Appendix D: Evidence Tables [update 2014]

D.5 Question 5

D.5.1 Evidence tables for first-line *H pylori* eradication

Bibliographic reference (Ref ID)	Abbas SZ et al, 2003 Abbas SZ et al, 2003
Study type	Randomised controlled trial
Number	85
Characteristics of patients	Mean age (yr): 59 Number of males: 70 Inclusion criteria: Patients positive for *H pylori* with a previously documented duodenal ulcer Exclusion criteria: Patients under 18 or over 80 years of age, patients who had previous *H pylori* eradication therapy, patients who needed to continue receiving drugs that may interact with the study drugs e.g. warfarin, carbamazepine and lithium, patients with hypersensitivity to the study drugs, pregnant and breast-feeding mothers, patients with mental impairment who could not comply or consent Dyspeptic condition types(s): Previously documented duodenal ulcer Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment; None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (ome/cla/met) N=41	Triple (ome/cla/tin) N=44	p
Mean age, yr (SD)	57 (10.9)	61.7 (11.3)	0.052
Sex: males/females	31/10	39/5	N/R

Bibliographic reference (Ref ID)	**Abbas SZ et al, 2003 Abbas SZ et al, 2003**
Intervention	Regimen: Triple (ome/cla/met) Dose and timing: 7 days; ome (20 mg b.i.d) / cla (250 mg b.i.d) / met (400 mg b.i.d) Route: Oral
Comparator	Regimen: Triple (ome/cla/tin) Dose and timing: 7 days; ome (20 mg b.i.d) / cla (250 mg b.i.d) / tin (500 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Location	UK
Outcomes measures and effect sizes	

	Triple (ome/cla/met)				Triple (ome/cla/tin)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	41	36	87.8	77.8 to 97.8	44	44	100	93.4 to 100	0.023
Adverse events (diarrhoea/loose stools)	41	8	19.5	N/R	44	2	45.5	N/R	N/R

Source of funding	Astra pharmaceuticals
Comments	Compliance was assessed but not reported as all subjects were considered compliant by the authors
Bibliographic reference (Ref ID)	**Antos D et al, 2006**
Study type	Randomised controlled trial
Location	Germany
Number	61
Characteristics of	Mean age (yr): 51

Bibliographic reference (Ref ID)	Abbas SZ et al, 2003 Abbas SZ et al, 2003
patients	Number of males: 30 Inclusion criteria: *H pylori* positive (culture and histology), 18-80yrs, recommended for treatment based on Maastricht Consensus Report Exclusion criteria: Intolerance to study drugs, contradiction to biopsy taking, complicated peptic ulcer (bleeding, perforation, or stenosis), regular NSAIDs, antibiotics of bismuth within 4 weeks of study entry. History of gastrectomy or proximal selective vagomtomy, malignant disease or severe concomitant disease. Dyspeptic condition types(s): Active peptic ulcer, erosive gastritis and or duodentisis, functional dyspepsia Previous antibiotics: Reported mixed Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (eso/amo/lev) N=30	Triple (eso/amo/cla) N=31	p
Median age, yr (range)	49 (21-70)	53 (18-79)	N/R
Sex male/female	13/17	17/14	N/R
Peptic ulcer	9	12	N/R
Erosive gastritis/or duodenitis	10	13	N/R
Functional dyspepsia	11	6	N/R
NSAID use	5	12	N/R
Number with previous treatment failures: 1 failure 2 or more	 2 (6.7%) 9 (30%)	 1 (3.2%) 6 (19.4%)	N/R
Mteronidazole sensitive	14	22	N/R

Bibliographic reference (Ref ID)	Abbas SZ et al, 2003 Abbas SZ et al, 2003

Metronidazole resistant	16	9	N/R
Clarithromycin sensitive	25	30	N/R
Clarithromycin resistant	5	1	N/R
Amoxicillin sensitive	30	31	N/R
Levofloxacin sensitive	29	30	N/R
Levofloxacin resistant	1	1	N/R

Intervention

Regimen: Triple (eso/amo/lev)
Dose and timing: 7 days; eso (40 mg b.i.d.) / amo (1000 mg b.i.d.) / lev (500 mg b.i.d.)
Route: Oral

Comparator

Regimen: Triple (eso/amo/cla)
Dose and timing: 7 days; eso (20 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.)
Route: Oral

Length of follow up

Follow-up occurred 6 weeks following treatment

Outcomes measures and effect sizes

	Triple (eso/amo/lev)				Triple (eso/amo/cla)				
	N	k	mean/ %	95% CI	N	k	mean/ %	95% CI	p
Eradication rate ITT	30	26	86.7	68-96	31	26	83.9	66-93	0.65
Eradication rate PP	28	26	92.9	76-99	31	26	83.9	66-93	0.22
Adverse events (dermatitis)	30	2	6.7	N/R	31	0	0	N/R	N/R
Adverse	3	9	30%	N/R	3	1	32.2	N/R	N/R

Bibliographic reference (Ref ID)	Abbas SZ et al, 2003 Abbas SZ et al, 2003
	events (diarrhoea/loose stools) 0 1 0
Source of funding	Not reported
Comments	Compliance was assessed but not reported as all subjects were considered compliant by the authors. 18 of the randomised participants had had a previous eradication attempt (15 had had at least two attempts)

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Bibliographic reference (Ref ID)	Arkkila PET et al, 2005
Study type	Randomised controlled trial
Location	Finland
Number	115
Characteristics of patients	Mean age (yr): 52.7 Number of males: 72 Inclusion criteria: Patients of both sexes between 18 and 85 years old, endoscopically proven duodenal or gastric ulcer, *H pylori* positive by urease test and histological evaluation, capable of communicating with the investigator, reliable at taking oral medication and remaining compliant for the duration of treatment and assessment, fertile females had to use contraception during the study. Use of NSAIDS or ASA was not an exclusion criteria Exclusion criteria: Patients who needed urgent surgery, such as for severe pyloric stenosis or continuous bleeding, or who had undergone partial gastrectomy were excluded, as were patients suffering from any other major disease that would have an impact on life expectancy during the study period or having any condition associated with poor patient compliance. Pregnant and lactating women and patients with known hypersensitivity or any drug reaction to any agent structurally related to the compounds investigated were also excluded Dyspeptic condition types(s): Peptic ulcer Previous antibiotics: Reported mixed Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None

Bibliographic reference (Ref ID)	Arkkila PET et al, 2005
	Baseline clinical patient characteristics:

	Mono (lan) N=30	Dual (lan/amo) N=30	Triple (lan/amo/cla) N=27	Quad (bis/lan/met/tet) N=28	p
Age, mean yr ± SD	53.4 ± 10.3	52.0 ± 11.4	52.0 ± 11.2	53.4 ± 8.3	N/S
Sex: males/females	17/13	21/9	19/8	15/13	N/S
Smokers	14	15	18	12	N/S
Use of alcohol	24	24	18	22	N/S
Previous peptic ulcer	9	10	14	15	N/S
Gastric/duodenal/both	0/8/1	1/9/0	4/9/1	3/11/1	N/S
Metronidazole resistant	12	9	5	8	N/R

Intervention	Regimen: Quad (bis/lan/met/tet) Dose and timing: 14 days; bis (120 mg q.i.d) / lan (30 mg b.i.d) / met (200 mg t.i.d) / tet (500 mg q.i.d) Route: Oral
Comparator	Regimen: Mono (lan) Dose and timing: 14 days; lan (30 mg b.i.d) plus placebo t.i.d days 1-14 and placebo (x2) q.i.d days 1-14 Route: Oral Regimen: Dual (lan/amo) Dose and timing: 14 days; lan (30 mg b.i.d) / amo (500 mg q.i.d) plus placebo t.i.d and q.i.d days 1-14 Route: Oral Regimen: Triple (lan/amo/cla) Dose and timing: 14 days; lan (30 mg b.i.d) / amo (500 mg q.i.d) / cla (250 mg t.i.d) plus placebo q.i.d days 1-14 Route: Oral

Bibliographic reference (Ref ID)	Arkkila PET et al, 2005
Length of follow up	All groups were followed up for a maximum of 52 weeks
Outcomes measures and effect sizes	

	Eradication rate ITT N, K, % (95% CI)	P (compared to mono (lan))	Eradication rate PP N, K, % (95% CI)	P (compared to mono (lan))
Mono (lan)	29, 0, 0 (0-12)	-	29, 0, 0 (0-12)	-
Dual (lan/amo)	29, 5, 83 (64-94)	0.01	27, 22, 81 (62-94)	0.01
Triple (lan/amo/cla)	27, 27, 100 (87-100)	0.01	27, 27, 100 (87-100)	0.01
Quad (bis/lan/met/tet)	27, 25, 93 (76-99)	0.01	27, 25, 93 (76-99)	0.01

Source of funding	Drugs for the study were provided by the Orion Pharma and Yamanouchi Pharna pharmacuetical companies
Comments	Patients took placebos to match active group comparators to ensure blinding as needed. Mixed population was 9 out of the 115 patients included in the study; adverse events are reported but arms of data have been pooled so are not available for analysis

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Bibliographic reference (Ref ID)	Basu PP et al, 2011
Study type	Randomised controlled trial
Location	USA
Number	270
Characteristics of patients	Mean age (yr): 37 Number of males: 156 Inclusion criteria: *H pylori* induced gastritis Exclusion criteria: Partial gastorectomy, gastric malignancy, active bleeding <20 years, pregnancy, prior *H pylori* infection/treatment,

Bibliographic reference (Ref ID)	Basu PP et al, 2011
	recent C. difficile infection, current use of PPI, H2RA, antacid, anticoagulant, misoprostol, recent use of antibiotics (6 weeks) or allergy to study medication Dyspeptic condition types(s): Dyspeptic symptoms (gastritis, peptic ulcer, gastric erosion) Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (7) (ome/dox/lev/nit) n=90	Quad (10) (ome/dox/lev/nit) n=90	Triple (lan/amo/cla) n= 90	p
Mean age, yr (range)	37 (26-58)	36 (22-48)	37(28-52)	N/S
Sex: male/female	52/38	51/39	53/37	N/S
Peptic ulcer	12	12	11	N/S
Gastric erosion	23	22	23	N/S
Regular gastritis	28	26	23	N/S
Nodular gastritis	5	10	12	N/S
Gastritis without intestinal metaplasia	22	22	22	N/S
Gastritis with intestinal metaplasia	34	32	33	N/S

Intervention	Regimen: Triple (lan/amo/cla) Dose and timing: 10 days; lan (30 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral

Bibliographic reference (Ref ID)	**Basu PP et al, 2011**
Comparator	Regimen: Quad (ome/dox/lev/nit) Dose and timing: 10 days; ome (40 mg m.a.n.e.) / dox (100 mg m.a.n.e.) / lev (250 mg m.a.n.e.) / nit (500 mg b.i.d.) Route: Oral Regimen: Quad (ome/dox/lev/nit) Dose and timing: 7 days; ome (40 mg m.a.n.e.) / dox (100 mg m.a.n.e.) / lev (250 mg m.a.n.e.) / nit (500 mg b.i.d.) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment.
Outcomes measures and effect sizes	

	Quad (7) (ome/dox/lev/nit)				Quad (10) (ome/dox/lev/nit)				Triple (lan/am/cla)				
	N	k	X %	95 % CI	N	k	X %	95% CI	N	k	X %	95 % CI	p
Eradication rate ITT	90	81	90	N/R	90	80	89	N/R	90	66	73	N/R	0.0003
Eradication rate PP	86	81	94	N/R	86	80	93	N/R	85	66	88	N/R	0.00035
Adherence to medication	90	87	97	N/R	90	85	94	N/R	90	85	94	N/R	N/R

Source of funding	Not reported
Comments	Adverse events are reported but arms of data have been pooled so are not available for analysis

Bibliographic reference (Ref ID)	Bayerdorffer E et al, 1999
Study type	Multicentre randomised controlled trial
Location	Germany
Number	75
Characteristics of patients	Mean age (yr): not reported for relevant population Number of males: not reported for relevant population Inclusion criteria: >18 years, active duodenal ulcer (at least 5mm in diameter), no more than one previous eradication attempt Exclusion criteria: Concurrent gastric, prepyloric ulcers or current complications of duodenal ulcer disease (pyloric stenosis, bleeding, perforation), treatment with H2RAs, antacids or PPI within 3 days of 13C UBT. History of gastric surgery, pregnancy, contradictions to study drugs, treatment with amo, met or bis within 1 month prior to entry, regular NSAID, severe concurrent disease and suspected/confirmed malignancy. Dyspeptic condition types(s): duodenal ulcer Previous antibiotics: Reported mixed Lead-in treatment: None Lead-out treatment; None Concomitant treatment: None Baseline clinical patient characteristics: Patient characteristics were not reported for the German cohort of participants specifically
Intervention	Regimen: Triple (ome/amo/met) Dose and timing: 7 days; ome (20 mg b.i.d.) / amo (1000 mg b.i.d.) / met (800 mg b.i.d.) Route: Oral
Comparator	Regimen: Triple dose x 3 (ome/amo/met) Dose and timing: 7 days; ome (40 mg) / amo (500 mg t.d.s.) / met (400 mg t.d.s.) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment
Outcomes measures and effect sizes	Triple (ome/amo/met) | Triple t.d.s. (ome/amo/met)

Bibliographic reference (Ref ID)	Bayerdorffer E et al, 1999

	N	k	mean/ %	95% CI	N	k	mean/ %	95% CI	p
Eradication rate ITT	38	32	84	69-94	35	29	83	66-93	N/R
Eradication rate PP	35	32	91	77-98	26	23	88	70-98	N/R

Source of funding	Astra Hassle Sweden
Comments	Also included data from Hungary and Czech republic, demographic data was not split by geographical regions. 3% off the study population had had previous eradication attempt. Helisal screening plus by either/both 13C UBT and histopathological assessment.

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Bibliographic reference (Ref ID)	Chiba N et al, 1996
Study type	Randomised controlled trial
Location	Canada
Number	65
Characteristics of patients	Mean age (yr): 56 Number of males: 35 Inclusion criteria: 18-80yr, no previous eradication attempt, no prior gastric resection, no antibiotics in preceding month, not pregnant/lactating, adequate contraception were appropriate Exclusion criteria: No previous eradication attempt, no prior gastric resection, no antibiotics in preceding month, not pregnant/lactating, adequate contraception were appropriate Dyspeptic condition types(s): Inactive peptic ulcer disease (duodenal ulcer, gastric ulcer), non-ulcer dyspepsia Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment: None

Bibliographic reference (Ref ID)	Chiba N et al, 1996
	Concomitant treatment: None Baseline clinical patient characteristics:

	Dual (ome/cla) n=31	Triple (ome/cla/met) n=34
Mean age, yr (range)	56 (29-79)	49 (20-77)
Sex: male/female	17/14	18/16
Duodenal ulcer	10	16
Gastric ulcer	6	1
Non-ulcer dyspepsia	15	17

Intervention	Regimen: Triple (ome/cla/met) Dose and timing: 14 days; ome (20 mg b.i.d.) / cla (250 mg b.i.d) / met (400 mg b.i.d.) Route: Oral
Comparator	Regimen: Dual (ome/cla) Dose and timing: 14 days; ome (20 mg b.i.d.) / cla (250 mg b.i.d.) Route: Oral
Length of follow up	Follow-up occurred 6 weeks following treatment
Outcomes measures and effect sizes	

	Dual (ome/cla)				Triple (ome/cla/met)				
	N	k	mean/%	95% CI	N	k	mean/%	95% CI	p
Eradication rate ITT	31	18	58	N/R	34	29	82	N/R	0.03
Eradication rate PP	29	18	62	N/R	30	29	93	N/R	0.004

Bibliographic reference (Ref ID)	Chiba N et al, 1996									
	Adverse events (diarrhoea/loose stools)	31	5	16	N/R	34	6	18	N/R	N/R
	Adherence to medication	N/R	N/R	97.2	93-102	N/R	N/R	97	93-100	N/R
Source of funding	Not reported									
Comments	N/A									

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Bibliographic reference (Ref ID)	Dore MP et al, 2011
Study type	Randomised controlled trial
Location	Italy
Number	417
Characteristics of patients	Mean age (yr): 53 Number of males: 153 Inclusion criteria: >18yrs, dyspeptic symptoms, *H pylori* positive Exclusion criteria: Bismuth, anti-secretory drugs or antibiotics within 4 weeks of endoscopy. Pregnancy/lactation, regular NSAID/corticosteroids use, malignancy, severe liver, heart, kidney or endocrine disease. Alcohol abuse, drug addiction, history of allergy to study medication or prior *H pylori* eradication. Dyspeptic condition types(s): Dyspeptic symptoms Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (14)	Quad (10)

Bibliographic reference (Ref ID)	Dore MP et al, 2011

	(bis/pan/met/tet) N=202	(bis/pan/met/tet) N=215
Mean age, yr	53	52
Sex male/female	72/130	81/134
Erosions	3	2
Gastric ulcer	5	7
Duodenal ulcer	2	2
Polyps	8	5
Lymphoma	1	0
Adenocarcinoma	2	3
Partial gastrectomy	3	2
Smokers	47	41
Ex -smokers	17	21

Intervention

Regimen: Quad (bis/pan/met/tet)
Dose and timing: 14 days; bis (240 mg b.i.d.) / pan (20 mg b.i.d.) / met (500 mg b.i.d.) / tet (500 mg b.i.d.)
Route: Oral

Comparator

Regimen: Quad (bis/pan/met/tet)
Dose and timing: 10 days; bis (240 mg b.i.d.) / pan (20 mg b.i.d.) / met (500 mg b.i.d.) / tet (500 mg b.i.d.)
Route: Oral

Length of follow up

Follow-up occurred 6-8 weeks following treatment

Outcomes measures and effect sizes

	Quad (14) (bis/pan/met/tet)				Quad (10) (bis/pan/met/tet)				
	N	k	mean /%	95% CI	N	k	mean /%	95% CI	p

Bibliographic reference (Ref ID)	Dore MP et al, 2011

Eradication rate ITT	202	185	91.5	87-95	215	199	92	88-96	N/R
Eradication rate PP	192	185	96	92-98	209	199	95	91-98	N/R
Adverse events (diarrhoea /loose stools)	202	3	1.5	N/R	215	5	2.3	N/R	.551
Adherence to medication	192	187	97	N/R	209	207	99	N/R	N/R

Source of funding	Institute of Clinica Medica
Comments	N/A

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Bibliographic reference (Ref ID)	Ecclissato C et al, 2002
Study type	Randomised controlled trial
Location	Brazil
Number	92
Characteristics of patients	Mean age (yr): 41.5 Number of males: 62 Inclusion criteria: Individuals with *H pylori* infection and active gastroduodenal ulcer disease were included in the study Exclusion criteria: Presence of malignancy at endoscopy, prior gastroduodenal surgery or *H pylori* treatment, drugs in the previous month and pregnancy or lactation. Patients who did not return to follow-up were also excluded from the study Dyspeptic condition types(s): Active gastroduodenal ulcer disease (peptic ulcers) Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None

Bibliographic reference (Ref ID)	Ecclissato C et al, 2002
	Lead-out treatment: None Baseline clinical patient characteristics:

	Triple (lan/amo/cla) N=46	Triple (bis/fur/tet) N=46	p
Mean age, yr (range)	42 (23 - 73)	41 (20 – 70)	N/S
Sex: males/females	27/19	35/11	N/S
Smokers	17	18	N/S

Intervention	Regimen: Triple (lan/amo/cla) Dose and timing: 7 days; lan (30 mg b.i.d) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral
Comparator	Regimen: Triple (bis/fur/tet) Dose and timing: 7 days; bis (125 mg q.i.d) / fur (200 mg b.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up was 30 days following completion of therapy
Outcomes measures and effect sizes	

	Triple (lan/amo/cla)				Triple (bis/fur/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	46	27	59	N/R	46	24	52	N/R	0.05
Eradication rate PP	41	27	66	N/R	40	24	60	N/R	0.05

Source of funding	This work was supported by a grant from Fundacao de Amparo a Pesquisa do Estado de Sao Paulo. Lansoprazole/clarithromycin and bismuth subcitrate were a generous gift from Abbott, Brazil and Farmasa, Brazil, respectively
Comments	Compliance was assessed but not reported as all subjects were considered compliant by the authors. Secondary antibiotic resistance to macrolides, nitrofurans and penicillins was reported but it was not possible to determine how many people in each arm

Bibliographic reference (Ref ID)	Ecclissato C et al, 2002
	were tested

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Bibliographic reference (Ref ID)	Ellenrieder V et al, 1998
Study type	Randomised controlled trial
Location	Germany
Number	163
Characteristics of patients	Median age (yr): 55.3 Number of males: 97 Inclusion criteria: Patients with endoscopically confirmed gastritis, or active gastric or duodenal ulcer and *H pylori* infection confirmed by histology and rapid urease test Exclusion criteria: Pregnant or lactating women, patients treated with antibiotics within the past 14 days, patients with previous treatment for *H pylori*, impaired liver function, MALT-lymphoma, other malignancies, or prior stomach resection or vagotomy Dyspeptic condition types(s): Gastritis, or active gastric or duodenal ulcer Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None Baseline clinical patient characteristics:

	Triple (pan/cla/met) – 250 mg cla N=82	Triple (pan/cla/met) – 500 mg cla N=81	p
Median age, yr (range)	57.5 (22-90)	53 (19-84)	N/R
Sex: males/females	45/37	52/29	N/R
Chronic gastritis	57	56	N/R
Duodenal ulcer	9	13	N/R
Gastric ulcer	16	10	N/R

Bibliographic reference (Ref ID)	Ellenrieder V et al, 1998

Gastric and duodenal ulcer	0	1	N/R
T-cell lymphoma	0	1	N/R

Intervention

Regimen: Triple (pan/cla/met)
Dose and timing: 7 days; pan (40 mg b.i.d) / cla (250 mg b.i.d) / met (500 mg b.i.d)
Route: Oral

Comparator

Regimen: Triple (pan/cla/met)
Dose and timing: 7 days; pan (40 mg b.i.d) / cla (500 mg b.i.d) / met (500 mg b.i.d)
Route: Oral

Length of follow up

Follow-up occurred 4 weeks after treatment ended

Outcomes measures and effect sizes

	Triple (pan/cla/met) – 250 mg cla				Triple (pan/cla/met) – 500 mg cla				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	82	62	75.6	N/R	80	63	78.8	N/R	N/R
Eradication rate PP	69	62	89.9	N/R	70	63	90.0	N/R	N/R
Eradication rate PP (gastritis subgroup)	49	43	87.8	N/R	50	44	88.0	N/R	N/R
Eradication rate PP (ulcer subgroup)	20	19	95.0	N/R	20	19	95.0	N/R	N/R
Adverse events (diarrhoea/loose stools)	71	4	5.6	N/R	72	5	6.9	N/R	N/R

Source of funding

Not reported

Bibliographic reference (Ref ID)	Ellenrieder V et al, 1998
Comments	Compliance was assessed but not reported as all subjects were considered compliant by the authors

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Bibliographic reference (Ref ID)	Hsu C-C et al, 2001
Study type	Randomised controlled trial
Location	Taiwan
Number	120
Characteristics of patients	Mean age (yr): 51 Number of males: 78 Inclusion criteria: 19-80 yrs, gastric, duodenal ulcers or non-ulcer dyspepsia. No previous eradication attempt. *H pylori* positive Exclusion criteria: Use of PPI, bismuth or antibiotics 4 weeks prior to enrolment, history of ulcer surgery, allergy to study medications, pregnancy/lactation, severe concomitant disease and suspected non-compliance. Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer non-ulcer dyspepsia Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment: Yes, allowed to take antacids (ditopax) after eradication therapy Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (fam/amo/tin) N=60	Triple (ome/amo/tin) N=60
Median age, yr (range)	52 (20-80)	50 (22-78)
Sex: male/female	36/22	40/20
Duodenal ulcer	9	12
Gastric ulcer	10	13
Non-ulcer dyspepsia	11	6
Smokers	6	7

Bibliographic reference (Ref ID)	Hsu C-C et al, 2001

Metronidazole sensitive	34*	50*
Metronidazole resistant	24	10
Antibiotic resistance: no data	2	0

*P<0.05

Intervention	Regimen: Triple (fam/amo/tin) Dose and timing: 14 days; fam (40 mg b.i.d.) / amo (1000 mg b.i.d.) / tin (500 mg b.i.d.) Route: Oral
Comparator	Regimen: Triple (ome/amo/tin) Dose and timing: 14 days; ome (20 mg b.i.d.) / amo (1000 mg b.i.d) / tin (500 mg b.i.d.) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment
Outcomes measures and effect sizes	

	Triple (fam/amo/tin)				Triple (ome/amo/tin)				
	N	k	mean/ %	95% CI	N	k	mean/ %	95% CI	p
Eradication rate ITT	60	48	80	74-93	60	50	83.3	74-93	N/R
Eradication rate PP	53	48	90.6	83-98	57	50	87.7	79.-96	N/R
Eradication rate ITT (MR)	24	18	75	N/R	10	7	70	N/R	N/R
Eradication	2	1	90	N/R	1	7	70	N/R	N/R

Bibliographic reference (Ref ID)	Hsu C-C et al, 2001

rate PP (MR)	0	8			0				
Eradication rate ITT (MS)	34	30	88	N/R	50	43	88	N/R	N/R
Eradication rate PP (MS)	33	30	91	N/R	47	43	92	N/R	N/R
Adverse events (diarrhoea/loose stools)	60	4	7	N/R	60	3	5	N/R	N/R

MS (metronidazole susceptible); MR (metronidazole resistant)

Source of funding	Not reported
Comments	N/A

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Bibliographic reference (Ref ID)	Katelaris PH et al, 2000
Study type	Multicentre randomised controlled trial
Location	Australia and New Zealand
Number	227
Characteristics of patients	Mean age (yr): 50 Number of males: 154 Inclusion criteria: >18 years, informed consent, endoscopically proven active duodenal ulcer (>5mm), *H pylori* positive by urease test/histology Exclusion criteria: Previous eradication therapy or gastric surgery, current gastric ulceration, ulcerative oesphagitis, antibiotic or bismuth use in preceding 30 days. Dyspeptic condition types(s): Duodenal ulcer Previous antibiotics: Reported naïve

Bibliographic reference (Ref ID)	Katelaris PH et al, 2000
	Lead-in treatment: None Lead-out treatment; Yes, 7 day of ome therapy for all (20mg m.a.n.e.) Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (ome/amo/met) N=111	Triple (ome/cla/met) N=109
Mean age, yr ± SD	49.5 +14.3	50.3 +13.8
Sex male/female	77/34	77/32
Number of duodenal ulcers = 1	99	87
Number of duodenal ulcers > 1	12	22
Size of ulcer (mm)	7.4 +2.1	7.9 +2.4
Regular smokers	32	37

Intervention	Regimen: Triple (ome/amo/met) Dose and timing: 7 days; ome (40 mg m.a.n.e.) / amo (500 mg t.d.s) / met (400 mg t.d.s) Route: Oral
Comparator	Regimen: Triple (ome/cla/met) Dose and timing: 7 days; ome (20 mg b.i.d.) / cla (250 mg b.i.d) / met (400 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment
Outcomes measures and effect sizes	

	Triple (ome/amo/met)				Triple (ome/cla/met)				
	N	k	mea	95% CI	N	k	mea	95% CI	p

Bibliographic reference (Ref ID)	Katelaris PH et al, 2000

			n/%				n/%		
Eradication rate ITT	111	64	58	49-67	109	89	82	74-89	N/R
Eradication rate PP	96	62	63	52-72	99	84	85	76-91	N/R
Eradication rate ITT (MR)	38	17	45	29-62	45	36	80	65-90	N/R
Eradication rate ITT (CR)	3	1	33	N/R	5	2	40	5-85	N/R
Eradication rate ITT (MS)	34	27	79	62-91	31	29	94	79-99	N/R
Eradication rate ITT (CS)	69	43	62	50-74	70	62	89	79-95	N/R
Adverse events (diarrhoea/loose stools)	114	13	11	N/R	113	6	5	N/R	N/R
Adverse events (liver events)	114	6	5	N/R	113	7	6	N/R	N/R

CS (clarithromycin susceptible); CR (clarithromycin resistant); MS (metronidazole susceptible); MR (metronidazole resistant)

Source of funding	Astra Australia Pharmaceutical
Comments	Placebos used as appropriate within study. Compliance was assessed by tablet counting but no outcome data was reported

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Bibliographic reference (Ref ID)	Katelaris PH et al, 2002
Study type	Randomised controlled trial

Bibliographic reference (Ref ID)	Katelaris PH et al, 2002
Location	Australia and New Zealand
Number	405
Characteristics of patients	Mean age (yr): 51 Number of males: 185 Inclusion criteria: Age 18 years or over, written informed consent, dyspepsia with *H pylori* infection confirmed (by urease test initially and then also histology and C-urea breath test), and no evidence of peptic ulcer disease or oesphagitis at endoscopy Exclusion criteria: Patients were excluded if there had been any prior attempt at *H pylori* eradication or concomitant or recent (within 30 days) use of PPIs, antibiotics, bismuth, or nonsteroidal anti-inflammatory drugs Dyspeptic condition types(s): Ulcer negative dyspepsia Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None Baseline clinical patient characteristics:

	Triple (pan/amo/cla) N=134	Triple (bis/met/tet) N=137	Quad (pan/bis/met/tet) N=134	p
Mean age, yr ± SD	51 ± 14	52 ± 14	50 ± 14	N/R
Sex: males/females	58 /76	58 /79	69 /65 f	N/R
Caucasian	111	115	117	N/R
Asian	5	7	7	N/R
Height (cm): mean ± SD	Males: 174 ± 8 Females: 159 ± 6	Males: 173 ± 9 Females: 161 ± 7	Males: 171 ± 12 Females: 161 ± 7	N/R
Weight (kg): mean ± SD	Males: 80 ± 18 Females: 69 ± 15	Males: 80 ± 13 Females: 68 ± 17	Males: 81 ± 16 Females: 70 ± 16	N/R
Nonsmoker	99	103	93	N/R
Metronidazole resistant	23/46 tested	29/50 tested	21/41 tested	N/S
Clarithromycin resistant	4/46 tested	4/50 tested	3/41 tested	N/S

Bibliographic reference (Ref ID)	Katelaris PH et al, 2002				
	Tetracycline resistant	0/46 tested	1/50 tested	0/41 tested	N/S
Intervention	Regimen: Quad (pan/bis/met/tet) Dose and timing: 7 days; pan (40 mg b.i.d) / bismuth subcitrate (108 mg q.i.d) / met (200 mg t.i.d daily and 400 mg at night) / tet (500 mg q.i.d) Route: Oral				
Comparator	Regimen: Triple (bis/met/tet) Dose and timing: 14 days; bis (108 mg q.i.d) / met (200 mg t.i.d) / tet (500 mg q.i.d) Route: Oral				
Length of follow up	Patients were reviewed 2 and 8 weeks after treatment				

Outcomes measures and effect sizes

	Triple (pan/amo/cla)1				Triple (bis/met/tet)2				Quad (pan/bis/met/tet)3				
	N	K	Mean %	95% CI	N	K	Mean %	95% CI	N	K	Mean %	95% CI	p
Eradication rate ITT	134	104	77.6	N/R	137	95	69.3	N/R	134	110	82.1	N/R	N/S* 0.04**
Eradication rate PP	114	94	82.5	N/R	101	75	74.3	N/R	105	92	87.6	N/R	N/S* 0.04**
Eradication rate ITT (CS)	42	36	85.7	N/R	46	29	63.0	N/R	38	30	78.9	N/R	N/R
Eradication rate ITT (CR)	4	1	25.0	N/R	4	3	75.0	N/R	3	3	100	N/R	N/R
Eradication rate ITT (MS)	23	17	73.9	N/R	21	16	76.2	N/R	20	16	80.0	N/R	N/R

Bibliographic reference (Ref ID)	Katelaris PH et al, 2002

Eradication rate ITT (MR)	23	20	87.0	N/R	29	16	55.2	N/R	21	17	81.0	N/R	N/R
Adverse events (diarrhoea/loose stools)	134	34	25.4	N/R	137	53	38.7	N/R	134	46	34.3	N/R	N/R
Adverse events (rash)	134	4	3.0	N/R	137	16	11.7	N/R	134	7	5.2	N/R	N/R
Adherence to medication	134	130	97.0	N/R	137	116	84.7	N/R	134	126	94.0	N/R	N/R

*1 vs. 2

**2 vs. 3

CS (clarithromycin susceptible); CR (clarithromycin resistant); MS (metronidazole susceptible); MR (metronidazole resistant)

Source of funding	Supported by Pharmacia Australian Propietary Limited, study was conducted by the Australian pantoprazole *H pylori* study group investigators
Comments	N/A

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Bibliographic reference (Ref ID)	Koivisto TT et al, 2005
Study type	Randomised controlled trial
Location	Finland
Number	329
Characteristics of patients	Mean age (yr): 57 Number of males: 154 Inclusion criteria: Patients aged 18-75 who had been referred for upper endoscopy from primary health care with a positive rapid urease test for *H pylori*

Bibliographic reference (Ref ID)	Koivisto TT et al, 2005

Exclusion criteria: Previous *H pylori* eradication therapy, PPI or H2RAs used regularly within 2 weeks before endoscopy, antibiotic therapy within 4 weeks before endoscopy, known hypersensitivity to any of the study medications for eradication therapy, pregnancy or lactation, confirmed or suspected malignant disease, gastric resection, advanced kidney disease (s-creatinine >200 mmol/L), severe liver disease, any serious illness with expected lifetime <2 years, and need for over 4 weeks of PPI or H2RA after the eradication therapy

Dyspeptic condition types(s): Gastric or duodenal ulcer patients and non-ulcer patients

Previous antibiotics: Reported naïve

Lead-in treatment: None

Concomitant treatment: None

Lead-out treatment: None

Baseline clinical patient characteristics:

	Triple (lan/amo/met) N=106	Triple (lan/amo/cla) N=110	Quad (bis/ran/met/tet) N=113	p
Mean age, yr	57	56	57	N/S
Smokers (%, 95% CI)	21 (13-29)	28 (20-37)	20 (13-28)	N/S
Alcohol consumption (cL/week, 95% CI)	5.4 (3.5-7.3)	8.6 (5.4-11.7)	6.0 (4.0-8.0)	<0.05*
Previous/present peptic ulcer (%, 95% CI)	27 (19-36)	33 (24-42)	30 (22-39)	N/S
Active peptic ulcer (%, 95% CI)	20 (12-27)	24 (16-32)	21 (14-29)	N/S
NSAIDs or ASA used (%, 95% CI)	66 (57-75)	54 (44-63)	60 (51-69)	N/S
Macrolide resistance (%, 95% CI)	1 (0-6)	3 (1-9)	3 (1-8)	N/S
Metronidazole resistance (%, 95% CI)	40 (30-51)	34 (24-44)	38 (29-47)	N/S

*LAC vs. LAM P < 0.05, LAC vs. Quad P < 0.05, LAM vs. Quad P = N/S

Bibliographic reference (Ref ID)	Koivisto TT et al, 2005
Intervention	Regimen: Triple (lan/amo/met) Dose and timing: 7 days; lan (30 mg b.i.d) / amo (1 g b.i.d) / met (400 mg t.i.d) Route: Oral
Comparator	Regimen: Triple (lan/amo/cla) Dose and timing: 7 days; lan (30 mg b.i.d) / amo (1 g b.i.d) / cla (500 mg b.i.d) Route: Oral Regimen: Quad (bis/ran/met/tet) Dose and timing: 7 days; ranitidine bismuth citrate (400 mg b.i.d) / met (400 mg t.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up was 4 weeks after completion of treatment regimens
Outcomes measures and effect sizes	

	Triple (lan/amo/met)1				Triple (lan/amo/cla)2				Quad (bis/ran/met/tet)3				
	N	K	Mean %	95% CI	N	K	Mean %	95% CI	N	K	Mean %	95% CI	p
Eradication rate ITT	106	83	78.3	N/R	110	100	90.9	N/R	113	92	81.4	N/R	0.01* 0.04**
Eradication rate ITT (MS)	56	52	92.9	N/R	61	58	95.1	N/R	64	58	90.6	N/R	0.01*
Eradication rate ITT (MR)	38	20	52.6	N/R	31	26	83.9	N/R	39	26	66.7	N/R	N/S

*1 vs. 2 p = 0.01
**2 vs. 3 p = 0.04
MS (metronidazole susceptible); MR (metronidazole resistant)

Source of funding	This work was supported by a grant from the Helsinki University EVO foundation, the Finnish Foundation for Gastroenterological Research and the Viipuri Tuberculosis Foundation. The study was also supported by Glaxo-Welcome, Wyeth-Lederle, Orion

Bibliographic reference (Ref ID)	Koivisto TT et al, 2005
	Pharma and Orion Diagnostica
Comments	Although compliance and adverse events were monitored in this study they were not reported in a way that the data could be extracted

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Bibliographic reference (Ref ID)	Laine L et al, 2000
Study type	Randomised controlled trial
Location	USA
Number	Study 1 (448), study 2 (98)
Characteristics of patients	Median age (yr): Study 1 (48), study 2 (41) Number of males: Study 1 (279), study 2 (58) Inclusion criteria: Patients 18-75 years of age with baseline endoscopic documentation of at least one duodenal ulcer (> 0.5 cm in diameter) or with a history of duodenal ulcer documented by endoscopy or upper gastrointestinal radiogram within the past 5 years. Inclusion also required a positive CLOtest of a gastric biopsy specimen for confirmation of *H pylori* infection. Women enrolled were required to be postmenopausal, to have been surgically sterilised, or to have a negative prestudy pregnancy test and to use a reliable method of contraception throughout the study Exclusion criteria: Pyloric obstruction, gastric ulcer, pyloric channel ulcer, erosive esophagitis, or Barrett's oesophagus at baseline endoscopy, history of refractory duodenal ulcer or Zollinger-Ellison syndrome, bleeding disorder or gastrointestinal bleeding at baseline or within the previous year, need for PPIs 2 weeks before, during, or 4 weeks after treatment period, a course of *H pylori* eradication therapy in the preceeding 1 year, need for concurrent therapy with anticholinergics, prostaglandin analogues, anti-neoplastic agents, NSAIDS (except aspirin of < 165 mg/day), steroids, sucralfate, H2RAs, quinidine, disopyramide phosphate, nefazodone hydrochloride, or anticoagulants; need for terfenadine, cisapride, or pimozide 1 week before or during treatment; need for astemizole 2 week before or during treatment; need for amiodarone 4 months before or during the study; known hypersensitivity to esomeprazole, omeprazole, amoxicillin, clarithromycin or Gelusil; use of an investigational drug within 4 weeks; pancreatitis, malabsorbtion, inflammatory bowel disease, severe pulmonary or liver disease, renal disease, active malignancy, unstable diabetes, hypertension with diastolic > 110 mm Hg, unstable heart disease, cerebral vascular disease currently or within 3 months, or alcohol or other substance abuse in prior 1 year; requirement for inpatient surgery during the study; or clinically significant, abnormal laboratory values Dyspeptic condition types(s): Duodenal ulcer

Bibliographic reference (Ref ID)	Laine L et al, 2000

Previous antibiotics: Reported mixed
Lead-in treatment: None
Concomitant treatment: None
Lead-out treatment: None
Baseline clinical patient characteristics:

Study 1	Dual (eso/cla) N=215	Triple (eso/amo/cla) N=233	p
Mean age, yr	48	48	N/S
Sex: males/females (%)	63/37	62/38	N/S
Race: white (%)	68	73	N/S
Race: black (%)	26	22	N/S
Race: other (%)	7	4	N/S
Smoker (%)	34	30	N/S
Active duodenal ulcer (%)	78	79	N/S
Previous *H pylori* therapy (%)	11	13	N/S

Baseline clinical patient characteristics:

Study 2	Mono (eso) N=24	Triple (eso/amo/cla) N=74	p
Mean age, yr	40	42	N/S
Sex: males/females (%)	50/50	62 /38	N/S
Race: white (%)	63	70	N/S
Race: black (%)	29	28	N/S
Race: other (%)	8	1	N/S
Smoker (%)	54	51	N/S

Bibliographic reference (Ref ID)	Laine L et al, 2000
	Active duodenal ulcer (%) | 100 | 89 | N/S Previous *H pylori* therapy (%) | 0 | 9 | N/S
Intervention	Study 1 Regimen: Triple (eso/amo/cla) Dose and timing: 10 days; eso (40 mg m.a.n.e) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral Study 2 Regimen: Triple (eso/amo/cla) Dose and timing: 10 days; eso (40 mg m.a.n.e) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral
Comparator	Study 1 Regimen: Dual (eso/cla) Dose and timing: 10 days; eso (40 mg m.a.n.e) / cla (500 mg b.i.d) Route: Oral Study 2 Regimen: Mono (eso) Dose and timing: 10 days; eso (40 mg m.a.n.e) Route: Oral
Length of follow up	Follow-up was carried out 4 weeks after completion of the study treatments
Outcomes measures and effect sizes	Study 1

	Dual (eso/cla)				Triple (eso/amo/cla)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p

Bibliographic reference (Ref ID)	Laine L et al, 2000

Eradication rate ITT	215	112	52	45-59	233	179	77	71-82	0.001
Eradication rate PP	187	103	55	48-62	196	164	84	78-89	0.001

Study 2

	Mono (eso)				Triple (eso/amo/cla)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	24	1	4	0-21	74	58	78	68-87	0.001
Eradication rate PP	22	1	5	0-23	67	57	85	74-93	0.001

Source of funding	This research was supported by AstraZeneca
Comments	Mixed population was: study 1 (11% EC; 13% EAC) and study 2 (0% E, 9% EAC). Although compliance was monitored in the study, insufficient data was reported and therefore it has not been included in the outcome table above. In addition, for antibiotic resistance, data for all 3 studies combined is reported but only studies 1 and 2 have arms of interest to our review question therefore this data has not been included in the outcome table above

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Bibliographic reference (Ref ID)	Laine L et al, 2003
Study type	Randomised controlled trial
Location	USA
Number	275
Characteristics of	Mean age (yr): 47

Bibliographic reference (Ref ID)	Laine L et al, 2003
patients	Number of males: 166 Inclusion criteria: Patients were eligible for the study if they had an active duodenal ulcer (>3 mm) at baseline endoscopy or a history of duodenal ulcer (within the last 5 years) documented by endoscopy or radiology plus confirmed *H pylori* infection Exclusion criteria: Evidence of upper GI bleeding within the past month, prior attempt to treat *H pylori*, use of antibiotics or bismuth in the prior 30 days, regular use of a PPI in the 15 days or of an H2RA, sucralfate or misoprostol in the 7 days before baseline, chronic use of NSAIDS (except for acetyl-salicylic acid < 325 mg daily), contraindication to the study medications, pregnancy or lactation, other serious medical conditions, or clinically significant laboratory abnormalities at baseline Dyspeptic condition types(s): Active duodenal ulcer Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None Baseline clinical patient characteristics:

	Triple (ome/amo/cla) N=137	Quad (bis/ome/met/tet) N=138	p
Age, mean yr ± SD	47 ± 15	47 ± 13	N/S
Sex: males/females	80/57	86 /52	N/S
Active duodenal ulcer	13	15	N/S
Metronidazole resistance	44	52	N/S
Clarithromycin resistance	14	13	N/S

Intervention	Regimen: Triple (ome/amo/cla) Dose and timing: 10 days; ome (20 mg b.i.d) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral
Comparator	Regimen: Quad (bis/ome/met/tet) Dose and timing: 10 days; bis (140 mg q.i.d) / ome (20 mg b.i.d) / met (125 mg q.i.d) / tet (125 mg q.i.d) Route: Oral
Length of follow up	Follow-up was carried out within 4 days after completion of therapy, at least 29 days after the end of treatment and, if the urea breath test was negative, the patient returned at least 57 days after the end of treatment

Bibliographic reference (Ref ID)	**Laine L et al, 2003**

Outcomes measures and effect sizes

	Triple (ome/amo/cla)				Quad (bisome/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	137	114	83.2	77.0 to 89.5	138	121	87.7	82.2 to 93.2	0.29
Eradication rate PP	124	108	87.1	81.2 to 93.0	120	111	92.5	87.8 to 97.2	0.16
Eradication rate ITT (CS)	101	93	92.1	N/R	98	111	88.3	N/R	0.36
Eradication rate ITT (CR)	14	3	21.4	N/R	13	10	76.9	N/R	0.04
Eradication rate PP (CS)	93	88	84.6	N/R	97	89	91.8	N/R	0.43
Eradication rate PP (CR)	13	3	23.1	N/R	10	9	90.0	N/R	0.001
Eradication rate ITT (MS)	71	60	84.5	N/R	74	68	91.7	N/R	0.18
Eradication rate ITT (MR)	44	36	81.8	N/R	51	41	80.4	N/R	0.90
Eradication rate PP (MS)	64	55	85.9	N/R	63	60	95.2	N/R	0.07
Eradication rate PP (MR)	42	36	85.7	N/R	45	39	86.7	N/R	0.90
Adverse events (diarrhoea/loose stools)	152	23	15	N/R	147	13	8.8	N/R	N/R

Bibliographic reference (Ref ID)	Laine L et al, 2003
	Adherence to medication: 137, 129, 94.2, N/R, 138, 126, 91.3, N/R, N/R CS (clarithromycin susceptible); CR (clarithromycin resistant); MS (metronidazole susceptible); MR (metronidazole resistant)
Source of funding	This study was sponsored by a grant by Axcan Pharma, Canada
Comments	N/A

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Bibliographic reference (Ref ID)	Lee JM et al, 1999
Study type	Randomised controlled trial
Location	Ireland
Number	308
Characteristics of patients	Mean age (yr): 47.5 Number of males: 156 Inclusion criteria: Consecutive patients with *H pylori* infection referred for diagnostic upper gastrointestinal endoscopy were considered Exclusion criteria: Patients under 18 or over 80 years of age, patients who had previous *H pylori* eradication therapy, patients who needed to continue receiving drugs that may interact with the study drugs e.g. warfarin, carbamazepine and lithium, patients with hypersensitivity to the study drugs, pregnant and breast-feeding mothers, patients with mental impairment who could not comply or consent Dyspeptic condition types(s): Dyspepsia Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment; None Concomitant treatment: None Baseline clinical patient characteristics: Baseline characteristic age given for all patients included in study: mean age 47.5 years, range 18-80 years. Triple (ome/amo/cla) group included 116 patients whilst the triple (ome/cla/met) group included 192 patients. No other baseline characteristics were given.

Bibliographic reference (Ref ID)	Lee JM et al, 1999
Intervention	Regimen: Triple (ome/amo/cla) Dose and timing: 7 days; ome (20 mg b.i.d) / amo (1000 mg b.i.d) / cla 500 mg b.i.d) Route: Oral
Comparator	Regimen: Triple (ome/cla/met) Dose and timing: 7 days; ome (20 mg b.i.d) / cla (250 mg b.i.d) / met (400 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred one month following treatment
Outcomes measures and effect sizes	

	Triple (ome/amo/cla)				Triple (ome/cla/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	116	83	71.6	63-80	192	140	72.9	67-79	0.80
Eradication rate PP	106	83	78.3	N/R	177	140	79.1	N/R	N/R

Source of funding	Health Research Board of Ireland
Comments	N/A

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Bibliographic reference (Ref ID)	Lerang F et al, 1997[a]
Study type	Randomised controlled trial
Location	Norway
Number	231
Characteristics of	Mean age (yr): 58

Bibliographic reference (Ref ID)	Lerang F et al, 1997[a]
patients	Number of males: 145 Inclusion criteria: Patients aged 18-80 with peptic ulcer disease and *H pylori* infection (confirmed by culture and urease test) who gave informed consent Exclusion criteria: Pregnancy or lactation, history of ulcer surgery (except highly selective vagotomy or oversewing of ulcer perforation), reflux esophagitis > grade 2 (Savary-Miller) or pathological 24 hr pH assessment, daily use of NSAID or ASA, known hypersensitivity to relevant medication, chronic alcoholism, suspected lack of compliance, severe liver or kidney disease, malignancy and previous anti-*H pylori* therapy Dyspeptic condition types(s): Peptic ulcer disease Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None Baseline clinical patient characteristics:

	Triple (ome/amo/met) N=77	Triple (ome/cla/met) N=76	Triple (bis/cla/met) N=78	p
Mean age, yr (range)	57 (24-80)	57 (30-77)	59 (32-80)	N/S
Sex: males/females	44/33	49/27	52/26	N/S
Smokers	39	38	37	N/S
Mean duration of disease, yr (range)	10 (0-44)	10 (0-41)	9 (0-43)	N/S
History of ulcer bleeding	14	16	13	N/S
Active ulcer	41	49	53	N/S
First time ulcer	20	24	30	N/R
Duodenal ulcer	56	59	62	N/R
Gastric ulcer	13	13	7	N/R
Pyloric ulcer	8	4	9	N/R

Bibliographic reference (Ref ID)	Lerang F et al, 1997[a]				
	Metronidazole resistance	22	18	24	N/S
Intervention	Regimen: Triple (ome/amo/met) Dose and timing: 10 days; ome (20 mg b.i.d) / amo (750 mg b.i.d) / met (400 mg b.i.d) Route: Oral				
Comparator	Regimen: Triple (ome/cla/met) Dose and timing: 10 days; ome (20 mg b.i.d) / cla (250 mg b.i.d) / met (400 mg b.i.d) Route: Oral Regimen: Triple (bis/cla/met) Dose and timing: 10 days; bis (DeNol tablets 240 mg b.i.d) / cla (250 mg b.i.d) / met (400 mg b.i.d) Route: Oral				
Length of follow up	Follow-up was conducted at least two months after starting therapy				

Outcomes measures and effect sizes

	Triple (ome/amo/met)				Triple (ome/cla/met)				Triple (bis/cla/met)				
	N	K	Mean %	95% CI	N	K	Mean %	95% CI	N	K	Mean %	95% CI	p
Eradication rate ITT	77	70	91	82-96	76	72	95	97-99	78	74	95	87-99	0.63*
Eradication rate PP	76	70	92	N/R	75	72	96	N/R	77	74	96	N/R	N/R
Eradication rate ITT (MS)	50	48	96	86-100	48	45	94	83-99	50	47	94	84-99	0.91**
Eradication rate	22	17	77	55-92	18	17	94	73-100	24	23	96	79-100	0.13¥

Bibliographic reference (Ref ID)	Lerang F et al, 1997[a]

ITT (MR)													
Eradication rate ITT (MUS)	3	3	100	N/R	8	8	100	N/R	4	4	100	N/R	N/R
Eradication rate ITT (MIS)	2	2	100	N/R	2	2	100	N/R	-	-	-	-	N/R

MS (metronidazole sensitive); MR (metronidazole resistant); MIS (metronidazole intermediate susceptibility); MUS (metronidazole unknown susceptibility)

*OAM vs. OCM vs. BCM: p = 0.63

** OAM vs. OCM vs. BCM (MS subgroup): p = 0.91

¥ OAM vs. OCM vs. BCM (MR subgroup): p = 0.13

Source of funding	This study was supported in part by a financial grant from Astra Norway
Comments	Compliance was not reported in the study in such a way that the data could be extracted e.g. the study found that 226 patients (98%) had completed the treatment course and had taken all the pills prescribed. In addition, adverse event data could not be recorded either as it was reported as none, mild, moderate or severe as opposed to what the event was (e.g. rash). In addition, antibiotic susceptibility was measured but the data could not be extracted per group and has therefore not been reported in the outcome table above

Bibliographic reference (Ref ID)	Lerang F et al, 1997[b]
Study type	Randomised controlled trial
Location	Norway
Number	100
Characteristics of	Mean age (yr): 53

Bibliographic reference (Ref ID)	Lerang F et al, 1997[b]
patients	Number of males: 79 Inclusion criteria: *H pylori* positive, 18-80yrs, informed consent Exclusion criteria: Pregnancy/lactation, history of ulcer surgery, pyloric stenosis, concurrent gastric ulcer or esophagitis. Use of NSAIDS, ASA, warfarin, steroids, bismuth, antibiotics during 4 weeks prior to endoscopy. Known contradiction to medication, alcoholism, suspected lack of compliance, severe liver disease, malignancy, in vitro antibiotic resistance (met/tet/amp), previous *H pylori* eradication Dyspeptic condition types(s): Relapsing duodenal ulcer disease Previous antibiotics: Reported naïve Lead-in treatment: None Lead-out treatment; None Concomitant treatment: None Baseline clinical patient characteristics: The study reported that there were no differences between groups with regard to age (mean 53yr), gender (56% male), smoking (56%), duration of disease (mean 14yr), or history of ulcer bleeding (26%)
Intervention	Regimen: Triple (ome/amo/met) Dose and timing: 14 days; ome (20 mg b.i.d.) / amo (750 mg b.i.d.) / met (400 mg b.i.d.) Route: Oral
Comparator	Regimen: Triple (bis/oxytet/met) Dose and timing: 14 days; bis (75 mg bid q.i.d.) / oxytet (500 mg q.i.d.) / met (400 mg b.i.d.) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Triple (bis/oxytet/met)				Triple (ome/amo/met)				
	N	k	mean/ %	95% CI	N	k	mean/ %	95% CI	p

Bibliographic reference (Ref ID)	Lerang F et al, 1997[b]

Eradication rate ITT	54	49	91	80-97	46	44	96	55-100	0.45
Adverse events (diarrhoea/loose stools)	54	41	76	N/R	46	30	65	N/R	N/R
Adverse events (rash)	54	9	17	N/R	46	9	20	N/R	N/R

Source of funding	Astra Hassle Sweden
Comments	H pylori status determined by endoscopy biopsies and resistant tested the strains plus serology for antibodies. Majority of patients tested for resistance to metronidazole and those found to be resistant were then in the non-randomised group. Study also had 41 patients that were not randomised as metronidazole resistant

21

Bibliographic reference (Ref ID)	Ohlin B et al, 2002
Study type	Randomised controlled trial
Location	Sweden
Number	177
Characteristics of patients	Median age (yr): 56.8 Number of males: 128 Inclusion criteria: Male and female patients aged between 18 and 80 years with *H pylori* infection, verified by positive CLO test, and a present recurrent duodenal ulcer and/or previous recurrent duodenal ulcer Exclusion criteria: Patients with treatment aimed at eradicating *H pylori* infection within 6 months before study entry, or known allergy to any of the study drugs were excluded. In addition, patients with severe reflux esophagitis were also excluded Dyspeptic condition types(s): Duodenal ulcer Previous antibiotics: Reported mixed Lead-in treatment: None Concomitant treatment: None

Bibliographic reference (Ref ID)	Ohlin B et al, 2002
	Lead-out treatment: None Baseline clinical patient characteristics:

	Dual (lan/amo) N=58	Dual (ome/amo) N=57	Triple (lan/amo/cla) N=62	p
Mean age, yr (range)	58.5 (21-78)	55.6 (22-78)	56.2 (24-79)	N/R
Sex: males/females	40/18	40/17	48/14	N/R
Height (m): mean (range)	1.74 (1.52-1.93)	1.72 (1.53-1.87)	1.73 (1.55-1.90)	N/R
Weight (kg): mean (range)	79.6 (53-118)	73.8 (53-110)	74.8 (52-105)	N/R
Patients with active ulcer	34	30	41	N/R

Intervention	Regimen: Triple (lan/amo/cla) Dose and timing: 14 days; lan (30 mg b.i.d) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral
Comparator	Regimen: Dual (lan/amo) Dose and timing: 14 days; lan (30 mg b.i.d) / amo (1000 mg b.i.d) plus placebo days 1-14 Route: Oral Regimen: Dual (ome/amo) Dose and timing: 14 days; ome (20 mg b.i.d) / amo (1000 mg b.i.d) plus placebo days 1-14 Route: Oral
Length of follow up	Follow-up was 6 weeks and 6 months after treatment was completed
Outcomes measures and effect sizes	

	Dual (lan/amo)1				Dual (ome/amo)2				Triple (lan/amo/cla)3				
	N	K	Mean %	95 % CI	N	K	Mean %	95 % CI	N	K	Mean %	95 % CI	p
Eradication rate PP	51	26	51.0	N/R	47	30	63.8	N/R	50	48	96.0	N/R	See *

Bibliographic reference (Ref ID)	Ohlin B et al, 2002

Antibiotic resistance to macrolides	25	0	0	N/R	16	0	0	N/R	1	0	0	N/R	N/R
Antibiotic resistance to penicillins	25	0	0	N/R	16	0	0	N/R	1	0	0	N/R	N/R
Adverse events (diarrhoea/loose stools)	51	5	9.8	N/R	47	5	10.6	N/R	50	18	36.0	N/R	N/R

*1 vs. 2 N/S; 1 vs. 3 and 2 vs. 3 p< 0.001

Source of funding	Not reported
Comments	Metronidazole resistant strains of *H pylori* were cultured from 9 patients at 6 weeks however this data was not recorded as the results were not reported per group.

22

Bibliographic reference (Ref ID)	Sullivan B et al, 2002
Study type	Randomised controlled trial
Location	USA
Number	56
Characteristics of patients	Mean age (yr): 40.5 Number of males: 43 Inclusion criteria: Individuals 18-80 years old with upper GI symptoms, peptic ulcer disease, history of peptic ulcer, chronic gastritis, gastric associated lymphoid tissue, intestinal metaplasia and positive for *H pylori* infection Exclusion criteria: History of previous treatment for *H pylori*, use of any of the proposed antibiotics in the previous 6 months, any known allergy to the proposed study medications Dyspeptic condition types(s): Patients with upper GI symptoms

Bibliographic reference (Ref ID)	Sullivan B et al, 2002
	Previous antibiotics: Reported naïve Lead-in treatment: None Concomitant treatment: None Lead-out treatment: None Baseline clinical patient characteristics:

	Quad (bis/lan/amo/azi) N=29	Quad (bis/lan/amo/cla) N=27	p
Mean age, yr	40	41	N/S
Sex: males/females	22 /7	21/6	N/S
Tobacco use	11	7	N/S
NSAID use	5	12	0.013
H2 blocker use	6	13	0.06

Intervention	Regimen: Quad (bis/lan/amo/azi) Dose and timing: 10 days; bis (2 tablets b.i.d) / lan (30 mg b.i.d) / amo (1000 mg b.i.d) / azi (250 mg m.a.n.e) Route: Oral
Comparator	Regimen: Quad (bis/lan/amo/cla) Dose and timing: 10 days; bis (2 tablets b.i.d) / lan (30 mg b.i.d) / amo (1000 mg b.i.d) / cla (500 mg b.i.d) Route: Oral
Length of follow up	Subjects were followed for 8 weeks including the treatment period
Outcomes measures and effect sizes	

	Quad (bis/lan/amo/azi)				Quad (bis/lan/amo/cla)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication	2	1	51.7	N/R	2	2	81.5	N/R	0.01

Bibliographic reference (Ref ID)	Sullivan B et al, 2002
	rate ITT: 9 / 5 / / / 7 / 2 / / / 9 Eradication rate PP: 27 / 15 / 55.5 / N/R / 26 / 22 / 84.6 / N/R / 0.021 Adverse events (diarrhoea/loose stools): 29 / 5 / 17.2 / N/R / 27 / 6 / 22.2 / N/R / N/S
Source of funding	Not reported
Comments	N/A

23

Bibliographic reference (Ref ID)	Vakil N et al, 2004
Study type	Randomised controlled trial
Location	USA
Number	803
Characteristics of patients	Mean age (yr): 46 Number of males: 362 Inclusion criteria: >18yrs, *H pylori* positive (serological test and urease test/culture), on-going gastrointestinal symptoms and/or findings on physical exam Exclusion criteria: Prior oesophageal/gastric surgery, erosive oesphagitis, pyloric stenosis, oesophageal/gastric varices, cancer, serious systemic diseases, previous *H pylori* eradication (with amoxicillin or clarithromycin): use of bismuth within 4 weeks of screening, treatment with prostaglandin analogue, sucralfate, PPI, H2RA with 2 weeks of screening, treatment with steroids, anticoagulants or anti-neoplastic drugs, aspirin, NSAIDs, COX-2 inhibitors, allergy to study medication, pregnancy/lactation, use of study medication in previous 30 days, any condition or situation that could lead to poor compliance, difficulty swallowing large capsules, poor medical/psychiatric condition. Dyspeptic condition types(s): Peptic ulcer disease , non-peptic ulcer disease Previous antibiotics: Reported naïve Lead-in treatment: None

Bibliographic reference (Ref ID)	Vakil N et al, 2004
	Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple 3 (rab/amo/cla) N=194	Triple 7 (rab/amo/cla) N=200	Triple 10 (rab/amo/cla) N= 202	Triple 10 (ome/amo/cla) N=207
Mean age, yr	45.1	46.9	48.2	45.6
Sex: male/female	83/111	94/106	96/106	89/118
Smokers	86	93	88	88
Alcohol intake	94	99	104	105
Peptic ulcer disease	93	103	100	104

Intervention	Regimen: Triple (rab/amo/cla) Dose and timing: 10 days; rab (20 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral
Comparator	Regimen: Triple (rab/amo/cla) Dose and timing: 7 days; rab (20 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral Regimen: Triple (ome/amo/cla) Dose and timing: 10 days: ome (20 mg b.i.d.) /amo (1000 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral Regimen: Triple (rab/amo/cla) Dose and timing: 3 days; rab (20 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.)

Bibliographic reference (Ref ID)	Vakil N et al, 2004
	Route: Oral
Length of follow up	Follow-up occurred 6 weeks following treatment
Outcomes measures and effect sizes	

	Eradication ITT n, k, % (95% CI)	P (compared to (ome /amo/cla)	Eradication PP n, k, % (95% CI)	P (compared to (ome/amo/ cla)
Triple 3 (rab/amo/cla)	187, 51, 27 (21-34)	N/R	167, 50, 30 923-37)	N/R
Triple 7 (rab/amo/cla))	194, 150, 77 (71-83)	N/D	166, 140, 84 (79-90)	N/D
Triple 10 (rab/amo/cla)	196, 153, 78 (72-84)	N/D	171, 147, 86 (91-91)	N/D
Triple (ome/amo/cla)	206, 151, 73 (67-79)	N/D	171, 146, 82 (76-87)	N/D
	Adverse events	n	k	%
Triple 3 (rab/amo/cla)	Diarrhoea/loose stools	188	17	9
Triple 7 (rab/amo/cla))	Diarrhoea/loose stools	195	22	11
Triple 10 (rab/amo/cla)	Diarrhoea/loose stools	198	11	6
Triple	Diarrhoea/loose	207	22	

Bibliographic reference (Ref ID)	Vakil N et al, 2004				
	(ome/amo/cla)	stools			11
	Sub groups				
	Non- ulcer peptic disease	Eradication ITT n, k, %	p	Eradication PP n, k, %	p
	Triple 3 (rab/amo/cla)	97,27, 28	N/R	89, 27, 30	N/R
	Triple 7 (rab/amo/cla))	93,68,73	N/R	79,63,80	N/R
	Triple 10 (rab/amo/cla)	99,78, 79	N/R	86,74,86	N/R
	Triple (ome/amo/cla)	103,74,72	N/R	92,74,80	N/R
	Peptic ulcer disease				
	Triple 3 (rab/amo/cla)	90, 24, 27	N/R	78, 23, 30	N/R
	Triple 7 (rab/amo/cla))	101, 82, 81	N/R	87,77,89	N/R
	Triple 10 (rab/amo/cla)	97, 75, 77	N/R	85, 73, 86	N/R
	Triple (ome/amo/cla)	103, 77, 75	N/R	87, 72, 83	N/R
	Sensitive to clarithromycin				

Bibliographic reference (Ref ID)	Vakil N et al, 2004				
	Triple 3 (rab/amo/cla)	134, 33, 25	N/R	121, 32, 26	N/R
	Triple 7 (rab/amo/cla))	145,103, 71	N/R	119, 95, 80	N/R
	Triple 10 (rab/amo/cla)	142, 111, 78	N/R	125, 106, 85	N/R
	Triple (ome/amo/cla)	139, 96, 79	N/R	122, 95, 79	N/R
	Resistant to clarithromycin				
	Triple 3 (rab/amo/cla)	9, 0, 0	N/R	8, 0, 0	N/R
	Triple 7 (rab/amo/cla))	16, 5, 31	N/R	14, 5, 36	N/R
	Triple 10 (rab/amo/cla)	9, 1,11	N/R	9, 1, 11	N/R
	Triple (ome/amo/cla)	18, 5, 28	N/R	15, 9, 60	N/R
Source of funding	Eisai Inc, Teaneck NJ and Janssen Pharmaceuticals Inc				
Comments	Patients took placebos to match active group comparators to ensure blinding as needed. Four arm study however only one valid comparison for the review as only the length of study and PPI are altered. Compliance was reported as greater than 95% in all treatment groups with specific data given				

24

Bibliographic reference (Ref ID)	van Zanten SV et al, 2003
Study type	Randomised controlled trial
Location	Canada

Bibliographic reference (Ref ID)	van Zanten SV et al, 2003
Number	305
Characteristics of patients	Mean age (yr): 52 Number of males: 244 Inclusion criteria: Chronic dyspepsia patients (with/without peptic ulcer disease). *H pylori* positive Exclusion criteria: Active duodenal ulcer, history of GERD or esophagitis that requires on-going treatment, renal insufficiency, serious comorbidity, allergy to study drugs. Use of bismuth or antibiotics in 4 weeks prior to study enrolment. NSAIDs not allowed during the study Dyspeptic condition types(s): Chronic dyspepsia patients (with/without peptic ulcer disease) Previous antibiotics: Reported mixed Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (ome/amo/cla) N=152	Triple (ran/bis/cla) n=153
Mean age, yr (range)	52 20-80	52 22-85
Sex male/female	80/72	79/74
Ulcer history Yes No	 59 93	 52 101
Previous eradication treatment Yes No	 8 144	 12 141

Intervention	Regimen: Triple (ome/amo/cla)

Bibliographic reference (Ref ID)	van Zanten SV et al, 2003
	Dose and timing: 7 days; ome (20 mg b.i.d.) / amo (1000 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral
Comparator	Regimen: Triple (bis/ran/cla) Dose and timing: 7 days; bis/ran (400 mg b.i.d.) / cla (500 mg b.i.d.) Route: Oral
Length of follow up	Follow-up occurred 12 weeks following treatment
Outcomes measures and effect sizes	

	Triple (ome/amo/cla)				Triple (ran/bis/cla)				
	N	k	mean/ %	95% CI	N	k	mean/ %	95% CI	p
Eradication rate ITT	152	118	78	71-84	153	101	66	59-74	0.03
Eradication rate PP	110	105	96	92-99	112	94	84	77-91	0.007
Adverse events (diarrhoea/loose stools)	156	64	41	N/R	156	45	29	N/R	N/R
Adherence to medication - mean pills taken	152	128	84.2	N/R	153	143	93.5	N/R	<0.05

Source of funding	GlaxoSmithKline (Canada) Incorporated
Comments	Study uses ranitidine bismuth citrate (this will be classed as two compounds -bismuth and ranitidine). Previous eradication in RBC-C group 8% and OCA 5%

25.5.2 Evidence tables for second-line *H pylori* eradication

26

Bibliographic reference (Ref ID)	Bago et al 2009
Study type	Randomised controlled trial
Location	Croatia
Number	160
Characteristics of patients	Mean age (yr): 45 Number of males: 59 Inclusion criteria: >18 years, non-ulcer dyspepsia, *H pylori* positive after first line eradication Exclusion criteria: Duodenal or gastric ulcer, gastrointestinal bleeding, contradiction to study medication. Use of NSAIDs, anti-coagulants, corticosteroids or gold based drugs or recent treatment with antimicrobials. Presence of severe disease, pregnancy/breast feeding or poor compliance Dyspeptic condition types(s): Non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (ome/met/mox) N=82	Quad (ome/bis/met/tet) N=78	p
Age (yr) (mean)	50 + 12	58 + 15	N/R
Gender male/female	42/40	41/37	N/R
Smoking	28	24	N/R

Intervention	Triple (ome/met/mox) Dose and timing: 7 days; ome (20 mg b.i.d) / met (500 mg t.i.d) / mox (400 mg m.a.n.e) Route: Oral

Bibliographic reference (Ref ID)	Bago et al 2009
Comparator	Quad (ome/bis/met/tet) Dose and timing: 7 days; ome (20 mg b.i.d) / bis (120 mg q.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 2 years following treatment
Outcomes measures and effect sizes	

	Triple (ome/met/mox)				Quad (ome/bis/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	82	60	73	64-82	78	42	53	43-64	0.018
Adverse events (diarrhoea/loose stools)	82	2	2.4	N/R	78	0	0	N/R	N/R
Adverse events (rash)	82	1	1.2	N/R	78	0	0	N/R	N/R
Adherence	82	76	92	N/R	78	65	83	N/R	0.114

Source of funding	Not reported
Comments	

27

Bibliographic reference (Ref ID)	Cheng et al 2007
Study type	Randomised controlled trial

Bibliographic reference (Ref ID)	Cheng et al 2007
Location	Taiwan
Number	124
Characteristics of patients	Mean age (yr): 42 Number of males: 63 Inclusion criteria: *H pylori* infection and previous eradication failure Exclusion criteria: Allergy to study medication Dyspeptic condition types(s): Duodenal ulcer, non-duodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (lan/amo/lev) N=62	Triple high (lan/amo/lev N=62	p
Age (yr) (mean)	41.8	42.2	N/R
Gender female %	50	51.6	N/R
Non duodenal ulcer	28	30	N/S
Duodenal ulcer	34	32	N/S

Intervention	Triple (lan/amo/lev) Dose and timing: 7 days; lan (30 mg b.i.d) / amo (1000mg b.i.d.) / lev (500mg b.i.d) Route: Oral
Comparator	Triple high dose (lan/amo/lev) Dose and timing: 7 days; lan (30 mg b.i.d) / amo (1000mg b.i.d.) / lev (500mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

Bibliographic reference (Ref ID)	Cheng et al 2007

	Triple (lan/amo/lev)				Triple high(lan/amo/lev)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	62	50	80.6	N/R	62	49	79	N/R	N/R
Adherence	62	57	91.9	N/R	62	56	90.3	N/R	N/R
Adverse events (diarrhoea/loose stools)	62	3	4.8	N/R	62	5	8.1	N/R	N/R

Source of funding	Research grant from National Scientific Council Taiwan
Comments	N/A

28

Bibliographic reference (Ref ID)	Cheon et al 2006[a]
Study type	Randomised controlled trial
Location	Korea
Number	54
Characteristics of patients	Mean age (yr): 56 Number of males: 31 Inclusion criteria: *H pylori* positive after previous eradication attempt Exclusion criteria: Concurrent critical illness, previous upper GI surgery, recent frequent NSAID, anticoagulation or steroid use. Study medication contradictions (allergy). Use of antimicrobials conditions associated with poor compliance. Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, gastroduodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA

Bibliographic reference (Ref ID)	Cheon et al 2006[a]
	Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (pan/bis/amo-cla/tet) N=25	Quad (pan/bis/met/tet) N=29	p
Age (yr) (mean)	58.6 + 10.1	54.7 + 12.3	0.21
Gender male/female	15/10	16/13	0.72
Gastric ulcer	7	7	N/R
Duodenal ulcer	17	20	N/R
Gastroduodenal ulcer	1	2	N/R
Amo res	4	3	1.0
Met res	12	8	0.477
Amo +Met res	2	2	1.0

Intervention	Regimen: Quad (pan/bisamo-cla//tet) Dose and timing: 7 days; pan (40 mg b.i.d) / bis (300 mg q.i.d.) / amo-cla (1000mg b.i.d) / tet (500 mg q.i.d) Route: Oral
Comparator	Regimen: Quad (pan/bis/met/tet) Dose and timing: 7 days; pan (40 mg b.i.d) / bis (300 mg q.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d.) Route: Oral
Length of follow up	Follow-up occurred 5 weeks following treatment
Outcomes measures and effect sizes	

	Quad (pan/bis/amo-	Quad

Bibliographic reference (Ref ID)	Cheon et al 2006[a]

	cla/tet)				(pan/bis/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	25	4	16	1.6-30.4	29	19	65.5	48.2-82.8	<0.0001
Adverse events (diarrhoea/loose stools)	25	4	16	N/R	29	1	3.4	NR	N/R

Source of funding	Liver Research Foundation Korea
Comments	Subgroups for resistance are reported but only as percentages for some of the data. Hence this data set was not extractable

29

Bibliographic reference (Ref ID)	Cheon et al, 2006[b
Study type	Randomised controlled trial
Location	Korea
Number	85
Characteristics of patients	Mean age (yr): 53 Number of males: 47 Inclusion criteria: Patients who had failed a first-line eradication treatment for *H pylori* Exclusion criteria: Patients with recurrent illness, a history of previous upper gastrointestinal surgery, contraindication to any of the study medication, recent frequent intake of NSAIDS, anticoagulants or steroids, an allergy to the study medications, pregnant or breast feeding women, recent use of antimicrobials and any condition probably associated with poor compliance such as drug abusers or alcoholics Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, gastroduodenal ulcer and non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None

Bibliographic reference (Ref ID)	Cheon et al, 2006[b
	Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (eso/amo/mox) n=41	Quad (bis/eso/met/tet)n=44	p
Mean age, yr (SD)	54.3 (11.7)	51.6 (12.5)	0.295
Sex: males/females	24/17	23/21	0.562
Gastric ulcer (n)	11	11	N/R
Duodenal ulcer (n)	20	24	N/R
Gastroduodenal ulcer (n)	2	1	N/R
Gastric adenoma (n)	4	3	N/R
Non-ulcer dyspepsia (n)	4	5	N/R

Intervention	Regimen: Triple (eso/amo/mox) Dose and timing: 7 days; eso (20 mg b.i.d) / amo (1 g b.i.d) / mox (400 mg q.i.d) Route: Oral
Comparator	Regimen: Quad (bis/eso/met/tet) Dose and timing: 7 days; bis (300 mg q.i.d) / eso (20 mg b.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment
Outcomes measures and effect sizes	

	Triple (eso/amo/mox)				Quad (bis/eso/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication	41	3	75.6	62.5-88.7	4	2	54.5	39.8-69.2	0.04

Bibliographic reference (Ref ID)	Cheon et al, 2006[b

rate ITT		1			4	4			2
Eradication rate PP	37	31	83.8	71.9-95.7	33	24	72.7	55.7-89.7	0.260
Adverse events (diarrhoea/loose stools)	41	1	2.4	N/R	44	0	0	N/R	N/R
Adherence to medication	41	37	90.2	N/R	44	33	75	N/R	N/R

Source of funding	This work was supported by a grant from the SNUBH research fund
Comments	N/A

30

Bibliographic reference (Ref ID)	Chi et al, 2003
Study type	Randomised controlled trial
Location	Taiwan
Number	100
Characteristics of patients	Mean age (yr): 45 Number of males: 51 Inclusion criteria: Patients who had failed a previous *H pylori* eradication regimen Exclusion criteria: Patients known to be allergic to bismuth, tetracycline or metronidazole were excluded. Patients with gastric malignancy were also excluded Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None

Bibliographic reference (Ref ID)	Chi et al, 2003
	Baseline clinical patient characteristics:

	Quad (bis/ome/amo/met) n=50	Quad (bis/ome/amo/tet) n=50	p
Mean age, yr	45.8	43.9	N/S
Sex: males/females	25/25	26/24	N/S
Diagnosis (duodenal ulcer/gastric ulcer/non-ulcer)	23/12/15	25/10/15	N/S

Intervention	Regimen: Quad (bis/ome/amo/met) Dose and timing: 7 days; bis (120 mg t.i.d) / ome (20 mg b.i.d) / amo (1 g b.i.d) / met (500 mg b.i.d) Route: Oral
Comparator	Regimen: Quad (bis/ome/amo/tet) Dose and timing: 7 days; bis (120 mg t.i.d) / ome (20 mg b.i.d) / amo (1 g b.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 6 weeks following treatment
Outcomes measures and effect sizes	

	Quad (bis/ome/amo/met)				Quad (bis/ome/amo/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	50	29	58	50.9-65.1	50	39	78	69.8-86.2	<0.05
Eradication rate PP	43	29	67.4	59.3-75.5	44	39	88.6	82.1-95.1	<0.05
Adverse events	50	3	6	N/R	50	3	6	N/R	N/R

Bibliographic reference (Ref ID)	Chi et al, 2003

(diarrhoea/loose stools)									
Adherence to medication	50	43	86	N/R	50	44	88	N/R	N/R
Eradication rate PP (CR)	11	6	54.5	N/R	11	8	72.7	N/R	N/S
Eradication rate PP (CS)	26	16	61.5	N/R	26	23	88.5	N/R	N/S
Eradication rate PP (MR)	15	5	33.3	N/R	16	13	81.3	N/R	0.05
Eradication rate PP (MS)	22	17	77.3	N/R	21	18	85.7	N/R	N/S

Clarithromycin resistant (CR); clarithromycin susceptible (CS); metronidazole resistant (MR); metronidazole susceptible (MS)

Source of funding	This study was supported by a research grant from the National Scientific Council, Taiwan
Comments	N/A

31

Bibliographic reference (Ref ID)	Chuah et al 2012
Study type	Randomised controlled trial
Location	Taiwan
Number	128
Characteristics of patients	Mean age (yr): 56 Number of males: 61 Inclusion criteria: Endoscopically proven peptic ulcer disease or gastritis, persistent *H pylori* (failed one eradication attempt) Exclusion criteria: Ingestion of antibiotic, bismuth, PPI, use of NSAIDs in 4 weeks prior to study, allergic reaction to study medication, previous gastric surgery, concomitant serious illness, pregnancy Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, gastric and duodenal ulcer, unspecified (includes peptic ulcer)

Bibliographic reference (Ref ID)	Chuah et al 2012
	Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: 3 weeks of antacid treatment for patients with gastritis, 3 weeks of esomeprazole 40mg once daily for peptic ulcer patients Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (eso/amo/lev) N=64	Triple (eso/amo/tet) N=64	p
Age (yr) (mean)	58.5 + 14	55.7 + 12.3	0.233
Gender male/female	26/38	35/29	0.11
Smoking	6	9	0.41
Alcohol	5	6	0.75
Gastric ulcer	18	24	N/R
Duodenal ulcer	17	19	N/R
Gastric and duodenal ulcer	11	5	N/R
unspecified	18	16	N/R
Tet (sus/res)	17/0	15/0	N/R
Amo (sus/res)	17/0	15/0	N/R
Lev (sus/res)	13/4	10/5	0.699

Intervention	Regimen: Triple (eso/amo/lev) Dose and timing: 7 days; eso (40 mg b.i.d) / amo (1000 mg b.i.d.) / lev (500 mg m.i.d.) Route: Oral
Comparator	Regimen: Triple (eso/amo/tet) Dose and timing: 14 days; eso (40 mg b.i.d) / amo (1000 mg b.i.d) / tet (500 mg q.i.d.)

Bibliographic reference (Ref ID)	Chuah et al 2012
	Route: Oral
Length of follow up	Follow-up occurred 126 days following treatment
Outcomes measures and effect sizes	

	Triple (eso/amo/lev)				Triple (eso/amo/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	64	50	78	N/R	64	48	75	N/R	0.67
Eradication rate ITT amo sen	17	11	65	N/R	15	9	60	N/R	N/R
Eradication rate ITT lev sus	13	9	69	N/R	N/A	N/A	N/A	N/A	N/A
Eradication rate ITT lev res	4	2	50	N/R	N/A	N/A	N/A	N/A	N/A
Eradication rate ITT tet sus	N/A	N/A	N/A	N/A	15	9	60	N/R	N/A
Adverse events (diarrhoea/loose stools)	64	0	0	N/R	64	0	0	N/R	N/R
Adverse events (rash)	64	0	0	N/R	64	1	NR	N/R	1.0

Bibliographic reference (Ref ID)	Chuah et al 2012
	Adherence to medication: 64 / 61 / 95 / N/R / 64 / 62 / 97 / N/R / 0.95
Source of funding	Research Foundation of Chang Gung Memorial Hospital Taiwan
Comments	Double blinded study

32

Bibliographic reference (Ref ID)	Di Caro et al, 2009
Study type	Randomised controlled trial
Location	Italy
Number	160
Characteristics of patients	Mean age (yr): Not reported Number of males: 72 Inclusion criteria: Patients *H pylori* positive who had failed previous eradication therapy Exclusion criteria: Patients taking PPIs, H2RAs or antibiotics in the 4 weeks preceeding the enrolment were excluded as were pregnant women, patients with known antibiotic allergy or hepatic impairment of kidney failure Dyspeptic condition types(s): Peptic ulcer, duodenitis, gastritis Previous 1st line eradication regimen: Standard first-line triple therapy (either amoxicillin or metronidazole based) Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics: 160 consecutive Caucasian patients (aged 18 – 70 years, 72 male patients). No additional baseline characteristics were provided.
Intervention	Regimen: Triple (eso/amo/lev) Dose and timing: 7 days; eso (20 mg b.i.d) / amo (1 g b.i.d) / lev (500 mg m.a.n.e) Route: Oral
Comparator	Regimen: Triple (eso/amo/lev)

Bibliographic reference (Ref ID)	Di Caro et al, 2009
	Dose and timing: 10 days; eso (20 mg b.i.d) / amo (1 g b.i.d) / lev (500 mg m.a.n.e) Route: Oral Regimen: Triple (eso/amo/lev) – double dose lev Dose and timing: 7 days; eso (20 mg b.i.d) / amo (1 g b.i.d) / lev (500 mg b.i.d) Route: Oral Regimen: Triple (eso/amo/lev) – double dose lev Dose and timing: 10 days; eso (20 mg b.i.d) / amo (1 g b.i.d) / lev (500 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred 6 weeks following treatment
Outcomes measures and effect sizes	

	Eradication ITT k, n, % (95% CI)	P	Eradication PP n, k, % (95% CI)
Triple 7 (eso/amo/lev)	26, 40, 65 (NR)	0.81 compared with Triple 7 (eso/amo/lev) – double dose lev <0.02 compared with Triple 10 (eso/amo/lev)	Same as ITT
Triple 10 (eso/amo/lev)	36, 40, 90 (NR)	0.73 compared with Triple 10 (eso/amo/lev) – double dose lev	Same as ITT
Triple 7 (eso/amo/lev) – double dose lev	28, 40, 70 (NR)	0.18 compared with Triple 10 (eso/amo/lev) – double dose lev	Same as ITT

Bibliographic reference (Ref ID)	Di Caro et al, 2009
	Triple 10 (eso/amo/lev) – double dose lev | 34, 40, 85 (NR) | 0.18 compared with Triple 7 (eso/amo/lev) – double dose lev | Same as ITT
	Adherence to medication (n) | Adherence to medication (k) | Adherence to medication (%)
	Triple 7 (eso/amo/lev) | 40 | 36 | 90
	Triple 10 (eso/amo/lev) | 40 | 33 | 82.5
	Triple 7 (eso/amo/lev) – double dose lev | 40 | 31 | 77.5
	Triple 10 (eso/amo/lev) – double dose lev | 40 | 36 | 90
Source of funding	Not reported
Comments	

33

Bibliographic reference (Ref ID)	Gisbert et al 2007
Study type	Randomised controlled trial
Location	Spain
Number	100
Characteristics of patients	Mean age (yr): 47 Number of males: 43 Inclusion criteria: Persistent *H pylori* infection, gastroduodenal ulcer disease, functional dyspepsia Exclusion criteria: <18 years, presence of clinically significant associated disease, previous gastric surgery, allergy to study medication Dyspeptic condition types(s): Gastroduodenal ulcer disease, functional dyspepsia

Bibliographic reference (Ref ID)	Gisbert et al 2007
	Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (ome/amo/lev) N=50	Quad (ran/bis/met/tet) N=50	p
Age (yr) (mean)	46	47	N/S
Gender male %	38	29	N/S
Smoking %	23	18	N/S
Functional dyspepsia %	82	81	N/S
Duodenal ulcer %	18	19	N/S

Intervention	Regimen: triple (ome/amo/lev) Dose and timing: 7 days; ome (20 mg b.i.d) / amo (1000 mg b.i.d) / lev (500 mg b.i.d) Route: Oral
Comparator	Regimen: quad (ran/bis/met/tet) Dose and timing: 7 days; ran/bis (400 mg b.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d.) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Triple (ome/amo/lev)				Quad (ran/bis/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p

Bibliographic reference (Ref ID)	Gisbert et al 2007

Eradication rate ITT	50	34	68	N/R	50	34	68	N/R	0.76
Adherence	50	45	90	N/R	50	45	90	N/R	N/R
Adverse events (diarrhoea/loose stools)	50	5	10	N/R	50	1	2	N/R	N/R
Adverse events (rash)	50	0	0	N/R	50	1	2	N/R	N/R

Source of funding	Instituto de Salud Carlos III
Comments	Open trial

34

Bibliographic reference (Ref ID)	Gisbert et al, 1999
Study type	Randomised controlled trial
Location	Spain
Number	60
Characteristics of patients	Mean age (yr): 45 Number of males: 28 Inclusion criteria: Patients in whom a first *H pylori* eradication therapy failed Exclusion criteria: Having had antibiotic or bismuth therapy within 30 days prior to entering the study, use of gastroerosive drugs, presence of associated conditions (hepatic, cardiorespiratory or renal diseases, diabetes, malign diseases, coagulopathy or previous gastric surgery) Dyspeptic condition types(s): Duodenal ulcer, non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None

Bibliographic reference (Ref ID)	Gisbert et al, 1999
	Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (bis/ome/met/tet) n=30	Quad (bis/ran/met/tet) n=30	p
Mean age, yr ± SD	47 ± 12	43 ± 11	0.19
Sex: males/females	14/16	14/16	0.79
Smoking (% smokers)	53	33	0.19
Diagnosis (% duodenal ulcer/non-ulcer)	27/73	17/83	0.54

Intervention	Regimen: Quad (bis/ome/met/tet) Dose and timing: 7 days; bismuth (120 mg q.i.d) / ome (20 mg b.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d) Route: Oral
Comparator	Regimen: Quad (bis/ran/met/tet) Dose and timing: 7 days; Ranitidine bismuth citrate (400 mg b.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 4 weeks following treatment
Outcomes measures and effect sizes	

	Quad (bis/ome/met/tet)				Quad (bis/ran/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	30	17	57	39-73	30	25	83	66-93	0.046
Eradication rate PP	29	17	59	41-14 (as	29	25	86	69-94	0.037

Bibliographic reference (Ref ID)	Gisbert et al, 1999

				reported by author)					
Adherence to medication	29	29	100	N/R	29	29	100	N/R	N/R

Source of funding	Not reported
Comments	Open trial. Adverse events were recorded in the study but was not reported in a way that the data could be extracted

35

Bibliographic reference (Ref ID)	Georgopoulos et al 2002
Study type	Randomised controlled trial
Location	Greece
Number	95
Characteristics of patients	Mean age (yr): 45 Number of males: 59 Inclusion criteria: Persistent *H pylori* (failed one eradication attempt) Exclusion criteria: Use of antibiotics, bismuth PPI, NSAIDs in month prior to study, pregnancy, lactation, previous gastric surgery, severe chronic disease Dyspeptic condition types(s): Duodenal ulcer, non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (ome/bis/met/tet) N=49	Quad (ome/bis/cla/met) N=46	p

Bibliographic reference (Ref ID)	Georgopoulos et al 2002

Age (yr) (median +range))	43(18-78)	44(19-78)	0.97
Gender male/female	31/18	28/18	0.81
Smoking %	50	39.5	0.24
Duodenal ulcer	13	17	0.27
Non ulcer dyspepsia	36	29	0.27
Met sus and Cla sus	20	16	N/R
Met sus Cla res	5	3	N/R
Met res Cla sus	8	11	N/R
Met res Cla res	4	6	N/R

Intervention	Regimen: Quad (ome/bis/cla/met) Dose and timing: 7 days; ome (20 mg b.i.d) / bis (120mg q.i.d) / cla (500 mg b.i.d) / met (500 mg b.i.d) Route: Oral
Comparator	Regimen: Quad (ome/bis/met/tet) Dose and timing: 7 days; ome (20 mg b.i.d) / bis (120 mg q.i.d) / met (500 mg b.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 49 days following treatment
Outcomes measures and effect sizes	

	Quad (ome/bis/met/tet)				Quad (ome/bis/cla/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	49	41	83.7	70-92	46	27	58	43-73	0.007

Bibliographic reference (Ref ID)	Georgopoulos et al 2002
	Adherence | 49 | 49 | 100 | 86-100 | 46 | 46 | 100 | 86-100 | 0.66
Source of funding	Not reported
Comments	Data could not be extracted on eradication rates in relation to resistance as the graphs were labelled incorrectly

36

Bibliographic reference (Ref ID)	Hu et al 2011
Study type	Randomised controlled trial
Location	Taiwan
Number	90
Characteristics of patients	Mean age (yr): 56 Number of males: 50 Inclusion criteria: Adult, endoscopically proven peptic ulcer disease, gastritis/normal endoscopy, *H pylori* positive Exclusion criteria: Previous *H pylori* eradication, ingestion of antibiotics ,bismuth, PPI within 4 weeks, use of NSAIDs within 4 weeks, history of allergic reaction to study medication, previous gastric surgery, serious concomitant illness, pregnancy. Dyspeptic condition types(s): Endoscopically proven peptic ulcer disease, gastritis Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: Esomeprazole 40mg daily for patients with peptic ulcers only Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (eso/amo/lev) N=45	Triple (eso/amo/met) N=45	p
Age (yr) (mean)	56 + 13.5	56.3 + 10.2	0.9
Gender male/female	21/24	29/16	0.13
Smoking	5	10	0.25
Alcohol consumption	5	12	0.10

Bibliographic reference (Ref ID)	Hu et al 2011

History of PU	30	32	0.8
Gastric ulcer	13	19	0.08
Duodenal ulcer	12	17	N/R
Gastric and dudodenal ulcer	8	5	N/R
Gastritis	12	4	N/R

Intervention

Regimen: Triple (eso/amo/lev)
Dose and timing: 7 days; eso (40 mg b.i.d) / amo((1000 mg b.i.d) / lev (500 mg daily)
Route: Oral

Comparator

Regimen: Triple (eso/amo/met)
Dose and timing: 14 days; eso (40 mg b.i.d) / amo (1000 mg b.i.d) / met (250 mg q.i.d)
Route: Oral

Length of follow up

Follow-up occurred 8 weeks following treatment

Outcomes measures and effect sizes

	Triple (eso/amo/lev)				Triple (eso/amo/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	45	32	68.9	N/R	45	38	84.4	N/R	0.134
Adverse events (diarrhoea/loose stools)	45	2	4.4	N/R	45	2	4.4	N/R	1.00
Adverse events (rash)	45	0	0	N/R	45	2	4.4	N/R	0.49
Adherence	45	43	95.6	N/R	45	45	100	N/R	0.49

Source of funding

Foundation of Chang Gung Memorial Hospital

Comments

N/A

37

Bibliographic reference (Ref ID)	Koksal et al, 2005
Study type	Randomised controlled trial
Location	Turkey
Number	56
Characteristics of patients	Mean age (yr): 44 Number of males: 25 Inclusion criteria: Patients who remained *H pylori* positive after an initial treatment failure Exclusion criteria: Patients who received bismuth compounds, anti-secretory drugs, or antibiotics during the 4 weeks before endoscopy were excluded from the study. Other exclusion criteria were age under 18 years, previous gastrointestinal surgery, concomitant diabetes, heart, liver or renal disease, malignancy, pregnancy or lactation, use of NSAIDS and allergy to penicillin, clarithromycin, bismuth or metronidazole Dyspeptic condition types(s): Gastric ulcer and non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (bis/ran/amo/cla) n=28	Quad (bis/ran/met/tet) n=28	p
Mean age, yr	46 ±11	42 ± 10	0.1
Sex: males/females	12/16	13/15	0.7
Smoking (% smokers)	17.8	32.1	0.2
Diagnosis (duodenal ulcer/gastric ulcer/non-ulcer)	0/2/26	0/1/27	0.5

Intervention	Regimen: Quad (bis/ran/amo/cla) Dose and timing: 10 days; ranitidine bismuth citrate (400 mg b.i.d) / amo (1 g b.i.d) / cla (500 mg b.i.d) Route: Oral

Bibliographic reference (Ref ID)	Koksal et al, 2005
Comparator	Regimen: Quad (bis/ran/met/tet) Dose and timing: 10 days; ranitidine bismuth citrate (400 mg b.i.d) / met (500 mg b.i.d) / tet (500 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Quad (bis/ran/amo/cla)				Quad (bis/ran/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	28	17	60.7	42-79	28	24	85.7	73-98	0.03
Eradication rate PP	28	17	60.7	42-79	28	24	85.7	73-98	0.03
Adverse events (diarrhoea/loose stools)	28	2	7.1	N/R	28	4	14.2	N/R	N/R
Adverse events (rash)	28	1	3.5	N/R	28	0	0	N/R	N/R
Adverse events (mouth dryness)	28	2	7.1	N/R	28	0	0	N/R	N/R
Adherence to medication	28	28	100	N/R	28	28	100	N/R	N/R

N.B. PP eradication rate not reported in table as results were the same as for ITT eradication

Bibliographic reference (Ref ID)	Koksal et al, 2005
Source of funding	Not reported
Comments	N/A

38

Bibliographic reference (Ref ID)	Kuo et al 2009
Study type	Randomised controlled trial
Location	Taiwan
Number	166
Characteristics of patients	Mean age (yr): 50 Number of males: 84 Inclusion criteria: *H pylori* positive after previous eradication attempt Exclusion criteria: Ingestion of antibiotics, bismuth PPI within 4 weeks, allergic reaction to study medication, previous gastric surgery, coexistence of serious concomitant illness, pregnancy. Dyspeptic condition types(s): Gastritis, gastric ulcer, duodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (eso/bis/met/tet) N=83	Triple (eso/amo/lev) N=83	p
Age (yr) (mean)	49.1 + 13.6	50.2 + 12.4	0.15
Gender male/female	40/43	44/39	0.45
Smoking	10	12	0.13
Gastric ulcer	21	19	N/R

Bibliographic reference (Ref ID)	Kuo et al 2009

Duodenal ulcer	33	34	N/R
Gastritis	29	30	N/R

Intervention

Regimen: Quad (eso/bis/met/tet)
Dose and timing: 7 days; eso (40 mg b.i.d) / bis (120 q.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d)
Route: Oral

Comparator

Regimen: Triple (eso/amo/lev)
Dose and timing: 7 days; eso (40 mg b.i.d) / amo (1000 mg b.i.d) / lev (500 mg m.a.n.e)
Route: Oral

Length of follow up

Follow-up occurred 120 days following treatment

Outcomes measures and effect sizes

	Quad (eso/bis/amo/tet)				Quad (eso/bis/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	83	53	63.9	53.6-74.2	83	58	69.9	60.1-79.7	0.89
Adherance to medication	71	66	92.7	N/R	80	79	99	N/R	0.32
Adverse events (diarrhoea/loose stools)	83	2	2.5	N/R	83	0	0	N/R	N/R
Adverse events (rash)	83	1	1	N/R	83	0	0	N/R	N/R

Source of funding

Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung Veterans General hospital

Bibliographic reference (Ref ID)	Kuo et al 2009
Comments	Blinded study. Levofloxacin resistance reported as 21% in study population

39

Bibliographic reference (Ref ID)	Mantzaris et al, 2005
Study type	Randomised controlled trial
Location	Greece
Number	115
Characteristics of patients	Mean age (yr): 40 Number of males: Not reported Inclusion criteria: Patients with persistent *H pylori* infection after first-line therapy and an active duodenal ulcer Exclusion criteria: Chronic alcoholism, chronic renal or hepatic failure, malignant disease, previous gastric surgery, treatment with anticoagulants, treatment with antibiotics other than those prescribed for the study, regular treatment with NSAIDS and well documented allergy to any of the study drugs Dyspeptic condition types(s): Duodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad 7 (bis/ome/met/tet) n=54	Quad 14 (bis/ome/met/tet) n=61	p
Mean age, yr (mean range)	38.5 (18-69)	40.5 (19-68)	N/S
Sex: males/females	30/24	33/28	N/S
Disease duration, yr (mean range)	4.2 (1-19)	5 (1-17)	N/S
Ulcer size (</> 1 cm)	23/31	24/37	N/S
Ulcer number (1 / > 1)	44/10	46/15	N/S

Bibliographic reference (Ref ID)	Mantzaris et al, 2005

Past bleeders	18	25	N/S
Smokers	34	38	N/S
Social drinkers	30	39	N/S
Occasional NSAID users	21	29	N/S

Intervention

Regimen: Quad (bis/ome/met/tet)
Dose and timing: 7 days; bismuth (120 mg q.i.d) / ome (20 mg b.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d)
Route: Oral

Comparator

Regimen: Quad (bis/ome/met/tet)
Dose and timing: 14 days; bismuth (120 mg q.i.d) / ome (20 mg b.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d)
Route: Oral

Length of follow up

Follow-up occurred 6 weeks following treatment

Outcomes measures and effect sizes

	Quad 7 (bis/ome/met/tet)				Quad 14 (bis/ome/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	54	36	66.7	N/R	61	48	78.7	N/R	0.215
Eradication rate PP	45	36	80	N/R	50	48	96	N/R	0.035
Adherence to medication	54	51	94.4	N/R	61	54	88.5	N/R	N/R
Recurrence	36	0	0	N/R	48	0	0	N/R	N/R

Source of funding

Not reported

Comments

Single-blind trial

40

Bibliographic reference (Ref ID)	Matsuhisa et al 2006
Study type	Randomised controlled trial
Location	Japan
Number	228
Characteristics of patients	Mean age (yr): 54 Number of males: 161 Inclusion criteria: *H pylori* positive after previous eradication attempt Exclusion criteria: Non stated Dyspeptic condition types(s): Peptic ulcer disease, atrophic gastritis, functional dyspepsia, MALT lymphoma (2%), early gastric cancer (<1%), gastric polyp (<0.5%) Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple low (ppi/amo/met) N=121	Triple high (ppi/amo/met) N=107	p
Age (yr) (mean)	55.7 + 12.1	51.2 + 10.7	0.0025
Gender male/female	82/39	79/28	0.36
PUD	91	83	0.67
Atrophic gastritis	21	18	0.91
Functional Gastritis	3	4	0.86
MALT lymphoma	3	2	0.889
Early gastric cancer	2	0	0.53
Gastric polyp	1	0	0.95

Intervention	Regimen: Triple low (ppi/amo/met)

Bibliographic reference (Ref ID)	Matsuhisa et al 2006
	Dose and timing: 7 days; PPI(- mg b.i.d) / amo (750 mg b.i.d) / met (250 mg b.i.d) Route: Oral
Comparator	Regimen: Triple high (ppi/amo/met) Dose and timing: 7 days; PPI(- mg b.i.d) / amo (750 mg b.i.d) / met (500 mg t.i.d) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Triple low (PPI/amo/met)				Triple high (PPI/amo/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	121	106	87.6	N/R	107	93	86	N/R	0.87
Adverse events (diarrhoea/loose stools)	118	9	7.6	N/R	106	25	23.6	N/R	0.0009

Source of funding	Not reported
Comments	N/A

41

Bibliographic reference (Ref ID)	Matsumoto et al, 2005
Study type	Randomised controlled trial
Location	Japan
Number	51
Characteristics of	Mean age (yr): 51

Bibliographic reference (Ref ID)	Matsumoto et al, 2005
patients	Number of males: 36 Inclusion criteria: Patients between 20 and 70 years of age with persistent *H pylori* infection after a standard triple therapy Exclusion criteria: Patients who had been taking aspirin, other NSAIDS, known drug allergy to the study drugs, gastric cancer, severe concomitant disease and previous gastric surgery were excluded Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, gastroduodenal ulcer and gastritis Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (lan/amo/lev) n=30	Triple (lan/amo/met) n=30	p
Mean age, yr	50.8 ± 13.5	52 ± 13	N/R
Sex: males/females	17/13	19/11	N/R
Gastric ulcer (n)	15	11	N/R
Duodenal ulcer (n)	6	8	N/R
Gastroduodenal ulcer (n)	2	2	N/R
Gastritis (n)	7	9	N/R
Smoking/non smoking	8/22	14/16	N/R
Drinking/non drinking	13/17	16/14	N/R
Amo S/R/unknown	17/0/13	18/0/12	N/R
Cla S/R/unknown	5/12/13	9/9/12	N/R
Lev S/R/unknown	15/2/13	15/3/12	N/R
Met S/R/Unknown	15/2/13	17/1/12	N/R

S = susceptible; R = resistant

Intervention	Regimen: Triple (lan/amo/lev)

Bibliographic reference (Ref ID)	Matsumoto et al, 2005
	Dose and timing: 7 days; lan (20 mg b.i.d) / amo (1 g b.i.d) / lev (300 mg b.i.d) Route: Oral
Comparator	Regimen: Triple (lan/amo/met) Dose and timing: 7 days; lan (20 mg b.i.d) / amo (1 g b.i.d) / met (500 mg b.i.d) Route: Oral
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Triple (lan/amo/lev)				Triple (lan/amo/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	30	21	70	45-95	30	29	96.7	90-100	0.006
Eradication rate PP	29	21	72.4	56-89	29	29	100	N/R	0.002
Adverse events (diarrhoea/loose stools)	30	3	10	N/R	30	6	20	N/R	N/R
Adverse events (rash)	30	1	3.3	N/R	30	0	0	N/R	N/R
Eradication rate PP (cla-S/lev-S)	4	3	75	N/R	N/A	N/A	N/A	N/A	N/R
Eradication rate PP (cla-R/lev-S)	10	6	60	N/R	N/A	N/A	N/A	N/A	N/R
Eradication	2	1	50	N/R	N/A	N/A	N/A	N/A	N/R

Bibliographic reference (Ref ID)	Matsumoto et al, 2005

rate PP (cla-R/lev-R)									
Eradication rate PP (cla-S/met-S)	N/A	N/A	N/A	N/A	8	8	100	N/R	N/R
Eradication rate PP (cla-S/met-R)	N/A	N/A	N/A	N/A	1	1	100	N/R	N/R
Eradication rate PP (cla-R/met-R)	N/A	N/A	N/A	N/A	8	8	100	N/R	N/R

Susceptible (S); Resistant (R)

Source of funding	Not reported
Comments	Open trial. Adherence to medication was assessed but data was not reported in a way that could be extracted - two patients did not complete the therapeutic regimens

42

Bibliographic reference (Ref ID)	Michopoulos et al 2000
Study type	Randomised controlled trial
Location	France
Number	156
Characteristics of patients	Mean age (yr): 48 Number of males: Not reported Inclusion criteria: 18-80 years, erosive duodentitis or duodenal ulcer failed eradication attempt and *H pylori* positive Exclusion criteria: Allergy to study medication, complications of ulcer disease, or taking omeprazole. Liver or kidney disease, severe cardiac or pulmonary, drug abuse malignancy, pregnancy, breast feeding or NSAID use Dyspeptic condition types(s): Duodenal ulcer

Bibliographic reference (Ref ID)	Michopoulos et al 2000
	Previous 1st line eradication regimen: PPI/AMO/CLA or dual therapy Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (ome/bis/met/tet) N=78	Quad (ran/bis/met/tet) N=78	p
Age (yr) (mean + SD)	47 (44-50)	49 (46-52)	0.35
Gender male/female	44/34	43/35	0.87
Smokers/non-smokers	34/44	35/43	0.87
Previous treatments dual/triple	40/38	40/38	1.00
Erosive duodenitis	19	18	0.85
Duodenal ulcer	59	60	0.85

Intervention	Regimen: Quad (ome/bis/met/tet) Dose and timing: 14 days; ome (20 mg b.i.d) / bis (120 mg t.i.d) / met (500 mg t.i.d) / tet (500 mg t.i.d) Route: Oral
Comparator	Regimen: Quad (ran/bis/met/tet) Dose and timing: 14 days; ran (300 mg b.i.d) / bis (120 mg t.i.d) / met (500 mg t.i.d) / tet (500 mg t.i.d) Route: Oral
Length of follow up	Follow-up occurred 4-6 weeks following treatment
Outcomes measures and effect sizes	

	Quad (ome/bis/met/tet)				Quad (ran/bis/met/tet)				
	N	k	Mean	95% CI	N	k	Mean	95% CI	p

Bibliographic reference (Ref ID)	Michopoulos et al 2000

			%				%		
Eradication rate ITT	76	76	100	N/R	76	74	97.4	N/R	0.79
Adverse events (diarrhoea/loose stools)	76	11	14.5	N/R	76	7	9.2	N/R	N/R
Adverse events (rash)	76	3	3.9	N/R	76	1	1.3	N/R	N/R

Source of funding	Not reported
Comments	Only subset of patients who received PPI/AMO/CLA as their first line therapy are applicable as the rest had a dual therapy as their previous eradication regimen

43

Bibliographic reference (Ref ID)	Nista et al, 2003
Study type	Randomised controlled trial
Location	Italy
Number	280
Characteristics of patients	Mean age (yr): 48 Number of males: 134 Inclusion criteria: *H pylori* patients with one failed eradication attempt Exclusion criteria: Recent (within the previous 30 days) use of antimicrobial agents, bismuth compounds, PPIs and H2RAs, hypersensitivity to one of the studied drugs, previous treatment with one of the studied combinations, pregnant or lactating women, patients with major concomitant diseases or who had undergone gastric surgery Dyspeptic condition types(s): Non-ulcer dyspepsia Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None

Bibliographic reference (Ref ID)	Nista et al, 2003
	Concomitant treatment: None Baseline clinical patient characteristics:

	Triple (rab/amo/lev) n=70	Triple (rab/lev/tin) n=70	Quad (bis/rab/met/tet) – 7 days n=70	Quad (bis/rab/met/tet) – 14 days n=70	p
Mean age, yr (SD)	47 ±10.4	48 ± 9.4	48 ± 9.9	49 ± 11.1	N/R
Sex: males/females	33/37	34/36	34/36	33/37	N/R
Ulcer-like dyspesia (%)	37	41	40	43	N/R
Dismotility-like dyspesia (%)	33	30	34	33	N/R
Reflux-like dyspepsia (%)	30	29	26	24	N/R

Intervention	Regimen: Triple (rab/amo/lev) Dose and timing: 10 days; rab (20 mg b.i.d) / amo (1 g b.i.d) / lev (500 mg m.a.n.e) Route: Oral
Comparator	Regimen: Triple (rab/lev/tin) Dose and timing: 10 days; rab (20 mg b.i.d) / lev (500 mg m.a.n.e) / tin (500 mg b.i.d) Route: Oral Regimen: Quad (bis/rab/met/tet) Dose and timing: 7 days; bismuth (120 mg q.i.d) / rab (20 mg b.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d) Route: Oral Regimen: Quad (bis/rab/met/tet) Dose and timing: 14 days; bismuth (120 mg q.i.d) / rab (20 mg b.i.d) / met (500 mg t.i.d) / tet (500 mg q.i.d) Route: Oral

Bibliographic reference (Ref ID)	Nista et al, 2003
Length of follow up	Follow-up occurred 6 weeks following treatment
Outcomes measures and effect sizes	

	Eradication ITT n, k, % (95% CI)	P	Eradication PP n, k, % (95% CI)	P
Triple (rab/amo/lev)	70, 66, 94.3, N/R	N/R	70, 66, 94.3, N/R	N/R
Triple (rab/lev/tin)	70, 63, 90, N/R	N/R	70, 63, 90, N/R	N/R
Quad 7 (bis/rab/met/tet)	70, 44, 62.9, N/R	N/R	64, 44, 68.8, N/R	N/R
Quad 14 (bis/rab/met/tet)	70, 48, 68.6, N/R	N/R	60, 48, 80, N/R	N/R
	Adverse events	n	k	%
Triple (rab/amo/lev)	Diarrhoea/loose stools	70	3	4.3
Triple (rab/lev/tin)	Diarrhoea/loose stools	70	3	4.3
Quad 7 (bis/rab/met/tet)	Diarrhoea/loose stools	70	1	1.4
Quad 14 (bis/rab/met/tet)	Diarrhoea/loose stools	70	6	8.6
Triple (rab/amo/lev)	Rash	70	0	0
Triple (rab/lev/tin)	Rash	70	0	0
Quad 7	Rash	70	0	0

Bibliographic reference (Ref ID)	Nista et al, 2003
	(bis/rab/met/tet) | | | | |
	Quad 14 (bis/rab/met/tet) | Rash | 70 | 1 | 1.4
Source of funding	This study was supported in part by an unrestricted grant from 'Fondazione Ricerca in Medicina', Bologna, Italy
Comments	N/A

44

Bibliographic reference (Ref ID)	Ueki et al 2009
Study type	Randomised controlled trial
Location	Japan
Number	104
Characteristics of patients	Mean age (yr): 55 Number of males: 67 Inclusion criteria: Persistent *H pylori* infection (failure of first line medication) Exclusion criteria: <18 yrs, pregnancy/lactation, allergy to study medication, contradiction to biopsy, peptic ulcer complications, regular NSAID use, chronic corticosteroid use Dyspeptic condition types(s): Gastric ulcer, duodenal ulcer, gastroduodenal ulcer, chronic gastritis, gastric adenoma (4%) Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (rab/amo/cla/met) N=52	Triple (rab/amo/met) N=52	p
Age (yr) (mean)	53.6 + 16.2	56.6 + 11.5	N/S

Bibliographic reference (Ref ID)	Ueki et al 2009

Gender male/female	37/15	30/22	N/S
Smoking	16	14	N/S
Alcohol consumption	21	24	N/S
Gastric ulcer	19	18	N/R
Duodenal ulcer	14	12	N/R
Gastroduodenal ulcer	2	7	N/R
Gastritis	15	13	N/R
Adenoma	2	2	N/R
Cla resistant	43	42	N/S
Amo resistant	2	3	N/S
Met resistant	0	0	N/S

Intervention

Regimen: Quad (rab/amo/cla/met)
Dose and timing: 7 days; rab (10 mg b.i.d) / amo (750mg b.i.d) / cla (200 mg b.i.d) / met (250 mg b.i.d)
Route: Oral

Comparator

Regimen: Triple (rab/amo/met)
Dose and timing: 7 days; rab (10 mg b.i.d) /amo (750 mg b.i.d) / met (250 mg b.i.d)
Route: Oral

Length of follow up

Follow-up occurred 12 weeks following treatment

Outcomes measures and effect sizes

	Quad (rab/amo/cla/met)				Triple (rab/amo/met)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication	52	4	88.5	79-97	5	4	82.3	72.7-92.7	0.40

Bibliographic reference (Ref ID)	Ueki et al 2009

rate ITT		5			2	3			7
Eradication rate ITT cla res	40	37	92.5	84-100	42	35	83	72-95	N/R
Adverse events (diarrhoea/loose stools)	52	8	15.4	N/R	52	6	11.5	N/R	N/R
Adverse events (rash)	52	2	3.8	N/R	52	0	0	N/R	N/R

Source of funding	Not reported
Comments	Single blinded

45

Bibliographic reference (Ref ID)	Uygun et al 2008
Study type	Randomised controlled trial
Location	Turkey
Number	300
Characteristics of patients	Mean age (yr): 42 Number of males: 161 Inclusion criteria: *H pylori* positive after previous eradication attempt Exclusion criteria: Active peptic ulcer, previous gastric surgery, malignancy, allergy to any first line drugs, fertile women not on contraception. Dyspeptic condition types(s): Non-ulcer dyspepsia (dyspepsia and gastritis and/or duodenitis) Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None

Bibliographic reference (Ref ID)	Uygun et al 2008
	Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (lan/bis/amo/met) N=100	Quad (lan/bis/amo/tet)) N=100	Quad (lan/bis/met/tet) N=100	p
Age (yr) (mean)	41.12 + 12.5	45.17 + 13.5	41.64 + 11.7	N/R
Gender male/female	57/34	47/45	48/47	N/R

Intervention	Regimen: Quad (lan/bis/amo/met) Dose and timing: 14 days; lan (30 mg b.i.d) / bis (300 mg q.i.d) / amo (1000 mg q.i.d) / met (500 mg q.i.d) Route: Oral
Comparator	Regimen: Quad (lan/bis/amo/tet) Dose and timing: 7 days; lan (30 mg b.i.d) / bis (300 mg q.i.d) /amo (1000 mg q.i.d) / tet (500 mg q.i.d) Route: Oral Regimen: Quad (lan/bis/amo/tet) Dose and timing: 14 days; lan (30 mg b.i.d) / bis (300 mg q.i.d) /amo (1000 mg q.i.d) / tet (500 mg q.i.d) Route: Oral
Length of follow up	Follow-up occurred 9 weeks following treatment
Outcomes measures and effect sizes	

	Quad lan/bis/amo/met			Quad (lan/bis/amo/tet)			Quad (lan/bis/met/tet)				
	N	k	Mean %	N	k	Mean %	N	K	Mean%	p	p
Eradication	91	6	81.5	9	7	80.9	9	78	82.2	N/R	0.76

Bibliographic reference (Ref ID)	Uygun et al 2008									
	rate ITT		8		2	5		5		
Source of funding	Not reported									
Comments	N/A									

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Bibliographic reference (Ref ID)	Wu et al 2011
Study type	Randomised controlled trial
Location	Taiwan
Number	120
Characteristics of patients	Mean age (yr): 54 Number of males: 60 Inclusion criteria: *H pylori* positive after previous eradication attempt Exclusion criteria: Ingestion of antibiotics, bismuth, PPI within 2 weeks of investigation, allergy to study medication, previous gastric surgery, coexistence of serious Dyspeptic condition types(s): Gastritis, gastric ulcer, duodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: Esomeprazole 40mg daily for patients with peptic ulcers only Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (eso/bis/amo/tet) N=58	Quad (eso/bis/met/tet) N=62	p
Age (yr) (mean)	54.3 + 11	53.6 + 11.7	0.75
Gender male/female	30/28	30/32	0.72
Smoking	9	8	0.68

Bibliographic reference (Ref ID)	Wu et al 2011

Alcohol consumption	3	5	N/R
Gastric ulcer	8	9	N/R
Duodenal ulcer	12	22	N/R
Gastritis	34	27	N/R
Tet (sus/res)	24/1	30/0	0.46
Amo (sus/res)	25/0	30/0	N/R
Met (sus/res)	11/14	15/15	0.66

Intervention

Regimen: Quad (eso/bis/amo/tet)
Dose and timing: 7 days; eso (40 mg b.i.d) / bis (120 mg q.i.d) / amo (500 mg q.i.d) / tet (500 mg q.i.d)
Route: Oral

Comparator

Regimen: Quad (eso/bis/met/tet)
Dose and timing: 7 days; eso (40 mg b.i.d) / bis (120 mg q.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d)
Route: Oral

Length of follow up

Follow-up occurred 8 weeks following treatment

Outcomes measures and effect sizes

	Quad (eso/bis/amo/tet)				Quad (eso/bis/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	58	36	62	N/R	62	50	81	N/R	0.02
Eradication rate ITT tet susceptible	24	16	67	N/R	30	24	80	N/R	N/R

Bibliographic reference (Ref ID)	Wu et al 2011

Eradication rate ITT amo susceptible	25	16	64	N/R	N/A	N/A	N/A	N/A	N/A
Eradication rate ITT met susceptible	N/A	N/A	N/A	N/R	15	11	73	N/A	N/A
Eradication rate ITT met resistant	N/A	N/A	N/A	N/R	15	13	87	N/A	N/A
Adherence	58	56	97	N/R	62	60	97	N/R	1.0
Adverse events (diarrhoea/loose stools)	58	0	0	N/R	62	2	3.2	N/R	0.39
Adverse events (rash)	58	0	0	N/R	62	0	0	N/R	1.0

Source of funding	Kaohsiung Veterans General Hospital and Department of Health Taiwan
Comments	N/A

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Bibliographic reference (Ref ID)	Wu et al 2006
Study type	Randomised controlled trial
Location	Taiwan
Number	93
Characteristics of patients	Mean age (yr): 50 Number of males: 46 Inclusion criteria: *H pylori* positive after previous eradication attempt

Bibliographic reference (Ref ID)	Wu et al 2006
	Exclusion criteria: Ingestion of antibiotics, bismuth, PPI within 2 weeks of investigation, allergy to study medication, previous gastric surgery, coexistence of serious Dyspeptic condition types(s): Gastritis, gastric ulcer, duodenal ulcer Previous 1st line eradication regimen: PPI/AMO/CLA Lead-in treatment: None Lead-out treatment: None Concomitant treatment: None Baseline clinical patient characteristics:

	Quad (eso/bis/met/tet) N=46	Quad (eso/cla/met/tet) N=47	p
Age (yr) (mean)	49.9 + 13.5	51.7 + 12.8	0.50
Gender male/female	20/26	26/21	0.25
Smoking	12	9	0.42
Alcohol consumption	4	4	0.98
Gastric ulcer	5	4	N/R
Duodenal ulcer	20	19	N/R
Gastritis	21	24	N/R
Tet (sus/res)	23/0	21/0	N/R
Amo (sus/res)	13/10	9/12	0.37
Met (sus/res)	7/16	7/14	0.84

Intervention	Regimen: Quad (eso/bis/met/tet) Dose and timing: 7 days; eso (40 mg b.i.d) / bis (120 mg q.i.d) / met (500 mg q.i.d) / tet (500 mg q.i.d) Route: Oral
Comparator	Regimen: Quad (eso/cla/met/tet) Dose and timing: 7 days; eso (40 mg b.i.d) / cla (500 mg b.i.d) / met (250 mg q.i.d) / tet (500 mg q.i.d) Route: Oral

Bibliographic reference (Ref ID)	**Wu et al 2006**
Length of follow up	Follow-up occurred 8 weeks following treatment
Outcomes measures and effect sizes	

	Quad (eso/bis/met/tet)				Quad (eso/cla/met/tet)				
	N	k	Mean %	95% CI	N	k	Mean %	95% CI	p
Eradication rate ITT	46	34	74	N/R	47	36	77	N/R	0.76
Eradication rate ITT met susceptible	9	9	100	N/R	13	9	69	N/R	N/R
Eradication rate ITT cla susceptible	N/A	N/A	N/A	N/A	7	4	57	N/R	N/R
Eradication rate ITT cla res	N/A	N/A	N/A	N/A	16	12	75	N/R	N/R
Eradication rate ITT met resistant	12	8	67	N/R	10	7	70	N/R	N/R
Adherence	47	45	96	N/R	46	43	94	N/R	0.68
Adverse events (diarrhoea/loose stools)	47	1	2.1	N/R	46	4	6.3	N/R	0.20
Adverse events (rash)	47	0	0	N/R	47	2	4.3	N/R	0.87

Bibliographic reference (Ref ID)	Wu et al 2006
Source of funding	Kaohsiung Veteans General Hospital and National Science Council Taiwan
Comments	N/A

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49 D.6 Question 6

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Bibliographic reference (Ref ID)	**Anvari M, Allen C., Marshall J. et al. (2006) A randomized controlled trial of laparoscopic nissen fundoplication versus proton pump inhibitors for treatment of patients with chronic gastroesophageal reflux disease: One-year follow-up. Surgical Innovation 13 (4): 238-249 (#341)** **&** **Goeree R, Hopkins R., Marshall J.K. et al. (2011) Cost-utility of laparoscopic Nissen fundoplication versus proton pump inhibitors for chronic and controlled gastroesophageal reflux disease: a 3-year prospective randomized controlled trial and economic evaluation. Value in Health 14 (2): 263-273 (#40)**
Study type & aim	Blinded: No Crossover trial: No Multicentre: Not reported
Number and characteristics of patients	Gender: 55 Male and 49 Female Age range: 18 years and older Reflux confirmed): 24hr pH monitoring Exclusions: GERD score >18, Symptoms persisting for 1 year, Symptoms not expected to last 2 years, previous surgery, cancer within last 1 year (except basal cell cancer) Baseline characteristics:

	lap fundoplication			PPI medical management				
	N	K	MEAN	N	K	MEAN	Δ	*P*

Bibliographic reference (Ref ID)	**Anvari M, Allen C., Marshall J. et al. (2006) A randomized controlled trial of laparoscopic nissen fundoplication versus proton pump inhibitors for treatment of patients with chronic gastroesophageal reflux disease: One-year follow-up. Surgical Innovation 13 (4): 238-249 (#341)** **&** **Goeree R, Hopkins R., Marshall J.K. et al. (2011) Cost-utility of laparoscopic Nissen fundoplication versus proton pump inhibitors for chronic and controlled gastroesophageal reflux disease: a 3-year prospective randomized controlled trial and economic evaluation. Value in Health 14 (2): 263-273 (#40)**
	Demographics: Age mean (SD) 52 52 42.9 (N/R) 52 52 42.1 (SD N/R) 0.8 N/S GERSS off medication mean (SD) 52 52 29.6 (14.2) 52 52 31.0 (10.6) 1.4 N/S
Intervention(s)	Laparoscopic fundoplication: N: 52 (k = 51) Laporoscopic Nissen fundoplication with 2.5 to 3 cm 360 degree wrap PPI medication: N: 52 (k = 50) PPI medication as at baseline and adjusted to control symptoms using a standardised treatment algorithm
Concomitant treatments	Other medication allowed: not reported
Length of follow up	Outcomes on or off med? pH monitoring ON medication in PPI arm and OFF medication in Lap fundoplication arm If off washout period (d): Not reported. Follow-up: 12 months ,and 36 months
Location	Country: USA
Outcomes measures and effect sizes	lap fundoplication PPI medical N K MEAN/% N K MEAN/% Δ *P*

Bibliographic reference (Ref ID)	**Anvari M, Allen C., Marshall J. et al. (2006) A randomized controlled trial of laparoscopic nissen fundoplication versus proton pump inhibitors for treatment of patients with chronic gastroesophageal reflux disease: One-year follow-up. Surgical Innovation 13 (4): 238-249 (#341)** **&** **Goeree R, Hopkins R., Marshall J.K. et al. (2011) Cost-utility of laparoscopic Nissen fundoplication versus proton pump inhibitors for chronic and controlled gastroesophageal reflux disease: a 3-year prospective randomized controlled trial and economic evaluation. Value in Health 14 (2): 263-273 (#40)**

Symptoms VAS	Continuous	52		89.2 (SD 13.5)	52		73.5 (SD 19.7)	-15.6 (95% CI -23.7 to -8.0)	< 0.001
GERSS 12 months	Continuous	52		8.3 (SD 8.4)	52		13.6 (SD 9.5)	5.3 (95% CI 2.0 to 8.7)	= 0.0020
GERSS 60 months	Continuous	52			52			2.66 (95% CI -1.11 to 6.43)	= 0.1660
Mortality	Dichotomous	52	0		52	0		N/S	N/S
SF-36 General Health	Continuous	52		75.4 (SD 23.2	52		66.4 (SD 23.6).	-12.3 (95% CI -20.8 to -3.7)	= 0.0048
% time <pH 4	Continuous	52			52			3.63 (95% CI 1.15 to 6.120	= 0.0042
Dysphagia at 3 months	Dichotomous	50	4		51	0		OR 9.97 (95% CI 0.52 to 190.17)	= 0.1264

Authors' conclusion	No statistically significant differences in GORD symptom scores, but laparoscopic fundoplication resulted in fewer heartburn days, and improved QOL
Source of funding	Supported by Canadian institute of Health research and Ontario ministry of Health
Comments	Control arm medication regimen tightly managed making direct comparison to other studies difficult. No comparison of patient characteristics between study arms reported. Complications in assessment of outcomes made off medication for surgery and on medication in the control arm

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Bibliographic reference (Ref ID)	Galmiche JP, Hatlebakk J., Attwood S. et al. (2011) Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial. JAMA 305 (19): 1969-1977. (#52)
Study type & aim	Blinded: No Crossover trial: No Multicentre: Not reported
Number and characteristics of patients	Gender: 398 male 156 female. Age range: 18 years and older (mean 45 years) Reflux confirmed): with GORD clinical history, endoscopy, or pH monitoring positive. Exclusions: required who did not respond positively to PPI in 3 motnh run-in Baseline characteristics:

	lap fundoplication			PPI medical management				
	N	K	MEAN / %	N	K	MEAN / %	Δ	*P*
Demographics:								
Age mean (SD)	288	288	45.0 (10.9)	266	266	45.0 (11.5)	0.0	N/S
Severe heartburn	288	44	15%	266	48	18%	3%	N/S

Intervention(s)	Laparoscopic fundoplication: N: 288 Laparoscopic fundoplication (not otherwise described) PPI: N: 266 PPI esomeprazole 20mg/day adjusted up to 20mg / twice day
Concomitant treatments	Other medication allowed: not reported
Length of follow up	Outcomes on or off med? Not reported

Bibliographic reference (Ref ID)	Galmiche JP, Hatlebakk J., Attwood S. et al. (2011) Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial. JAMA 305 (19): 1969-1977. (#52)
	If off washout period (d): Not reported. Follow-up: 60 months
Location	Country:
Outcomes measures and effect sizes	

		lap fundoplication			PPI medical				
		N	K	MEAN /%	N	K	MEAN/%	Δ	*P*
Remission	Dichotomous	168	142	85%	181	167	92%		= 0.048*
Acid regurgitation (any grade)	Dichotomous	180	4	2%	191	25	13%		< 0.001 *
% time <pH 4	Continuous	N/R	N/R	0.7	N/R	N/R	1.9	N/R	N/R

* P value reported from study text based on log-rank comparison between groups.

Authors' conclusion	Trial demonstrated that contemporary anti-reflux therapy for GORD either drug acid suppression with esomeprazole or Laparoscopic anti reflux surgery most patient achieve remission at 5 years follow up.
Source of funding	Supported by manufacturer
Comments	Analysis undertaken on IIT but also per protocol and best and worst case scenarios. Notdesigned as a superiority or equivalence trial. At 5 years 23.1% of patients in the med arm were recieving increased dose esomeprazole. No crossover was permitted in protocol

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Bibliographic reference (Ref ID)	**Grant AM, Wileman S.M., Ramsay C.R. et al. (2008) Minimal access surgery compared with medical management for chronic gastro-oesophageal reflux disease: UK collaborative randomised trial. *BMJ* 337: a2664.(#200)** **&** **Grant AM (2012)**
Study type & aim	Blinded: No Crossover trial: No Multicentre: 21 sites
Number and characteristics of patients	Gender: 236 male 121 female. Age range: 18 years and older (mean 46 years) Reflux confirmed): long term PPI treatment of 1 year, endoscopic or 24 hr pH evidence of GORD or both. Exclusions: Barrett's oesophagus >3cm, evidence of dysplasia, hernia, or stricture, BMI >40 Baseline characteristics:

		Sevelamer			Calcium Acetate				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
Age	Continuous	179		46.7 (SD 10.3)	178		45.9 (SD 11.9)		N/S
Duration of medication - months (IQR)	Continuous	179		33 [15–83]	178		31 [16–71]		N/S

Intervention(s)	Laparoscopic fundoplication: N: 179 Laparoscopic Fundoplication (type at the discression of the surgeon) Drug: N: 178 'Best medical management' according to Geneva workshop including PPI- with option for surgery if clear indication developed.
Concomitant treatments	Other medication allowed: Not reported
Length of follow up	Outcomes on or off med?: Not reported If off washout period (d):

Bibliographic reference (Ref ID)	**Grant AM, Wileman S.M., Ramsay C.R. et al. (2008) Minimal access surgery compared with medical management for chronic gastro-oesophageal reflux disease: UK collaborative randomised trial. *BMJ* 337: a2664.(#200)** **&** **Grant AM (2012)**
	Follow-up: 60 months
Location	Country: UK

Outcomes measures and effect sizes

		lap fundoplication			PPI medical				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
REFLUX score 12 months (SD)	Continuous	179	179	84.6 (17.9)	178	178	73.4 (23.3)	18.3 (95% CI 13.8 to 22.9)	<0.001*
VAS scale 12 months (SD)	Continuous	179	179	74.3 (18.0)	178	178	75.9 (17.8)	N/R	N/R
EQ-5D score 12 months (SD)	Continuous	179	179	0.75 (0.25)	178	178	0.71 (0.27)	0.047 (95% CI -0.001 to 0.10) *	= 0.07 *
Visceral injury 12 months	Dichotomous	178	2		179	0		5.085 (95% CI 0.24 to 106.68)	= 0.295
REFLUX score 60 months (SD)	Continuous	179	179	86.7 (13.8)	178	178	80.7 (20.3)	6.4 (95% CI 1.6 to 11.2)	= 0.009 *
SF-36 score 60 months (SD)	Continuous	179	179	44.1 (10.3)	178	178	43.2 (11.5)	2.76 (95% CI 0.21 to 5.31) *	= 0.034 *
EQ-5D score 60 months (SD)	Continuous	179	179	0.77 (0.26)	178	178	0.76 (0.28)	0.047 (95% CI -0.01 to 0.11) *	= 0.126 *

* Mean difference and P value reported from study text with correction for baseline characteristics.

Bibliographic reference (Ref ID)	**Grant AM, Wileman S.M., Ramsay C.R. et al. (2008) Minimal access surgery compared with medical management for chronic gastro-oesophageal reflux disease: UK collaborative randomised trial. *BMJ* 337: a2664.(#200)** **&** **Grant AM (2012)**
Authors' conclusion	At 5 years follow up Laparoscopic fundoplciation continues to provide better GORD symptom relief, and improved health related QOL. Complications were uncommon.
Source of funding	Funded by NIHR HTA programme
Comments	Patients with strong preference for either arm were invited into a separate preference trail. All types of lap fundopication considered the same. 2% conversion to open surgery (across both randomised and open study). 21 centre UK study. High attrition rate in the Surgery arm. Surgery group were younger, more male, and had taken medication for longer than control group.

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Bibliographic reference (Ref ID)	**Mahon D, Rhodes M., Decadt B. et al. (2005) Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux. *British Journal of Surgery* 92 (6): 695-699 (#466)**
Study type & aim	Blinded: No Crossover trial: No Multicentre: 2 sites
Number and characteristics of patients	Gender: 149 Male and 38 female Age range: 18 years and older (mean 48 years) Reflux confirmed):. Patients with pathological reflux on endoscopy Exclusions: with symptoms of GORD for <6 months, not dependent on PPIs, BMI>35. Baseline characteristics:

		Sevelamer			Calcium Acetate				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
Age (IQR)	Continuous	109		48 (39 to 56)	108		47 (35 to 57)		N/S

Bibliographic reference (Ref ID)	**Mahon D, Rhodes M., Decadt B. et al. (2005) Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux. *British Journal of Surgery* 92 (6): 695-699 (#466)**									
	Duration of medication - months (IQR)	Continuous	109		30 (12 to 56)	108		24 (12 to 16)*		N/S
	Grade 3 or 5 oesophagitis	Dichotamous	109	22		108	15		1.52 Chi ^{2}	N/S
	* Figure for IQR maximum as reported in study manuscript.									
Intervention(s)	Laparoscopic fundoplication: N: 109 Laparoscopic fundoplication with 5 port entry creating a 3 cm wrap (proportion of circumference not reported) with division og short gastric vessels as necessary Drug: N: 108 PPI medication using rabeprazole 10mg, pantoprazole 20mg, lansoprazole 20g, omeprazole 20mg, or esopemprazole 20mg and adjusted to control symptoms.									
Concomitant treatments	Other medication allowed: Not reported									
Length of follow up	Outcomes on or off med?: Baseline measurements taken off medication. Follow up pH and manometry studies in the med group undertaken on medication. For Laparoscopic fundoplication not reported whether on or off any medication. If off washout period (d): 5 days Follow-up: 12 months									
Location	Country: UK									
Outcomes measures and effect sizes			lap fundoplication			PPI medical				
			N	K	MEAN/%	N	K	MEAN/%	Δ	*P*

Bibliographic reference (Ref ID)	**Mahon D, Rhodes M., Decadt B. et al. (2005) Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux. *British Journal of Surgery* 92 (6): 695-699 (#466)**								
	GI wellbeing score 12 months (SD)	Continuous	108	80	37.0 (5.4)	109	86	35.0 (7.3)	3.0 (95% CI 1.1 to 4.9)	= 0.003
	General wellbeing score 12 months (SD)	Continuous	108	79	106.2 (16.3)	109	86	100.4 (18.9)	7.1 (95% CI 2.5 to 11.7)	= 0.003
	Major intraoperative complication.	Dichotamous	109	4		108	0		9.26 (95% CI 0.49to 174.05)	= 0.137
	Dysphagia >3 months.	Dichotamous	109	5		108	0		11.42 (95% CI 0.62 to 209.14)	= 0.101
Authors' conclusion	Laparoscopic fundoplication leads to significantly less acid exposure at 3 months and significantly greater improvements in GI and general well being at 12 months compared to PPI treatment.									
Source of funding	Supported by manufacturer									
Comments	PPI medication considered a class effect in the study with no subgroup analysis. Two surgeons undertook all procedures.									

D.7 Question 8

Bibliographic reference (Ref ID)	Cooper,G.S., Kou,T.D., Chak,A.. Receipt of previous diagnoses and endoscopy and outcome from esophageal adenocarcinoma: a population-based study with temporal trends. American Journal of Gastroenterology 2009;104(6):1356-62. (#10399)
Study type & aim	Study type: Cohort study (retrospective)
Number and characteristics of patients	n = 2,754 with cancer (proportion with BO at baseline not reported) Gender: Male 80% Age: 78 years (mean) Barrett's Oesophagus defined as: N/R Exclusions: N/R Baseline characteristics: These characteristics relate to all patients with cancer for retrospective analysis:

Bibliographic reference (Ref ID)	Cooper,G.S., Kou,T.D., Chak,A.. Receipt of previous diagnoses and endoscopy and outcome from esophageal adenocarcinoma: a population-based study with temporal trends. American Journal of Gastroenterology 2009;104(6):1356-62. (#10399)

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	N/R	N/A

Prevalent cancer / HGD excluded up to 6 months?: Yes, patients analysed for factors relating to cancer stage and survival from 3 years to 6 months retrospectively.

Intervention(s)	Surveillance: Surveillance protocol not reported Initial frequency of recall (for BO with no dysplasia): N/R No Surveillance: N/R
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 6 months to 3 years (retrospective)
Location	Country: USA

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/ %	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous	N/R			N/A			N/R	N/R
100 patient year incidence of HDG	Dichotomous	N/R			N/A			N/R	N/R

Bibliographic reference (Ref ID)	Cooper,G.S., Kou,T.D., Chak,A.. Receipt of previous diagnoses and endoscopy and outcome from esophageal adenocarcinoma: a population-based study with temporal trends. American Journal of Gastroenterology 2009;104(6):1356-62. (#10399)						
	Mortality from cancer	Dichotomous	N/R		N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	N/R		N/A	N/A	N/A
	Independent predictor of early stage on presentation	Dichotomous	N/S				
	Independent predictor of Survival	Dichotomous	HR 0.45	(95% CI 0.25 to 0.80)			
	Factors included in multivariate analysis include: Site / centre, Age (5 year bands), sex, ethnicity, income , education, comorbidity, and year of diagnosis (year on year).						
Authors' conclusion	Despite the development of practice guidelines, we were unable to demonstrate any temporal increases in diagnostic frequency or endoscopic utilization, which highlights the challenges that clinicians face						
Source of funding	Supported by national grants, no COI						
Comments	Retrospective analysis. No detials provided of the denominator with BO at baseline and proportion that did not progress to cancer.						

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Bibliographic reference (Ref ID)	**Fitzgerald,R.C., Saeed,I.T., Khoo,D., Farthing,M.J., Burnham,W.R.. Rigorous surveillance protocol increases detection of curable cancers associated with Barrett's esophagus. Digestive Diseases & Sciences 2001;46(9):1892-98. (#7697)**
Study type & aim	Study type: Cohort study
Number and characteristics of patients	n = 204 (108 Surveillance, 96 No surveillance) Gender: Male 76% Age range: 64 years

Bibliographic reference (Ref ID)	Fitzgerald,R.C., Saeed,I.T., Khoo,D., Farthing,M.J., Burnham,W.R.. Rigorous surveillance protocol increases detection of curable cancers associated with Barrett's esophagus. Digestive Diseases & Sciences 2001;46(9):1892-98. (#7697)
	Barrett's Oesophagus defined as: Patients with endoscopically confirmed BO Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment		N/A
Degree of dysplasia (if any)	82% No, 13% Low, 3% High , 2% Cancer	N/A

Prevalent cancer / HGD excluded up to 6 months?: No – patients with cancer at baseline are included.

Intervention(s)	Surveillance: Surveillance protocol not reported Initial frequency of recall (for BO with no dysplasia): 1 year No Surveillance: Follow up of patients not in surveillance arm is not described
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 108 patient years for formal surveillance, 375 patient years for informal surveillance.
Location	Country: UK

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			1.85			0.00	N/R	N/R

Bibliographic reference (Ref ID)	Fitzgerald,R.C., Saeed,I.T., Khoo,D., Farthing,M.J., Burnham,W.R.. Rigorous surveillance protocol increases detection of curable cancers associated with Barrett's esophagus. Digestive Diseases & Sciences 2001;46(9):1892-98. (#7697)									
	100 patient year incidence of HDG	Dichotomous			2.78			0.27	N/R	N/R
	Mortality from cancer	Dichotomous	108	N/R		96	N.R		N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	108	2		96	0		N/A	N/A
Authors' conclusion	In conclusion, a rigorous biopsy protocol increases the detection of early cancer in Barrett's esophagus									
Source of funding	Lead author is national research counsel fellow									
Comments	'no surveillance' was not described,. It is unlikely to be true no surveillance, but patients followed up with ad hoc surveillance. Few outcomes were reported comparing the two groups.									

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Bibliographic reference (Ref ID)	Gladman,L., Chapman,W., Iqbal,T.H., Gearty,J.C., Cooper,B.T.. Barrett's oesophagus: an audit of surveillance over a 17-year period. European Journal of Gastroenterology & Hepatology 2006;18(3):271-76 (#7801)
Study type & aim	Study type: Cohort Study
Number and characteristics of patients	n = 343 (195 Surveillance, 148 No Surveillance) Gender: Age range: Barrett's Oesophagus defined as: Patients with BO but no Intestinal metaplasia Exclusions: Patients with severe concurrent illness (including cancer) were exluded from surveillance. Baseline characteristics: SURVEILLANCE NO SURVEILLANCE

Bibliographic reference (Ref ID)	Gladman,L., Chapman,W., Iqbal,T.H., Gearty,J.C., Cooper,B.T.. Barrett's oesophagus: an audit of surveillance over a 17-year period. European Journal of Gastroenterology & Hepatology 2006;18(3):271-76 (#7801)

	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/R
Degree of dysplasia (if any)	No dysplasia	No dysplasia

Prevalent cancer / HGD excluded up to 6 months?: Yes – up to 2 years.

Intervention(s)

Surveillance: Surveillance with 'multiple biopsies at 1 cm intervals
Initial frequency of recall (for BO with no dysplasia): mixed

No Surveillance: Endoscopy as required based on symptoms.

Concomitant treatments

Patients on PPI for GORD?: N/R

Length of follow up

Follow-up: 5.5 years

Location

Country: UK

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.37			N/R	N/R	N/R
100 patient year incidence of HDG	Dichotomous			0.19			N/R	N/R	N/R
Mortality from cancer	Dichotomous	195	N/R		148	N/R		N/R	N/R
Absolute number of patients developing cancer	Dichotomous	195	4		148	N/R		N/R	N/R

Bibliographic reference (Ref ID)	Gladman,L., Chapman,W., Iqbal,T.H., Gearty,J.C., Cooper,B.T.. Barrett's oesophagus: an audit of surveillance over a 17-year period. European Journal of Gastroenterology & Hepatology 2006;18(3):271-76 (#7801)
Authors' conclusion	The incidence of adenocarcinoma was low compared with many published series, and we speculate whether this is the result of maintenance PPI therapy
Source of funding	No conflicts of interest
Comments	Most endoscopies and biospies assessed by 1 person which suggests low variability. Incidence of cancer not reported between groups.

D.8 Question 8

Bibliographic reference (Ref ID)	Macdonald,C.E., Wicks,A.C., Playford,R.J.. Final results from 10 year cohort of patients undergoing surveillance for Barrett's oesophagus: observational study. BMJ 2000;321(7271):1252-55. (#8414)
Study type & aim	Study type: Cohort study
Number and characteristics of patients	n = 409 (143 surveillance, 266 No surveillance) Gender: 52% Male Age: 63 years Barrett's Oesophagus defined as: Patients with BO >3cm on endoscopy and biopsy detected columnar metaplasia Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A

Bibliographic reference (Ref ID)	Macdonald,C.E., Wicks,A.C., Playford,R.J.. Final results from 10 year cohort of patients undergoing surveillance for Barrett's oesophagus: observational study. BMJ 2000;321(7271):1252-55. (#8414)
	Degree of dysplasia (if any) N/R N/A Prevalent cancer / HGD excluded up to 6 months?: N/R
Intervention(s)	Surveillance: Biopsy from 4 quadrants and other areas showing abnormality. Endoscopies used to investigate deteriorating symptoms in patients in the surveillance group were excluded. Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: Endoscopy when symptoms suggest it
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.4 years
Location	Country: UK
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.79			N/R	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R			N/R	N/A	N/A
Mortality from cancer	Dichotomous	143	3		266	1		N/R	N/R
Absolute number of patients developing cancer	Dichotomous	143	5		266	N/R		N/A	N/A

Bibliographic reference (Ref ID)	**Macdonald,C.E., Wicks,A.C., Playford,R.J.. Final results from 10 year cohort of patients undergoing surveillance for Barrett's oesophagus: observational study. BMJ 2000;321(7271):1252-55. (#8414)**
	Rate of cancer incidence possible to calculate for surveillance cohort, but only cancer death available from no surveillance group.
Authors' conclusion	The current surveillance strategy has limited value, and it may be appropriate to restrict surveillance to patients with additional risk factors such as stricture, ulcer, or long segment (>80 mm) Barrett's oesophagus.
Source of funding	No conflicts of interest.
Comments	High attrition in the surveillance group. Mostly through death from other causes 20%, comorbidity 27%, age 32%, loss to follow up 11%, moving from area 10%. Patients excluded from surveillance were older and more likely to have comorbidity. If these patients are more likely to develop cancer then the incidence rate in the surveillance programme will appear artificially low

Bibliographic reference (Ref ID)	**Corley DA, Mehtani K, Quesenberry C, et al. Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus–Associated Esophageal Adenocarcinomas. Gastroenterology 2013; 145:312-319.**
Study type & aim	Study type: Case control study
Number and characteristics of patients	n = 139 (38 cases in surveillance, 101 controls in surveillance) Gender: Cases (89.5% male); controls (92.1% male) Age: Mean age: Cases = 73.5 years; controls = 73.8 years Barrett's Oesophagus defined as: The presence of visible endoscopic changes consistent with BO and the histologic presence of esophageal intestinal metaplasia. Exclusions: had only gastric-type metaplasia of the esophagus, had columnar metaplasia without intestinal metaplasia, lacked endoscopic changes indicating BO; or lacked an esophageal biopsy. Baseline characteristics:

	CASES IN SURVEILLANCE	CONTROLS IN SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN

Bibliographic reference (Ref ID)	**Corley DA, Mehtani K, Quesenberry C, et al. Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus–Associated Esophageal Adenocarcinomas. Gastroenterology 2013; 145:312-319.**
	Length of BO segment <3cm: 1 (2.6%) / 15 (14.9%) ≥3cm: 31 (81.6%) / 79 (78.2%) Not defined: 6 (15.8%) / 7 (6.9%) Degree of dysplasia (if any): N/R / N/R Prevalent cancer / HGD excluded up to 6 months?: N/A
Intervention(s)	Cases: People who were diagnosed with esophageal or gastroesophageal junction adenocarcinoma before September 2007; had a Barrett's esophagus diagnosis (as defined earlier) 6 months or more before their cancer diagnosis; and subsequently died of esophageal/gastroesophageal junction adenocarcinoma or its complications before December 31, 2009. Controls: People with a diagnosis of Barrett's esophagus (confirmed as described earlier) who did not die of esophageal or gastroesophageal junction adenocarcinoma through the end of the follow-up evaluation. Controls were matched to cases by age at Barrett's esophagus diagnosis, year of Barrett's esophagus diagnosis, medical center of Barrett's esophagus diagnosis, sex, and race.
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 14 years
Location	Country: USA
Outcomes measures and effect sizes	CASES IN SURVEILLANCE / CONTROLS IN SURVEILLANCE RISK OF DEATH FROM OESOPHAGEAL CANCER: N (%) / N (%) / ADJ OR (95%CI)

Bibliographic reference (Ref ID)	Corley DA, Mehtani K, Quesenberry C, et al. Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus–Associated Esophageal Adenocarcinomas. Gastroenterology 2013; 145:312-319.
	Adjusted for dysplasia status: 21 (55.3%) / 61 (60.4%) / 0.99 (0.36 to 2.75) Adjusted for dysplasia status and BO length: 21 (55.3%) / 61 (60.4%) / 1.14 (0.39 to 3.32)
Authors' conclusion	Endoscopic surveillance of Barrett's esophagus was not associated with any substantial decrease in the risk of death from esophageal adenocarcinoma, within a large, community-based population. The results cannot exclude a small to moderate benefit or a benefit from more intensive surveillance (eg, annual); however, many patients had cancer-related deaths and some were not able to be treated despite detection of early stage disease, a finding at least partially influenced by the risks, acceptability, and effectiveness of standard existing treatments.
Source of funding	No conflicts of interest.
Comments	This study had several limitations. It cannot exclude the possibility of a small to moderate benefit from surveillance; however, if present, the benefit would be much smaller than those incorporated into widely used cost-effectiveness analyses. Second, endoscopic surveillance performed in the community may not be performed optimally, even if it is performed at appropriate intervals.

Bibliographic reference (Ref ID)	Abela,J.E., Going,J.J., Mackenzie,J.F., McKernan,M., O'Mahoney,S., Stuart,R.C.. Systematic four-quadrant biopsy detects Barrett's dysplasia in more patients than nonsystematic biopsy. American Journal of Gastroenterology 2008;103(4):850-55. (#7020)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 180 Gender: 66% Male Age range: 64 years (mean) Barrett's Oesophagus defined as: Barrett's Oesophagus >3cm, with histology of intestinal metaplasia

Bibliographic reference (Ref ID)	**Abela,J.E., Going,J.J., Mackenzie,J.F., McKernan,M., O'Mahoney,S., Stuart,R.C.. Systematic four-quadrant biopsy detects Barrett's dysplasia in more patients than nonsystematic biopsy. American Journal of Gastroenterology 2008;103(4):850-55. (#7020)**
	Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	78% No, 19% LGD, 3% HGD	N/A

Prevalent cancer / HGD excluded up to 6 months?: N/R

Intervention(s)	Surveillance: quad biopsy every 2cm. All biopsies examined at minimum of 3 levels, at 1 lab, to Vienna classification Initial frequency of recall (for BO with no dysplasia): 1 year No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: not reported
Length of follow up	Follow-up: 3 years
Location	Country: UK

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	FREQ	N	K	FREQ	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.37	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			1.67	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Abela,J.E., Going,J.J., Mackenzie,J.F., McKernan,M., O'Mahoney,S., Stuart,R.C.. Systematic four-quadrant biopsy detects Barrett's dysplasia in more patients than nonsystematic biopsy. American Journal of Gastroenterology 2008;103(4):850-55. (#7020)**								
	Mortality from cancer	Dichotomous	180	0	N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	180	2	N/A	N/A	N/A	N/A	N/A
	Progression to high grade dysplasia or to cancer are not reported separately								
Authors' conclusion	Our data support the hypothesis that systematic four-quadrant biopsy is considerably more effective than nonsystematic biopsy sampling in detecting Barrett's dysplasia and early adenocarcinoma								
Source of funding	none – salaries paid by University								
Comments	Patients selected for systematic Quad biopsy or standard biopsy on consultant preference. Only Quad biopsy data are extracted here.								

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Bibliographic reference (Ref ID)	**Ajumobi,A., Bahjri,K., Jackson,C., Griffin,R.. Surveillance in Barrett's esophagus: an audit of practice. Digestive Diseases & Sciences 2010;55(6):1615-21. (#7045)**		
Study type & aim	Study type: Case series		
Number and characteristics of patients	n = 165 Gender: not reported Age: 65 years mean Barrett's Oesophagus defined as: patients with Barrett's Oesophagus – not otherwise described Exclusions: N/R Baseline characteristics:		
		SURVEILLANCE	NO SURVEILLANCE
		MEAN / MEDIAN	MEAN / MEDIAN
	Length of BO segment	N/R	N/A

Bibliographic reference (Ref ID)	Ajumobi,A., Bahjri,K., Jackson,C., Griffin,R.. Surveillance in Barrett's esophagus: an audit of practice. Digestive Diseases & Sciences 2010;55(6):1615-21. (#7045)
	Degree of dysplasia (if any) — No dysplasia 59%, LGD 38%, HGD 4%. — N/A Prevalent cancer / HGD excluded up to 6 months?
Intervention(s)	Surveillance: N/R Initial frequency of recall (for BO with no dysplasia): Frequency of recall not reported – analysis of variation from national recommended intervals was undertaken. No details given of treatment regimen while under surveillance No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.2 months
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/ %	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.00	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.0086	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	165	0		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	165	0		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Ajumobi,A., Bahjri,K., Jackson,C., Griffin,R.. Surveillance in Barrett's esophagus: an audit of practice. Digestive Diseases & Sciences 2010;55(6):1615-21. (#7045)**
Authors' conclusion	Veteran patients with Barrett's esophagus undergoing SE rarely progress to high-grade dysplasia or esophageal adenocarcinoma.
Source of funding	N/R
Comments	More patients in the study regressed to normal mucosa (11.5%) than progressed to HGD (3.6%) or Caner (0.0%). Of patients who missed recall by twice the recommended interval none progressed to HGD or cancer

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Bibliographic reference (Ref ID)	**Bani-Hani,K., Sue-Ling,H., Johnston,D., Axon,A.T., Martin,I.G.. Barrett's oesophagus: results from a 13-year surveillance programme. European Journal of Gastroenterology & Hepatology 2000;12(6):649-54.(#7146)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 357 Gender: 58% male Age: 65 years Barrett's Oesophagus defined as: Patients with columnar epithelium >3cm above gastro-oesophageal junction, or specialised type epithelium anywhere in oesophagus Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	6.1 cm (mean)	N/A
Degree of dysplasia (if any)	N/R	N/A

Prevalent cancer / HGD excluded up to 6 months?

Intervention(s)	Surveillance: No mandatory biopsy protocol used. Initial frequency of recall (for BO with no dysplasia): 1 year

Bibliographic reference (Ref ID)	**Bani-Hani,K., Sue-Ling,H., Johnston,D., Axon,A.T., Martin,I.G.. Barrett's oesophagus: results from a 13-year surveillance programme. European Journal of Gastroenterology & Hepatology 2000;12(6):649-54.(#7146)**
	No Surveillance: N/R
Concomitant treatments	Patients on PPI for GORD? N/R
Length of follow up	Follow-up: 3.8 years
Location	Country: UK
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.9	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	357	0		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	357	12		N/A	N/A	N/A	N/A	N/A

Authors' conclusion	Whilst the role of screening patients with Barrett's oesophagus remains controversial, this study supports the routine surveillance of male patients with specialized epithelium
Source of funding	N/R
Comments	No mandatory biopsy protocol used. 12 patients lost to follow up (no record available)

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Bibliographic reference (Ref ID)	**Conio,M., Blanchi,S., Lapertosa,G., Ferraris,R., Sablich,R., Marchi,S., et al. Long-term endoscopic surveillance of patients with Barrett's esophagus. Incidence of dysplasia and adenocarcinoma: a prospective study. American Journal of Gastroenterology 2003;98(9):1931-39. (#7428)**
Study type & aim	Study type: Case series
Number and	n = 166

Bibliographic reference (Ref ID)	**Conio,M., Blanchi,S., Lapertosa,G., Ferraris,R., Sablich,R., Marchi,S., et al. Long-term endoscopic surveillance of patients with Barrett's esophagus. Incidence of dysplasia and adenocarcinoma: a prospective study. American Journal of Gastroenterology 2003;98(9):1931-39. (#7428)**
characteristics of patients	Gender: 78% Male Age range: 60 years Barrett's Oesophagus defined as: Detectable upward displacement of the squamocolumnar junction at endoscopy, with intestinal metaplasia Exclusions: N/R Baseline characteristics: Prevalent cancer / HGD excluded up to 6 months?: N/R
Intervention(s)	Surveillance: Endoscopy with multiple biopsies Initial frequency of recall (for BO with no dysplasia): 2 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 5.5 years
Location	Country: Italy
Outcomes measures and effect sizes	

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	no dysplasia 90%, LGD 10%	N/A

Bibliographic reference (Ref ID)	**Conio,M., Blanchi,S., Lapertosa,G., Ferraris,R., Sablich,R., Marchi,S., et al. Long-term endoscopic surveillance of patients with Barrett's esophagus. Incidence of dysplasia and adenocarcinoma: a prospective study. American Journal of Gastroenterology 2003;98(9):1931-39. (#7428)**

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.54	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.33	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	166	0		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	166	5		N/A	N/A	N/A	N/A	N/A

Authors' conclusion	In our patient cohort, surveillance involved a large expenditure of effort but did not prevent any cancer deaths. The benefit of surveillance remains uncertain
Source of funding	N/R
Comments	Patients who missed some surveillance endoscopies were analysed separately as 'partially compliant'. 8/174 patients lost to follow up and excluded from analysis – no comparison made to completers

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Bibliographic reference (Ref ID)	**Cooper,S.C., El-agib,A., Dar,S., Mohammed,I., Nightingale,P., Murray,I.A., et al. Endoscopic surveillance for Barrett's oesophagus: the patients' perspective. European Journal of Gastroenterology & Hepatology 2009;21(8):850-54 (#7443)**
Study type & aim	Study type: Case series
Number and characteristics of	n = 151 Gender: 67% Male

Bibliographic reference (Ref ID)	**Cooper,S.C., El-agib,A., Dar,S., Mohammed,I., Nightingale,P., Murray,I.A., et al. Endoscopic surveillance for Barrett's oesophagus: the patients' perspective. European Journal of Gastroenterology & Hepatology 2009;21(8):850-54 (#7443)**
patients	Age: 66 years Barrett's Oesophagus defined as: Patients with red columnar lined oesophagus above the proximal margins of the upper folds, and intestinal metaplasia on biopsy. Exclusions: Exclusions not reported Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	90% no, 3% indefinite, 7% LGD, 0% HGD	N/A

Prevalent cancer / HGD excluded up to 6 months?: N/R

Intervention(s)	Surveillance:. Surveillance protocol not reported. Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: N/R
Location	Country: UK
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Cooper,S.C., El-agib,A., Dar,S., Mohammed,I., Nightingale,P., Murray,I.A., et al. Endoscopic surveillance for Barrett's oesophagus: the patients' perspective. European Journal of Gastroenterology & Hepatology 2009;21(8):850-54 (#7443)									
	100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
	Mortality from cancer	Dichotomous	151	N/R		N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	151	N/R		N/A	N/A	N/A	N/A	N/A
	Patient information	Categorical	Too little information 29% (43/151), no information 22% (33/151), desire for more information 85% (129/151)							
	Perception of benefit of surveillance	Categorical	Reduce risk of Oesophageal cancer 74% (109/151), completely negate risk 5% (7/151), greatly reduce risk 49% (72/151)							
	Hospital anxiety and depression (HAD) Anxiety	Conrinous	6.1 points (SD 4.2 points)							
	Hospital anxiety and depression (HAD) Depression	Continous	4.0 points (SD 3.5 points)							
	Trust in Physician score (TIPS) (11 to 55 points higher score better)	Continous	44 points (range 27 to 55 points)							
	SF-36	Continous	Pain 57.2 points, General perception of health 53.9 points, mental health 72.4 points, physical functioning 57.0 points, role limitations emotional 63.0, role limitations physical 50.9, social functioning 88.1, energy 53.1							
	All SF-36 domains were significantly lower in the BO surveillance patients than in an age, sex, and socio-economic adjusted general population cohort except for mental health									
Authors' conclusion	Patients undergoing endoscopic surveillance for BO suffer anxiety and have impaired quality of life									
Source of funding	No conflicts of interests									
Comments	Questionnaire completed at a time independent to surveillance appointments. Proximity to next endoscopy may have influenced scores. 71% of patients invited to take part agreed to. And 151/178 patients completed the questionnaire in full. 3 study sites. Comparison between responders and those who did not take part showed no significant difference in demographic or clinical									

Bibliographic reference (Ref ID)	Cooper,S.C., El-agib,A., Dar,S., Mohammed,I., Nightingale,P., Murray,I.A., et al. Endoscopic surveillance for Barrett's oesophagus: the patients' perspective. European Journal of Gastroenterology & Hepatology 2009;21(8):850-54 (#7443)
	characteristics. UK perspective.

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Bibliographic reference (Ref ID)	de Jonge,P.J., van,Blankenstein M., Looman,C.W., Casparie,M.K., Meijer,G.A., Kuipers,E.J.. Risk of malignant progression in patients with Barrett's oesophagus: a Dutch nationwide cohort study. Gut 2010;59(8):1030-36. (#7502)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 16,365 Gender: 63% Male Age range: 82 years Barrett's Oesophagus defined as: Histologically confirmed Barrett's Oesophagus with no dysplasia or low grade dysplasia at baseline. Exclusions: Previous surgery, or malignancy Baseline characteristics: SURVEILLANCE: MEAN / MEDIAN NO SURVEILLANCE: MEAN / MEDIAN Length of BO segment: N/R / N/A Degree of dysplasia (if any): None 90%, LGD 10% / N/A Prevalent cancer / HGD excluded up to 6 months?: Yes – up to 12 months
Intervention(s)	Surveillance; not defined Initial frequency of recall (for BO with no dysplasia): not defined – mean of 3 endoscopies per patient over 4.8 years follow up. Significantly more pfrequent if LGD at baseline No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?:

Bibliographic reference (Ref ID)	de Jonge,P.J., van,Blankenstein M., Looman,C.W., Casparie,M.K., Meijer,G.A., Kuipers,E.J.. Risk of malignant progression in patients with Barrett's oesophagus: a Dutch nationwide cohort study. Gut 2010;59(8):1030-36. (#7502)
Length of follow up	Follow-up: 4.8 years
Location	Country: Holland
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.65	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.0021*	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	16,365	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	16,365	505		N/A	N/A	N/A	N/A	N/A

* possibly analysis of patients that developed HGD but not cancer

Authors' conclusion	In this largest reported cohort of unselected patients with BO, the annual risk of OAC was 0.4%. Male sex, older age and LGD at diagnosis are independent predictors of malignant progression
Source of funding	One author is on executive board of the National registry
Comments	Cancer / HGD incidence rates of patients not in surveillance are not reported. Patients in Surveillance programme significantly younger than those not included p<0.001. Patients with LGD were significantly older than those with no dysplasia (p<0.001) Younger (p<0.001) and male (p<0.001) patients were more likely to be in 'surveillance' group Follow up frequency was significantly shorter for patients with LGD (mean 1.4 years) than those with no dysplasia (mean 2.0 years) (p<0.001) Patients with LGD were significantly older than those with no dysplasia.

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Bibliographic reference (Ref ID)	**Drewitz,D.J., Sampliner,R.E., Garewal,H.S.. The incidence of adenocarcinoma in Barrett's esophagus: a prospective study of 170 patients followed 4.8 years. American Journal of Gastroenterology 1997;92(2):212-15. (#7576)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 170 Gender: 98% Male Age: 62 years Barrett's Oesophagus defined as: Patients with columnar epithelium on endoscopy and metaplasia on biopsy specimen Exclusions: N/R Baseline characteristics: SURVEILLANCE / NO SURVEILLANCE MEAN / MEDIAN / MEAN / MEDIAN Length of BO segment: 5cm / N/A Degree of dysplasia (if any): N/R / N/A Prevalent cancer / HGD excluded up to 6 months?: Yes
Intervention(s)	Surveillance: Dual biopsy rather than quad biopsy undertaken which might reduce detection rate Initial frequency of recall (for BO with no dysplasia): 1 to 2 years (mix) No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.8 years
Location	Country: USA
Outcomes measures and effect sizes	SURVEILLANCE / NO SURVEILLANCE

Bibliographic reference (Ref ID)	**Drewitz,D.J., Sampliner,R.E., Garewal,H.S.. The incidence of adenocarcinoma in Barrett's esophagus: a prospective study of 170 patients followed 4.8 years. American Journal of Gastroenterology 1997;92(2):212-15. (#7576)**

		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.48	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	170	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	170	4		N/A	N/A	N/A	N/A	N/A

Authors' conclusion	The current series is larger and has a longer follow-up period than previous prospective trials and demonstrates a lower incidence of adenocarcinoma. Surveillance of patients with Barrett's esophagus for dysplasia remains an appropriate clinical practice
Source of funding	N/R
Comments	Patients encouraged to enter surveillance at their own preference

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Bibliographic reference (Ref ID)	**Ferraris,R., Bonelli,L., Conio,M., Fracchia,M., Lapertosa,G., Aste,H.. Incidence of Barrett's adenocarcinoma in an Italian population: an endoscopic surveillance programme. Gruppo Operativo per lo Studio delle Precancerosi Esofagee (GOSPE). European Journal of Gastroenterology & Hepatology 1997;9(9):881-85 (#7686)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 187 Gender: 74% Male Age range: 19-75 years Barrett's Oesophagus defined as: Patients with columnar epithelium on endoscopy and metaplasia on biopsy specimen Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE

Bibliographic reference (Ref ID)	**Ferraris,R., Bonelli,L., Conio,M., Fracchia,M., Lapertosa,G., Aste,H.. Incidence of Barrett's adenocarcinoma in an Italian population: an endoscopic surveillance programme. Gruppo Operativo per lo Studio delle Precancerosi Esofagee (GOSPE). European Journal of Gastroenterology & Hepatology 1997;9(9):881-85 (#7686)**
	MEAN / MEDIAN — MEAN / MEDIAN Length of BO segment: N/R — N/A Degree of dysplasia (if any): 97% no dysplasia / indefinite, 3% LGD, 0% HGD — N/A Prevalent cancer / HGD excluded up to 6 months?: Yes – 12 months
Intervention(s)	Surveillance: Quad biopsy every 2 cm Initial frequency of recall (for BO with no dysplasia): 1 year No Surveillance:
Concomitant treatments	Patients on PPI for GORD?: Some patients on H2RAs – earlier in the cohort
Length of follow up	Follow-up: 3 years
Location	Country: Italy
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.53	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.01*	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	187	N/R		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Ferraris,R., Bonelli,L., Conio,M., Fracchia,M., Lapertosa,G., Aste,H.. Incidence of Barrett's adenocarcinoma in an Italian population: an endoscopic surveillance programme. Gruppo Operativo per lo Studio delle Precancerosi Esofagee (GOSPE). European Journal of Gastroenterology & Hepatology 1997;9(9):881-85 (#7686)**
	Absolute number of patients developing cancer — Dichotomous — 187 — 3 — N/A — N/A — N/A — N/A — N/A * possibly analysis of patients that developed HGD but not cancer
Authors' conclusion	The present report shows that the incidence of adenocarcinoma in Italian Barrett's oesophagus patients is in the range of that reported from other Western countries
Source of funding	N/R
Comments	51.7% (187/344) eligible complied with follow up (no difference in dysplasia status between groups). Patients over 75 years were excluded from surveillance and hence this study

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Bibliographic reference (Ref ID)	**Fisher,D., Jeffreys,A., Bosworth,H., Wang,J., Lipscomb,J., Provenzale,D.. Quality of life in patients with Barrett's esophagus undergoing surveillance. American Journal of Gastroenterology 2002;97(9):2193-2000 (#7695)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 15 Gender: 100% Male Age range: 67 years (median) Barrett's Oesophagus defined as: Patients with BO on endoscopy and biopsy. Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A

Bibliographic reference (Ref ID)	Fisher,D., Jeffreys,A., Bosworth,H., Wang,J., Lipscomb,J., Provenzale,D.. Quality of life in patients with Barrett's esophagus undergoing surveillance. American Journal of Gastroenterology 2002;97(9):2193-2000 (#7695)
	Degree of dysplasia (if any) N/R N/A Prevalent cancer / HGD excluded up to 6 months?: N/R
Intervention(s)	Surveillance N/R Initial frequency of recall (for BO with no dysplasia): N/R No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: All on PPI
Length of follow up	Follow-up: N/A
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	15	N/R	N/R	N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	15	N/R	N/R	N/A	N/A	N/A	N/A	N/A
QUALRAD total score	Continuous	15	N/R	6.8 points*	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Fisher,D., Jeffreys,A., Bosworth,H., Wang,J., Lipscomb,J., Provenzale,D.. Quality of life in patients with Barrett's esophagus undergoing surveillance. American Journal of Gastroenterology 2002;97(9):2193-2000 (#7695)
	* For all 5 domains of QOLRAD scores were significantly higher in patients in surveillance than gender matched cohort having endoscopy for upper GI symptoms – data not reported
Authors' conclusion	This population of BE patients had significantly higher QOLRD scores than a previously published population referred for endoscopy
Source of funding	A number of authors supported by national grants
Comments	Higher QOLRAD score denotes better QOL (scale 0 to 7). QOLRAD score did not correlate well with utility rating score (p=0.71)

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Bibliographic reference (Ref ID)	Hillman,L.C., Chiragakis,L., Clarke,A.C., Kaushik,S.P., Kaye,G.L.. Barrett's esophagus: Macroscopic markers and the prediction of dysplasia and adenocarcinoma. Journal of Gastroenterology & Hepatology 2003;18(5):526-33. (#7650)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 353 Gender: 71 Male Age: 60 years Barrett's Oesophagus defined as: Patients with BO (not otherwise described) Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	No dysplasia 83% , LGD 16% , HGD 1%	N/A

Prevalent cancer / HGD excluded up to 6 months?: No - excluded up to 2 months

Intervention(s)	Surveillance: Quad biopsy every 2 cm. Two or more independent pathologists undertook assessment of biopsy samples

Bibliographic reference (Ref ID)	Hillman,L.C., Chiragakis,L., Clarke,A.C., Kaushik,S.P., Kaye,G.L.. Barrett's esophagus: Macroscopic markers and the prediction of dysplasia and adenocarcinoma. Journal of Gastroenterology & Hepatology 2003;18(5):526-33. (#7650)
	Initial frequency of recall (for BO with no dysplasia): 1 year (3 to 6 months if severe oesophagitis) No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: Not all patients on PPIs some on H2RAs
Length of follow up	Follow-up: 4.5 years
Location	Country: Australia
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.05	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.05	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	353	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	353	9		N/A	N/A	N/A	N/A	N/A

1/3 patients with HGD at baseline regressed to LGD, 28/56 patients with LGD regressed to no dysplasia.

Authors' conclusion	The presence of severe esophagitis, Barrett's ulcer, nodularity or stricture at entry indicates a high-risk group for Barrett's esophagus.
Source of funding	N/R
Comments	Follow up was changed from retrospective to prospective during the study period.

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Bibliographic reference (Ref ID)	**Horwhat,J.D., Baroni,D., Maydonovitch,C., Osgard,E., Ormseth,E., Rueda-Pedraza,E., et al. Normalization of intestinal metaplasia in the esophagus and esophagogastric junction: incidence and clinical data. American Journal of Gastroenterology 2007;102(3):497-506. (#7978)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 101 Gender: 73% Male Age: 65 years Barrett's Oesophagus defined as: Patients with short segment BO, long segment BO, or specialized intestinal mucosa at the gastro-oesophageal junction. Confirmed endoscopically and histologically. Exclusions: Patients with history of oesophageal carcinoma or contraindication to endoscopy Baseline characteristics: SURVEILLANCE: MEAN / MEDIAN NO SURVEILLANCE: MEAN / MEDIAN Length of BO segment: 43% short segment Barrett's, 25% Long segment Barrett's; N/A Degree of dysplasia (if any): 32% specialist intestinal mucosa at Gastro-oesophageal junction; N/A Prevalent cancer / HGD excluded up to 6 months?: N/R
Intervention(s)	Surveillance: Quad biopsies every 2cm Initial frequency of recall (for BO with no dysplasia): N/R No Surveillance:
Concomitant treatments	Patients on PPI for GORD?: Yes

Bibliographic reference (Ref ID)	**Horwhat,J.D., Baroni,D., Maydonovitch,C., Osgard,E., Ormseth,E., Rueda-Pedraza,E., et al. Normalization of intestinal metaplasia in the esophagus and esophagogastric junction: incidence and clinical data. American Journal of Gastroenterology 2007;102(3):497-506. (#7978)**
Length of follow up	Follow-up: 3.7 years
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.54	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	101	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	101	2		N/A	N/A	N/A	N/A	N/A

Regression occurred in 30% (13/44) of patients with short segment BO

Authors' conclusion	Surveillance of long segment BO results in the greatest yield for identifying dysplasia and cancer
Source of funding	No conflicts
Comments	Only 68% (101/148) of patients undergoing surveillance were available for analysis. Endoscopy undertaken off PPI

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Bibliographic reference (Ref ID)	**Hur,C., Wittenberg,E., Nishioka,N.S., Gazelle,G.S.. Patient preferences for the management of high-grade dysplasia in Barrett's esophagus. Digestive Diseases & Sciences 2005;50(1):116-25. (#8007)**
Study type & aim	Study type: Case series
Number and	n = 20

Bibliographic reference (Ref ID)	Hur,C., Wittenberg,E., Nishioka,N.S., Gazelle,G.S.. Patient preferences for the management of high-grade dysplasia in Barrett's esophagus. Digestive Diseases & Sciences 2005;50(1):116-25. (#8007)
characteristics of patients	Gender: 55% Male Age: 65 years Barrett's Oesophagus defined as: Patients with BO confirmed on biopsy having an endoscopy or clinic visit, and asked to image that they had HGD Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment		N/A
Degree of dysplasia (if any)	90% none, 10% LGD (although asked to imagine they had HGD)	N/A

Prevalent cancer / HGD excluded up to 6 months?: N/R – not applicable

Intervention(s)	Surveillance: N/R – imagined surveillance scenario Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: N/R
Location	Country: USA
Outcomes measures and effect sizes	

Bibliographic reference (Ref ID)	Hur,C., Wittenberg,E., Nishioka,N.S., Gazelle,G.S.. Patient preferences for the management of high-grade dysplasia in Barrett's esophagus. Digestive Diseases & Sciences 2005;50(1):116-25. (#8007)									
			SURVEILLANCE			NO SURVEILLANCE				
			N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
	100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
	100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
	Mortality from cancer	Dichotomous	20	N/R		N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	20	N/R		N/A	N/A	N/A	N/A	N/A
	Preference for treatment of HGD Surveillance / oesophagectomy / PDT (0 to 100 scale – higher better)	Dichotomous	20		Surveillance 79.3 points (range 50 to 100), oesophagectomy 46.0 points (5 to 100), PDT 59.5 points (10 to 90)*					
	*Significantly more patients chose Surveillance 70% (14/20) , than oesophagectomy 15% (3/20) , and PDT 15% (3/20) (p=0.0024) two tailed Chi-square.									
Authors' conclusion	In summary, when patients with Barrett's esophagus were presented with three options to manage HGD, the majority chose endoscopic surveillance									
Source of funding	N/R									
Comments	Treatment scenarios (outcomes) presented to patients are open to debate – relating to cure and complications. No surveillance was									

Bibliographic reference (Ref ID)	Hur,C., Wittenberg,E., Nishioka,N.S., Gazelle,G.S.. Patient preferences for the management of high-grade dysplasia in Barrett's esophagus. Digestive Diseases & Sciences 2005;50(1):116-25. (#8007)
	not presented as an option (although unlikely in the situation where HGD diagnosed). Order of presenting scenarios might have affected preference. One interviewer undertook all sessions with patients

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Bibliographic reference (Ref ID)	Katz,D., Rothstein,R., Schned,A., Dunn,J., Seaver,K., Antonioli,D.. The development of dysplasia and adenocarcinoma during endoscopic surveillance of Barrett's esophagus. American Journal of Gastroenterology 1998;93(4):536-41. (#8138)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 102 Gender: 83% Male Age: 63 years Barrett's Oesophagus defined as: patients with endoscopic appearance of BO >3cm and specialized epithelium on at least 1 biopsy specimen. Exclusions: Patients with previous resection for cancer, current cancer or HGD were excluded. Baseline characteristics: SURVEILLANCE: MEAN / MEDIAN NO SURVEILLANCE: MEAN / MEDIAN Length of BO segment: N/A Degree of dysplasia (if any): Mixed no dysplasia / HGD; N/A Prevalent cancer / HGD excluded up to 6 months?: Patients with HGD at baseline were excluded
Intervention(s)	Surveillance Pathologists undertaking follow up biopsy review were blind to original diagnosis, and confirmed by 2 pathologists. Initial frequency of recall (for BO with no dysplasia): N/R No Surveillance:
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.8 years

Bibliographic reference (Ref ID)	**Katz,D., Rothstein,R., Schned,A., Dunn,J., Seaver,K., Antonioli,D.. The development of dysplasia and adenocarcinoma during endoscopic surveillance of Barrett's esophagus. American Journal of Gastroenterology 1998;93(4):536-41. (#8138)**
Location	Country: Holland
Outcomes measures and effect sizes	

		SURVEILLANCE BASELINE			SURVEILLANCE FOLLOW UP				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.36	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.71	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	102	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	102	2		N/A	N/A	N/A	N/A	N/A

Authors' conclusion	Our results suggest that surveillance endoscopy can be safely deferred for at least 2 yr following an initial biopsy that is negative or indeterminate for dysplasia
Source of funding	Lead author supported by fellowship from national institution and funding from university.
Comments	Method of biopsy changed during study period, with systematic quad biopsy sampling used later in the cohort (post 1983). 1/102 patients lost to follow up.

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Bibliographic reference (Ref ID)	**Kruijshaar,M.E., Kerkhof,M., Siersema,P.D., Steyerberg,E.W., Homs,M.Y., Essink-Bot,M.L., CYBAR Study Group. The burden of upper gastrointestinal endoscopy in patients with Barrett's esophagus. Endoscopy 2006;38(9):873-78 (#8221)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 192 Gender: 66% Male

Bibliographic reference (Ref ID)	**Kruijshaar,M.E., Kerkhof,M., Siersema,P.D., Steyerberg,E.W., Homs,M.Y., Essink-Bot,M.L., CYBAR Study Group. The burden of upper gastrointestinal endoscopy in patients with Barrett's esophagus. Endoscopy 2006;38(9):873-78 (#8221)**
	Age: 62 years Barrett's Oesophagus defined as: Patients with BO of 2cm or more, with pathology confirmed intestinal metaplasia. Exclusions: Patients with HGD or cancer at baseline were excluded. Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	78% no, 22% Low	N/A

Prevalent cancer / HGD excluded up to 6 months?:

Intervention(s)	Surveillance: endoscopy technique not reported, sedation not used in all patients Initial frequency of recall (for BO with no dysplasia): N/R No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 1 month
Location	Country: Holland
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Kruijshaar,M.E., Kerkhof,M., Siersema,P.D., Steyerberg,E.W., Homs,M.Y., Essink-Bot,M.L., CYBAR Study Group. The burden of upper gastrointestinal endoscopy in patients with Barrett's esophagus. Endoscopy 2006;38(9):873-78 (#8221)**									
	100 patient year incidence of HDG	Dichotomous		N/R	N/A	N/A	N/A	N/A	N/A	
	Mortality from cancer	Dichotomous	192	N/R	N/A	N/A	N/A	N/A	N/A	
	Absolute number of patients developing cancer	Dichotomous	192	N/R	N/A	N/A	N/A	N/A	N/A	
	HAD anxiety (0 to 21 lower scores better) 1 wk	Continous	102	From 6.0 (5.3 to 6.8) to 5.3 (4.6 to 6.0)				0.7	0.02	
	HAD depression (0 to 21 lower scores better) 1 wk	Continous	102	From 2.9 (2.5 to 3.2) to 2.4 (2.0 to 2.8)				0.5	<0.01	
	Anxiety scores before endoscopy (6.0 points) were significantly higher (worse) than in the general population (3.9 points) (p<0.0001)									
Authors' conclusion	Upper gastrointestinal endoscopy is burdensome for many patients with Barrett's esophagus and causes moderate distress. Perception of a high risk of adenocarcinoma may increase distress and the burden experienced from the procedure									
Source of funding	None									
Comments	3 centre study. Follow up was at 1 week and 1 month. 84% of patients had undergone a previous endoscopy. Not all outcomes described are reported in the results section, possible selective reporting. Throat ache was significantly higher following endoscopy 47% than at baseline 12% (p<0.01).									

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Bibliographic reference (Ref ID)	**Levine,D.S., Blount,P.L., Rudolph,R.E., Reid,B.J.. Safety of a systematic endoscopic biopsy protocol in patients with Barrett's esophagus. American Journal of Gastroenterology 2000;95(5):1152-57. (#8326)**
Study type & aim	Study type: Case series
Number and characteristics of	n = 705 Gender: N/R

Bibliographic reference (Ref ID)	**Levine,D.S., Blount,P.L., Rudolph,R.E., Reid,B.J.. Safety of a systematic endoscopic biopsy protocol in patients with Barrett's esophagus. American Journal of Gastroenterology 2000;95(5):1152-57. (#8326)**
patients	Age range: N/R Barrett's Oesophagus defined as: Patients with GORD or Barrett's oesophagus. Mixture of screening and surveillance patients, not all had BO at baseline Exclusions: Patients in whom endoscopy were contraindicated or who had limited life expectance were excluded. Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	N/R	N/A

Prevalent cancer / HGD excluded up to 6 months?:

Intervention(s)	Surveillance: Up to 10 samples for endoscopically visible lesion, and quad biopsies every 2 cm (or 1 cm is high grade dysplasia). Jumbo forceps used for sampling biopsies Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: N/R
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Levine,D.S., Blount,P.L., Rudolph,R.E., Reid,B.J.. Safety of a systematic endoscopic biopsy protocol in patients with Barrett's esophagus. American Journal of Gastroenterology 2000;95(5):1152-57. (#8326)										
	100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A	
	Mortality from cancer	Dichotomous	705	0		N/A	N/A	N/A	N/A	N/A	
	Absolute number of patients developing cancer	Dichotomous	N/R	N/R		N/A	N/A	N/A	N/A	N/A	
	Adverse event	Dichotomous	705	5		N/A	N/A	N/A	N/A	N/A	
	*Rate of adverse events calculated patient not per biopsy. 18 adverse events in 11 patients Adverse events that required hospitalisation were included in this analysis for event rate. Both bleeding events involved procedures with stricture										
Authors' conclusion	A rigorous, systematic endoscopic biopsy protocol in patients with Barrett's esophagus does not produce esophageal perforation or bleeding when performed by an experienced team of physicians, nurses, and technicians										
Source of funding	Supported by a national grant										
Comments	Patients pre-selected for suitability for endoscopy at baseline.										

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Bibliographic reference (Ref ID)	Murphy,S.J., Dickey,W., Hughes,D., O'Connor,F.A.. Surveillance for Barrett's oesophagus: results from a programme in Northern Ireland. European Journal of Gastroenterology & Hepatology 2005;17(10):1029-35 (#8559)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 178 Gender: 71% Male Age: 57 years Barrett's Oesophagus defined as: Patients with BO defined as columnar epithelium of any length and specialized intestinal metaplasia on biopsy.. Exclusions: Patients with significant comorbidity or unsuitability for oesophagectomy were excluded

Bibliographic reference (Ref ID)	**Murphy,S.J., Dickey,W., Hughes,D., O'Connor,F.A.. Surveillance for Barrett's oesophagus: results from a programme in Northern Ireland. European Journal of Gastroenterology & Hepatology 2005;17(10):1029-35 (#8559)**
	Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	63% No, 18% indefinite, 19% Low	N/A

Prevalent cancer / HGD excluded up to 6 months?: Yes. Patients with cancer at baseline or at up to 6 months FU were excluded as prevalent cancer

Intervention(s)	Surveillance: multiple samples taken from Barrett's segment and additional biopsies of suspicious areas Initial frequency of recall (for BO with no dysplasia): Mixed, 1 year at start of cohort then 2 years from 2001 No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 3.4 years
Location	Country: UK

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.49	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.98	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Murphy,S.J., Dickey,W., Hughes,D., O'Connor,F.A.. Surveillance for Barrett's oesophagus: results from a programme in Northern Ireland. European Journal of Gastroenterology & Hepatology 2005;17(10):1029-35 (#8559)								
	Mortality from cancer	Dichotomous	178	N/R	N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	178	3	N/A	N/A	N/A	N/A	N/A
Authors' conclusion	The incidence of adenocarcinoma in patients in Northern Ireland was similar to the incidence reported by other large institutions. Clinical benefit is suggested but is not certain from these data, because of biases that affect surveillance programmes. Large multicentre studies are required to determine whether surveillance is beneficial								
Source of funding	No conflicts on interest								
Comments	No standard biopsy protocol used, multiple samples taken from Barrett's segment and additional biopsies of suspicious areas								

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Bibliographic reference (Ref ID)	Nilsson,J., Skobe,V., Johansson,J., Willen,R., Johnsson,F.. Screening for oesophageal adenocarcinoma: an evaluation of a surveillance program for columnar metaplasia of the oesophagus. Scandinavian Journal of Gastroenterology 2000;35(1):10-16. (#8591)		
Study type & aim	Study type: Case series		
Number and characteristics of patients	n = 199 Gender: 70% Male Age range: 59 years Barrett's Oesophagus defined as: Patients with specialized columnar epithelium, or gastric type metaplasia. Endoscopic and biopsy confirmation. Exclusions: N/R Baseline characteristics:		
		SURVEILLANCE	NO SURVEILLANCE
		MEAN / MEDIAN	MEAN / MEDIAN

Bibliographic reference (Ref ID)	Nilsson,J., Skobe,V., Johansson,J., Willen,R., Johnsson,F.. Screening for oesophageal adenocarcinoma: an evaluation of a surveillance program for columnar metaplasia of the oesophagus. Scandinavian Journal of Gastroenterology 2000;35(1):10-16. (#8591)
	Length of BO segment: 67% 134/199 patients had long segment BO (>3cm). N/A Degree of dysplasia (if any): No dysplasia or LGD 100%. 68% patients with specialized columnar epithelium N/A Prevalent cancer / HGD excluded up to 6 months?: Yes
Intervention(s)	Surveillance: Not described. 6 or 8 biopsies per endoscopy. Initial frequency of recall (for BO with no dysplasia): Mixed, 6 months to 2 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.0 years
Location	Country: Sweden

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.63	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	199	N/R		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Nilsson,J., Skobe,V., Johansson,J., Willen,R., Johnsson,F.. Screening for oesophageal adenocarcinoma: an evaluation of a surveillance program for columnar metaplasia of the oesophagus. Scandinavian Journal of Gastroenterology 2000;35(1):10-16. (#8591)**
	Absolute number of patients developing cancer — Dichotomous — 199 — 5 — N/A — N/A — N/A — N/A — N/A HGD and cancer lumped for analysis of incidence. 1 in 159 patient years (95% CI 1 in 67 to 1 in 500).
Authors' conclusion	Low cancer incidence, high costs, and the doubtful prognosis for the patients with identified cancer question the benefits and cost-effectiveness of cancer screening among patients with columnar metaplasia in the oesophagus
Source of funding	N/R
Comments	All endoscopies performed by experienced endoscopists with >1000 endoscopies performed. 6 to 8 biopsies taken at each endoscopy

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Bibliographic reference (Ref ID)	**O'Connor,J.B., Falk,G.W., Richter,J.E.. The incidence of adenocarcinoma and dysplasia in Barrett's esophagus: report on the Cleveland Clinic Barrett's Esophagus Registry. American Journal of Gastroenterology 1999;94(8):2037-42. (#8613)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 136 Gender: 67% Male Age: 58 years Barrett's Oesophagus defined as: Patients with Barrett's Oesophagus with endoscopic and biopsy confirmation Exclusions: N/R Baseline characteristics: SURVEILLANCE — NO SURVEILLANCE MEAN / MEDIAN — MEAN / MEDIAN Length of BO segment — N/A

Bibliographic reference (Ref ID)	O'Connor,J.B., Falk,G.W., Richter,J.E.. The incidence of adenocarcinoma and dysplasia in Barrett's esophagus: report on the Cleveland Clinic Barrett's Esophagus Registry. American Journal of Gastroenterology 1999;94(8):2037-42. (#8613)
	Degree of dysplasia (if any) 92% No dysplasia, 7% LGD, 1% HGD N/A Prevalent cancer / HGD excluded up to 6 months?: Yes. Patients with <1 yr FU were excluded to avoid misclassification of prevalent dyplasia or cancer
Intervention(s)	Surveillance: Quad biopsy every 2 cm Initial frequency of recall (for BO with no dysplasia): 2 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: Patients treated with either H2RA or PPI
Length of follow up	Follow-up: 4.2 years
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.35	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.70	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	136	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	136	2		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	O'Connor,J.B., Falk,G.W., Richter,J.E.. The incidence of adenocarcinoma and dysplasia in Barrett's esophagus: report on the Cleveland Clinic Barrett's Esophagus Registry. American Journal of Gastroenterology 1999;94(8):2037-42. (#8613)
	9/136 patients lost to follow up none of whom had developed dysplasia
Authors' conclusion	The incidence of adenocarcinoma in Barrett's esophagus is lower than initially thought. However, large multicenter studies are required to clarify the epidemiological and clinical factors related to the development of dysplasia and adenocarcinoma in Barrett's esophagus
Source of funding	N/R
Comments	Patients treated with either H2RA or PPI – cancer incidence rate might be higher on PPI if acid suppression not so complete.

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Bibliographic reference (Ref ID)	Oberg,S., Johansson,J., Wenner,J., Johnsson,F., Zilling,T., von Holstein,C.S., et al. Endoscopic surveillance of columnar-lined esophagus: frequency of intestinal metaplasia detection and impact of antireflux surgery. Annals of Surgery 2001;234(5):619-26 (#8626)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 177 Gender: 76 Male Age range: 57 years Barrett's Oesophagus defined as: Patients with specialized columnar epithelium. Endoscopic and biopsy confirmation Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	67% 134/199 patients had long segment BO (>3cm).	N/A
Degree of dysplasia (if any)	No dysplasia or LGD 100%.	N/A

Bibliographic reference (Ref ID)	**Oberg,S., Johansson,J., Wenner,J., Johnsson,F., Zilling,T., von Holstein,C.S., et al. Endoscopic surveillance of columnar-lined esophagus: frequency of intestinal metaplasia detection and impact of antireflux surgery. Annals of Surgery 2001;234(5):619-26 (#8626)**
	Prevalent cancer / HGD excluded up to 6 months?: Yes
Intervention(s)	Surveillance: Quad biopsy every 2 cm. 6 to 8 biopsies taken at each endoscopy Initial frequency of recall (for BO with no dysplasia): Mixed, 6 months to 2 years No Surveillance:
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 5.1 years
Location	Country: Sweden
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	177	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	177	N/R		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Oberg,S., Johansson,J., Wenner,J., Johnsson,F., Zilling,T., von Holstein,C.S., et al. Endoscopic surveillance of columnar-lined esophagus: frequency of intestinal metaplasia detection and impact of antireflux surgery. Annals of Surgery 2001;234(5):619-26 (#8626)
	51% (35/69) of patients with no metaplasia at baseline developed it over the 5.5 year follow up
Authors' conclusion	Biopsy samples from a single endoscopy, despite an adequate biopsy protocol, are insufficient to rule out the presence of intestinal metaplasia. Patients in whom biopsy specimens from a segment of CLE show no intestinal metaplasia have a significant risk of having undetected intestinal metaplasia or of developing intestinal metaplasia with time.
Source of funding	N/R
Comments	As many as 143 of the patients reported here are also included in Nilsson (2000) within this review

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Bibliographic reference (Ref ID)	Olithselvan,A., Gorard,D.A., McIntyre,A.S.. A surveillance programme for Barrett's oesophagus in a UK general hospital. European Journal of Gastroenterology & Hepatology 2007;19(4):305-09. (#8653)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 121 Gender: 70% Male Age: 60 years Barrett's Oesophagus defined as: Patients with visible columnar lined mucosa >cm with histological confirmation. Exclusions: Patients over 75, with comorbidity, or condition that would limit oesophagectomy were excluded Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	N/R	N/A

Bibliographic reference (Ref ID)	Olithselvan,A., Gorard,D.A., McIntyre,A.S.. A surveillance programme for Barrett's oesophagus in a UK general hospital. European Journal of Gastroenterology & Hepatology 2007;19(4):305-09. (#8653)
	Grade of dysplasia not reported but study reports that it was not intending to study progression of LGD Prevalent cancer / HGD excluded up to 6 months?: No. results at index endoscopy were excluded from analysis of incidence
Intervention(s)	Surveillance: Quad biopsy every 2 to 4 cm Initial frequency of recall (for BO with no dysplasia): 2 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 3.5 years
Location	Country: UK
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.47	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			1.18	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	121	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	121	2		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Olithselvan,A., Gorard,D.A., McIntyre,A.S.. A surveillance programme for Barrett's oesophagus in a UK general hospital. European Journal of Gastroenterology & Hepatology 2007;19(4):305-09. (#8653)
Authors' conclusion	This surveillance programme for classical Barrett's oesophagus was effective with six cancers being detected early and treated
Source of funding	N/R
Comments	79/121 (65%) of patients available at final follow up

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Bibliographic reference (Ref ID)	Ramus,J.R., Gatenby,P.A., Caygill,C.P., Winslet,M.C., Watson,A.. Surveillance of Barrett's columnar-lined oesophagus in the UK: endoscopic intervals and frequency of detection of dysplasia. European Journal of Gastroenterology & Hepatology 2009;21(6):636-41. (#8832)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 817 Gender: 64% Male Age: 61 years Barrett's Oesophagus defined as: Patients with BO, not otherwise described Exclusions: Patients with only 1 follow up endoscopy were excluded from analysis. Patients that were excluded from surveillance were significantly older than those included (p<0.001) Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	91% No dysplasia, 7% LGD, 2% HGD	N/A

Prevalent cancer / HGD excluded up to 6 months?:

Intervention(s)	Surveillance: Not described. Only 7.6% of patients had quad biopsies during endoscopy Initial frequency of recall (for BO with no dysplasia): Mix – separate analysis for each period / frequency

Bibliographic reference (Ref ID)	**Ramus,J.R., Gatenby,P.A., Caygill,C.P., Winslet,M.C., Watson,A.. Surveillance of Barrett's columnar-lined oesophagus in the UK: endoscopic intervals and frequency of detection of dysplasia. European Journal of Gastroenterology & Hepatology 2009;21(6):636-41. (#8832)**
	No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?:
Length of follow up	Follow-up: 4.8 years
Location	Country: UK
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.21	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.53	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	817	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	817	13		N/A	N/A	N/A	N/A	N/A

Authors' conclusion	A variation in surveillance practice for CLO was observed throughout the UK. A large proportion of dysplastic disease is detected on specific surveillance endoscopies.
Source of funding	Supported by charity / trust / foundation
Comments	Male patients were significantly younger than female patients (p=0.016). 6 centre study. Separate analysis for different recall frequencies. No relationship found between detection of cancer and frequency if surveillance for HGC (p=0.299). Cancer incidence rate calculated for only cancers detected during surveillance endoscopy, not for those detected at additional endoscopy for

Bibliographic reference (Ref ID)	Ramus,J.R., Gatenby,P.A., Caygill,C.P., Winslet,M.C., Watson,A.. Surveillance of Barrett's columnar-lined oesophagus in the UK: endoscopic intervals and frequency of detection of dysplasia. European Journal of Gastroenterology & Hepatology 2009;21(6):636-41. (#8832)
	symptoms.. 6 centre study. Separate analysis for different recall frequencies

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Bibliographic reference (Ref ID)	Schnell,T.G., Sontag,S.J., Chejfec,G., Aranha,G., Metz,A., O'Connell,S., et al. Long-term nonsurgical management of Barrett's esophagus with high-grade dysplasia. Gastroenterology 2001;120(7):1607-19. (#9034)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 1099 Gender: N/R Age range: N/R Barrett's Oesophagus defined as: Patients with BO not otherwise described Exclusions: N/R Baseline characteristics: SURVEILLANCE: MEAN / MEDIAN NO SURVEILLANCE: MEAN / MEDIAN Length of BO segment: N/R / N/A Degree of dysplasia (if any): 22% No, 71% LGD, 7% HGD / N/A Prevalent cancer / HGD excluded up to 6 months?:
Intervention(s)	Surveillance: Circumferential quad biopsy not used in all patients . 2 endoscopists undertook all procedures, and 1 pathologist examined all specimens with endoscopist Initial frequency of recall (for BO with no dysplasia): Mixed. Recall period varied during the study No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: No. Patients earlier in the cohort were prescribed H2RAs

Bibliographic reference (Ref ID)	Schnell,T.G., Sontag,S.J., Chejfec,G., Aranha,G., Metz,A., O'Connell,S., et al. Long-term nonsurgical management of Barrett's esophagus with high-grade dysplasia. Gastroenterology 2001;120(7):1607-19. (#9034)
Length of follow up	Follow-up: 7.3 years
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.15	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.56	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	1099	1		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	1099	12		N/A	N/A	N/A	N/A	N/A

Length of BO segment at baseline was associated with incidence of cancer on multivariate analysis HR 1.38 (1.06 to 1.81).

Authors' conclusion	HGD without cancer in Barrett's esophagus follows a relatively benign course in the majority of patients. In the patients who eventually progress to cancer during regular surveillance, surgical resection is curative. Surveillance endoscopies with biopsy is a valid and safe follow-up strategy for Barrett's patients who have HGD without cancer
Source of funding	N/R
Comments	None

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Bibliographic reference (Ref ID)	**Schoenfeld,P., Johnston,M., Piorkowski,M., Jones,D.M., Eloubeidi,M., Provenzale,D.. Effectiveness and patient satisfaction with nurse-directed treatment of Barrett's esophagus. American Journal of Gastroenterology 1998;93(6):906-10. (#9038)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 123 Gender: 79% Male Age : 55 years Barrett's Oesophagus defined as: Patients with short or long segment BO, candidates for oesophagectomy or PDT, <80 years, no HGD or cancer at baseline Exclusions: N/R Baseline characteristics: SURVEILLANCE / NO SURVEILLANCE MEAN / MEDIAN / MEAN / MEDIAN Length of BO segment: N/R / N/A Degree of dysplasia (if any): N/R / N/A Prevalent cancer / HGD excluded up to 6 months?: No. Patients with HGD or cancer at index endoscopy were excluded from analysis
Intervention(s)	Surveillance Type of endoscopy and biopsy protocol not reported. Initial frequency of recall (for BO with no dysplasia): 2 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: PPIs used as a 2nd line treatment
Length of follow up	Follow-up: 4.0 years
Location	Country: USA
Outcomes measures	

Bibliographic reference (Ref ID)	**Schoenfeld,P., Johnston,M., Piorkowski,M., Jones,D.M., Eloubeidi,M., Provenzale,D.. Effectiveness and patient satisfaction with nurse-directed treatment of Barrett's esophagus. American Journal of Gastroenterology 1998;93(6):906-10. (#9038)**
and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.00	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.40	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	123	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	123	0		N/A	N/A	N/A	N/A	N/A
Adverse events	Dichotomous	123	0						

Authors' conclusion	The registered nurse in our clinical setting effectively administered clinical practice guidelines for the management of Barrett's esophagus without clinically significant morbidity or patient dissatisfaction
Source of funding	N/R
Comments	Patients treated by a specialty trained registered nurse.

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Bibliographic reference (Ref ID)	**Sikkema,M., Looman,C.W., Steyerberg,E.W., Kerkhof,M., Kastelein,F., van,Dekken H., et al. Predictors for neoplastic progression in patients with Barrett's Esophagus: a prospective cohort study. American Journal of Gastroenterology 2011;106(7):1231-38 (#9133)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 713 Gender: 74% Male Age: 61 years

Bibliographic reference (Ref ID)	**Sikkema,M., Looman,C.W., Steyerberg,E.W., Kerkhof,M., Kastelein,F., van,Dekken H., et al. Predictors for neoplastic progression in patients with Barrett's Esophagus: a prospective cohort study. American Journal of Gastroenterology 2011;106(7):1231-38 (#9133)**
	Barrett's Oesophagus defined as: Patients with BO >2cm at baseline with biopsy confirmation of no dysplasia or LGD. Exclusions: Patients with previous history of HGD or cancer were excluded. Baseline characteristics: SURVEILLANCE: MEAN / MEDIAN NO SURVEILLANCE: MEAN / MEDIAN Length of BO segment: N/R / N/A Degree of dysplasia (if any): 84% No, 16% LGD / N/A Prevalent cancer / HGD excluded up to 6 months?: Yes. HGD or cancer found within 6 months of index endoscopy were considered to be prevalent
Intervention(s)	Surveillance: Endoscopy protocol not surprised. Biopsy samples assessed by local pathologist and confirmed by investigating pathologists blinded to initial results. Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 3.5 years
Location	Country: Holland
Outcomes measures and effect sizes	SURVEILLANCE: N / K / MEAN/% NO SURVEILLANCE: N / K / MEAN/% Δ *P*

Bibliographic reference (Ref ID)	**Sikkema,M., Looman,C.W., Steyerberg,E.W., Kerkhof,M., Kastelein,F., van,Dekken H., et al. Predictors for neoplastic progression in patients with Barrett's Esophagus: a prospective cohort study. American Journal of Gastroenterology 2011;106(7):1231-38 (#9133)**
	100 patient year incidence of cancer — Dichotomous — N/R — N/A N/A N/A N/A N/A 100 patient year incidence of HDG — Dichotomous — 1.03 — N/A N/A N/A N/A N/A Mortality from cancer — Dichotomous — 713 N/R — N/A N/A N/A N/A N/A Absolute number of patients developing cancer — Dichotomous — 713 N/R — N/A N/A N/A N/A N/A HGD incidence rate calculated is for both HGD plus Cancer – not reported seperately. Author was contacted for data – no reponse.
Authors' conclusion	In patients with BE, the risk of developing HGD or EAC is predominantly determined by the presence of LGD, a known duration of BE of >=10 years, longer length of BE, and presence of esophagitis. One or combinations of these risk factors are able to identify patients with a low or high risk of neoplastic progression and could therefore be used to individualize surveillance intervals in BE
Source of funding	National grant , no conflicts of interest
Comments	LGD was an independent predictor of progression to HGD or cancer on multivariate analysis RR 9.7 (95% CI 4.4 to 21.5), other factors were oesophagitis RR 3.5, BO for >10 years at baseline RR 3.2, and longer length of BO RR 1.11 per cm

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Bibliographic reference (Ref ID)	**Streitz,J.M.,Jr., Ellis,F.H.,Jr., Tilden,R.L., Erickson,R.V.. Endoscopic surveillance of Barrett's esophagus: a cost-effectiveness comparison with mammographic surveillance for breast cancer. American Journal of Gastroenterology 1998;93(6):911-15 (#9242)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 136 Gender: N/R Age range: N/R

Bibliographic reference (Ref ID)	**Streitz,J.M.,Jr., Ellis,F.H.,Jr., Tilden,R.L., Erickson,R.V.. Endoscopic surveillance of Barrett's esophagus: a cost-effectiveness comparison with mammographic surveillance for breast cancer. American Journal of Gastroenterology 1998;93(6):911-15 (#9242)**
	Barrett's Oesophagus defined as: Patients with BO, not otherwise defined. Exclusions: N/R Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	Mixed	N/A

Prevalent cancer / HGD excluded up to 6 months?:

Intervention(s)	Surveillance: No details of endoscopy protocol but possibly not quad biopsy in the earlier cases at least Initial frequency of recall (for BO with no dysplasia): No details of endoscopy protocol or recall frequency. No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 3.8 years
Location	Country: USA

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			1.37	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Streitz,J.M.,Jr., Ellis,F.H.,Jr., Tilden,R.L., Erickson,R.V.. Endoscopic surveillance of Barrett's esophagus: a cost-effectiveness comparison with mammographic surveillance for breast cancer. American Journal of Gastroenterology 1998;93(6):911-15 (#9242)**									
	100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
	Mortality from cancer	Dichotomous	136	1		N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	136	7		N/A	N/A	N/A	N/A	N/A
	Adverse events	Dichotomous	136	0		N/A	N/A	N/A	N/A	N/A
	Of 7 cancers detected three stage o, two stage I and two stage IIA									
Authors' conclusion	Endoscopic surveillance of patients with Barrett's esophagus compares favorably with the common practice of surveillance mammography to detect early breast cancer									
Source of funding	N/R									
Comments	Costs and incidence compared to that for breast cancer surveillance									

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Bibliographic reference (Ref ID)	**Switzer-Taylor,V., Schlup,M., Lubcke,R., Livingstone,V., Schultz,M.. Barrett's esophagus: a retrospective analysis of 13 years surveillance. Journal of Gastroenterology & Hepatology 2008;23(9):1362-67. (#9260)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 212 Gender: 69% Male Age: 57 years Barrett's Oesophagus defined as: Patients with long segment (>3cm) BO with histological finding of columnar epithelium with intestinal metaplasia. Exclusions: Patients were excluded if thought to be unsuitable for oesophagectomy if required. Baseline characteristics:

Bibliographic reference (Ref ID)	Switzer-Taylor,V., Schlup,M., Lubcke,R., Livingstone,V., Schultz,M.. Barrett's esophagus: a retrospective analysis of 13 years surveillance. Journal of Gastroenterology & Hepatology 2008;23(9):1362-67. (#9260)

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment		N/A
Degree of dysplasia (if any)	70% no (dysplasia), 15% LGD, 3% HGD	N/A

Patients excluded from surveillance programme were significantly older than those included (p<0.05)

Prevalent cancer / HGD excluded up to 6 months?: N/R

Intervention(s)	Surveillance : Quad biopsy every 2 cm and multiple samples from areas of macroscopic abnormality. All endoscopies performed or supervised by an experienced gastroenterologist. Initial frequency of recall (for BO with no dysplasia): 3 years No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 4.0 years
Location	Country: New Zealand

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			1.00 (95% CI 0.45 to 1.9)	N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	Switzer-Taylor,V., Schlup,M., Lubcke,R., Livingstone,V., Schultz,M.. Barrett's esophagus: a retrospective analysis of 13 years surveillance. Journal of Gastroenterology & Hepatology 2008;23(9):1362-67. (#9260)									
	100 patient year incidence of HDG	Dichotomous			N/R	N/A	N/A	N/A	N/A	N/A
	Mortality from cancer	Dichotomous	212	2		N/A	N/A	N/A	N/A	N/A
	Absolute number of patients developing cancer	Dichotomous	212	9		N/A	N/A	N/A	N/A	N/A
Authors' conclusion	During 13 years of Barrett's surveillance, 88% of all adenocarcinoma occurred in a subset of only 11% patients. To stratify surveillance for Barrett's esophagus, programs could focus on male patients with dysplasia or ulcerations on index endoscopy									
Source of funding	Supported by local grant									
Comments	Patients were excluded if thought to be unsuitable for oesophagectomy if required									

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Bibliographic reference (Ref ID)	Wani,S., Falk,G., Hall,M., Gaddam,S., Wang,A., Gupta,N., et al. Patients with nondysplastic Barrett's esophagus have low risks for developing dysplasia or esophageal adenocarcinoma. Clinical Gastroenterology & Hepatology 2011;9(3):220-27 (#9465)
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 1204 Gender: 88% Male Age range: 59 years Barrett's Oesophagus defined as: Patients with presence of columnar lined mucosa in the distal oesophagus of any length, and intestinal metaplasia documented on histology. Exclusions: Patients with any dysplasia at baseline, and patients with no metaplasia on histology were excluded Baseline characteristics: SURVEILLANCE NO SURVEILLANCE

Bibliographic reference (Ref ID)	**Wani,S., Falk,G., Hall,M., Gaddam,S., Wang,A., Gupta,N., et al. Patients with nondysplastic Barrett's esophagus have low risks for developing dysplasia or esophageal adenocarcinoma. Clinical Gastroenterology & Hepatology 2011;9(3):220-27 (#9465)**

	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	N/R	N/A
Degree of dysplasia (if any)	100% No dysplasia	N/A

Prevalent cancer / HGD excluded up to 6 months?: Yes. Patients with HGD or cancer at up to 1 year FU were excluded as prevalent cases

Intervention(s)	Surveillance: Quad biopsy every 2 cm with standard or jumbo forceps Initial frequency of recall (for BO with no dysplasia): Mixed No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: N/R
Length of follow up	Follow-up: 5 years
Location	Country: USA

Outcomes measures and effect sizes

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.27	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.48	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	1204	N/R		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Wani,S., Falk,G., Hall,M., Gaddam,S., Wang,A., Gupta,N., et al. Patients with nondysplastic Barrett's esophagus have low risks for developing dysplasia or esophageal adenocarcinoma. Clinical Gastroenterology & Hepatology 2011;9(3):220-27 (#9465)**
	Absolute number of patients developing cancer Dichotomous 1204 18 N/A N/A N/A N/A N/A Mean time to development of cancer 5.29 (SD 3.83). No difference in progression to HGD or Cancer in Males of females. Patients with BO segment >6 cm had significantly higher cancer incidence rate 0.65 (95% CI 0.33 to 1.25) Vs 0.09
Authors' conclusion	There is a lower incidence of dysplasia and EAC among patients with NDBE than previously reported. Because most patients are cancer free after a long-term follow-up period, surveillance intervals might be lengthened, especially for patients with shorter segments of BE
Source of funding	Support from manufacturer. No conflict of interest.
Comments	5 centre study. All biopsies were reviewed by 2nd pathologist.

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Bibliographic reference (Ref ID)	**Weston,A.P., Sharma,P., Mathur,S., Banerjee,S., Jafri,A.K., Cherian,R., et al. Risk stratification of Barrett's esophagus: updated prospective multivariate analysis. American Journal of Gastroenterology 2004;99(9):1657-66 (#9495)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 324 Gender: 99% Male Age: 62 years Barrett's Oesophagus defined as: Patients with BO confirmed histologically. Exclusions: Patients with no biopsy follow up, follow up < 3 months, cancer or multi focal HGD within 3 months were excluded Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	Length of BO 3.7 cm	N/A

Bibliographic reference (Ref ID)	Weston,A.P., Sharma,P., Mathur,S., Banerjee,S., Jafri,A.K., Cherian,R., et al. Risk stratification of Barrett's esophagus: updated prospective multivariate analysis. American Journal of Gastroenterology 2004;99(9):1657-66 (#9495)
	Degree of dysplasia (if any) 77% no, 18% LGD, 5% HGD. N/A Prevalent cancer / HGD excluded up to 6 months?: No. Patients with Cancer or HGD within 3 months of FU were excluded
Intervention(s)	Surveillance:. All cancer biopsy samples were confirmed by a second pathologist. Quad biopsy ever 2cm or less and target biopsies of suspicious areas, using jumbo forceps. Initial frequency of recall (for BO with no dysplasia): 1 year No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: Not all patients were on PPIs
Length of follow up	Follow-up: 3.2 years
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			2.03	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.68	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	324	N/R		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	324	21		N/A	N/A	N/A	N/A	N/A

Bibliographic reference (Ref ID)	**Weston,A.P., Sharma,P., Mathur,S., Banerjee,S., Jafri,A.K., Cherian,R., et al. Risk stratification of Barrett's esophagus: updated prospective multivariate analysis. American Journal of Gastroenterology 2004;99(9):1657-66 (#9495)**
	Study end point of 'cancer' included a very conservative definition for cancer including patients with HGD and dysplasia related lesion or mass, and HGD in which intramucosal cancer couldn't be ruled out
Authors' conclusion	Endoscopic and histologic features of BE at initial diagnosis are predictive of index HGD and cancer as well as with risk of BE progression
Source of funding	Supported by national grant
Comments	324/550 patients were included in surveillance.

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Bibliographic reference (Ref ID)	**Wong,T., Tian,J., Nagar,A.B.. Barrett's surveillance identifies patients with early esophageal adenocarcinoma. American Journal of Medicine 2010;123(5):462-67 (#9535)**
Study type & aim	Study type: Case series
Number and characteristics of patients	n = 248 Gender: N/R – mostly Male – veterans affairs study Age: 63 years Barrett's Oesophagus defined as: Patients with specialised intestinal metaplasia above the gastro-oesophageal junction.. Exclusions: Patients over 80 years, or unfit for surgery were excluded Baseline characteristics:

	SURVEILLANCE	NO SURVEILLANCE
	MEAN / MEDIAN	MEAN / MEDIAN
Length of BO segment	63% <3cm, 37% >3cm.	N/A
Degree of dysplasia (if any)	100% no dysplasia	N/A

Prevalent cancer / HGD excluded up to 6 months?:

Intervention(s)	Surveillance:. Quad biopsy every 3 cms

Bibliographic reference (Ref ID)	**Wong,T., Tian,J., Nagar,A.B.. Barrett's surveillance identifies patients with early esophageal adenocarcinoma. American Journal of Medicine 2010;123(5):462-67 (#9535)**
	Initial frequency of recall (for BO with no dysplasia): 3 years, 72% of patients received surveillance endoscopy at recommended No Surveillance: N/A
Concomitant treatments	Patients on PPI for GORD?: Not all patients on PPIs some on H2RAs
Length of follow up	Follow-up: 4.0 years
Location	Country: USA
Outcomes measures and effect sizes	

		SURVEILLANCE			NO SURVEILLANCE				
		N	K	MEAN/%	N	K	MEAN/%	Δ	*P*
100 patient year incidence of cancer	Dichotomous			0.51	N/A	N/A	N/A	N/A	N/A
100 patient year incidence of HDG	Dichotomous			0.41	N/A	N/A	N/A	N/A	N/A
Mortality from cancer	Dichotomous	248	0		N/A	N/A	N/A	N/A	N/A
Absolute number of patients developing cancer	Dichotomous	248	5		N/A	N/A	N/A	N/A	N/A

Of 5 cancers detected in the surveillance group, four stage I and one stage II. Of 46 other cancers detected at same site three stage I, eight stage II, 34 stages III / IV

Authors' conclusion	Patients with Barrett's esophagus undergoing endoscopic surveillance benefit from early-stage cancer diagnosis. Progression to adenocarcinoma is low, but long-segment and high-grade dysplasias have an increased risk of cancer
Source of funding	No conflicts of interest
Comments	Patients in the surveillance cohort were compared to patients at the same centre with new on set cancer, but it is not clear whether these patients had BO at baseline, or what the total denominator was. Therefore study treated as a case series.

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