Appendix 2: Evidence Tables

I. On demand PPI vs Continuous PPI for maintenance therapy of reflux esophagitis and gastroesophageal reflux disease?[1]

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**On demand PPI**	**Continuous PPI**	**Relative (95% CI)**	**Absolute**		
Lack of Symptom Control [1–5]												
5[2,3]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	140/859 (16.3%)	73/794 (9.2%)	RR 1.71 (1.31 to 2.21)	7% (3 to 11%)	⊕⊕OO LOW	
Pill Use (tablets/week) (Better indicated by lower values) [1,2,5]												
3[6]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	571	581	-	MD 3.79 lower (4.73 to 2.84 lower)	⊕⊕⊕O MODERATE	
Satisfaction (unwilling to continue or inadequate relief) [1–5]												
5	randomised trials	serious[9]	no serious inconsistency	serious[10]	serious[11]	none	136/859 (15.8%)	70/794 (8.8%)	RR 1.82 (1.26 to 2.65)	7% (2 to 14%)	⊕OOO VERY LOW	

[1] Four studies used maintenance dose PPI on-demand (pantoprazole 20 mg/rabeprazole 10 mg/esomeprazole 20mg) while one study used healing dose PPI on-demand (pantoprazole 40 mg)

[2] Four studies did not report endoscopic findings

[3] Lack of symptom control defined as inadequate symptom relief or treatment failure (return of symptom(s) of at least moderate severity or symptoms incompatible with well-being)

[4] No low risk of bias trials (all studies with high risk of detection bias, three of five with high risk of attrition bias)

[5] 95% CI wide and close to line of no effect

[6] Studies used maintenance dose PPI on-demand (pantoprazole 20mg/rabeprazole 10 mg/esomeprazole 20mg)
[7] No low risk of bias trials (all three studies at high risk of detection and attrition bias)
[8] Statistically significant heterogeneity but not clinically important as all trials showed strong statistically significant benefit
[9] No low risk of bias trials (four studies at high risk of attrition and reporting bias)
[10] Evidence indirect as poor methods of satisfaction used (willingness to continue or "inadequate relief")
[11] 95% CI wide and close to line of no effect (for willingness to continue the result was not statistically significant)

II. Maintenance dose PPI vs Healing dose PPI for maintenance therapy of reflux oesophagitis and gastroesophageal reflux disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Maintenance dose PPI**	**Healing dose PPI**	**Relative (95% CI)**	**Absolute**		
Oesophagitis relapse (endoscopic findings) [6–11]												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	228/916 (24.9%)	186/1191 (15.6%)	RR 1.54 (1.25 to 1.89)	8% (4 to 14%)	⊕⊕⊕O MODERATE	
Symptom relapse [6–10]												
5[3,4]	randomised trials	serious[1]	serious[5]	no serious indirectness	no serious imprecision	none	343/810 (42.3%)	470/1102 (42.6%)	RR 1.16 (0.93 to 1.44)	7% (-3 to 19%)	⊕⊕OO LOW	[3,4]

[1] No low risk of bias trials (most trials had unclear risk of bias)
[2] 95% CI narrow and in favour of healing dose PPI, close to line of no effect
[3] Studies did not measure patient satisfaction
[4] Symptom relapse defined as return of symptom(s) of at least moderate severity(enough to interfere with normal activity) for three to seven consecutive days in five studies and return of symptom(s) of any severity in one study
[5] Statistically significant heterogeneity that was unexplained

III. H2 receptor antagonist vs Healing dose PPI for maintenance therapy of reflux esophagitis and gastroesophageal reflux disease[1]

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**H2 receptor antagonist**	**Healing dose PPI**	**Relative (95% CI)**	**Absolute**		
Esophagitis relapse (endoscopic findings) [7,12,13]												
3	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	121/242 (50%)	36/242 (14.9%)	RR 3.52 (1.8 to 6.87)	37% (12 to 87%)	⊕⊕⊕O MODERATE	
Symptom relapse [7,12,13]												
3[4,5]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision[6]	none	91/232 (39.2%)	49/236 (20.8%)	RR 1.92 (1.44 to 2.58)	19% (9 to 33%))	⊕⊕⊕O MODERATE	

[1] H2RA likely to increase pill burden as typically dosed twice daily

[2] No low risk of bias trials (most studies had unclear risk of bias)

[3] Statistically significant heterogeneity but not clinically important as all trials showed strong statistically significant benefit of standard dose PPI

[4] Studies did not measure patient satisfaction

[5] Symptom relapse defined as return of symptom(s) of at least moderate severity in two studies and at least mild severity in one study

[6] 95% CI narrow and in favour of healing dose PPI

IV. Abrupt discontinuation of PPI vs. continuation of PPI for maintenance therapy of reflux esophagitis and gastroesophageal reflux disease

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Deprescribing**	**Continued Use**	**Relative (95% CI)**	**Absolute**		
Lack of Symptom Control - Symptom Relapse Rate [14]												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	38/56 (67.9%)	11/49 (22.4%)	RR 3.02 (1.74 to 5.24)	453 more per 1000 (from 166 more to 952 more)	⊕OOO VERY LOW	
								22.5%		454 more per 1000 (from 167 more to 954 more)		
Adverse Drug Withdrawal Events (ADWE) - Relapse (Endoscopic Findings) [14]												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	39/56 (69.6%)	10/49 (20.4%)	RR 3.41 (1.91 to 6.09)	492 more per 1000 (from 186 more to 1000 more)	⊕OOO VERY LOW	
								20.4%		492 more per 1000 (from 186 more to 1000 more)		

[1] Concerns surrounding attrition bias and blinding

[2] 95% CI wide, number of participants and events small

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