Appendix Table 2. Detailed Summary of Meta-analyses Performed for the Consensus Conference

<table>
<thead>
<tr>
<th>Statement</th>
<th>Trials</th>
<th>Treatment</th>
<th>N</th>
<th>Justification for the statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>A6: Prokinetic agents should not be used routinely before endoscopy to increase the diagnostic yield</td>
<td>5 RCTs (21)</td>
<td>• Erythromycin</td>
<td>19</td>
<td>Prokinetic compared to placebo or no treatment</td>
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<tr>
<td></td>
<td></td>
<td>• No treatment</td>
<td>22</td>
<td>1) Main Outcome: Need for repeat endoscopy: OR=0.51 (95%CI 0.30; 0.88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carbonell 2006 (61)</td>
<td>Erythromycin</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Placebo</td>
<td>50</td>
<td>Duration of hospital stay: MD=-1.04 (95%CI -2.83; 0.76)</td>
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<tr>
<td></td>
<td></td>
<td>Frossard 2002 (62)</td>
<td>Erythromycin</td>
<td>51</td>
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<td></td>
<td></td>
<td>• Placebo</td>
<td>54</td>
<td>Comments: There exists heterogeneity in study populations: Some trials included patients admitted to intensive care because of bleeding, others not. Some trials included patients with hematemesis or bloody naso-gastric aspirate, while others included patients with clinical evidence of active hemorrhage and/or acute anemia requiring active resuscitation.</td>
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<tr>
<td></td>
<td></td>
<td>Habashi 2007 (abstract) (63)</td>
<td>Erythromycin or Metoclopramide</td>
<td>15</td>
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<td></td>
<td></td>
<td>• Placebo</td>
<td>15</td>
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<td></td>
<td></td>
<td>Sussman 2008 (abstract) (64)</td>
<td>Metoclopramide</td>
<td>13</td>
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<td></td>
<td></td>
<td>• No treatment</td>
<td>13</td>
<td></td>
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<tr>
<td>A8: Pre-endoscopic, proton pump inhibitor therapy may be considered to downstage the endoscopic lesion and decrease the need for endoscopic intervention, but should not delay endoscopy</td>
<td>6 RCTs (22)</td>
<td>• IV OME 80 mg bolus + 8 mg/h CI until endoscopy</td>
<td>314</td>
<td>Pre-endoscopic PPI compared to treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Placebo</td>
<td>317</td>
<td>1) Main outcome: Rebleeding: OR 0.81 (95%CI 0.62,1.06)</td>
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<tr>
<td></td>
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<td>2) Secondary outcomes: Mortality: OR 1.12 (95%CI 0.75,1.68)</td>
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<td></td>
<td>Surgery: OR 0.92 (95% CI 0.66, 1.29)</td>
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<td>Patients exhibiting high-risk stigmata of recent hemorrhage at the time of endoscopy: OR 0.67 (95% CI 0.54, 0.84)</td>
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<td>Need for endoscopic therapy: OR 0.68 (95%CI 0.50, 0.93)</td>
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<td>Comments: The statement was recommended (“do it”) based on cost-effectiveness studies with an attempt to better define a subgroup of patients at greater likelihood of having a high-risk lesion may optimize the cost-effectiveness of this approach, such as patients presenting with hematemesis.</td>
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<td>(95%CI 0.28, 1.81)</td>
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<td></td>
<td></td>
<td>Surgery: OR 1.16 (95%CI 0.39, 3.51)</td>
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<td></td>
<td>Mortality: OR 0.70 (95%CI 0.14, 3.57)</td>
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<td>Comments: A recommendation of “do it” because early endoscopy (&lt;24 hours) was adopted based on previously noted improvements in secondary outcome measures (15), however without the need for a more urgent timing of the endoscopy. It was noted that endoscopy may need to be delayed or deferred in selected high-risk patients (e.g., very elevated INR, active acute coronary syndrome, suspected perforation (38))</td>
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<td>(95%CI 0.14, 3.57)</td>
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<tr>
<td>B3: Early endoscopy (within 24 hours of presentation) is recommended in most patients with acute upper gastrointestinal bleeding</td>
<td>3 RCTs</td>
<td>• EGD within 6 h</td>
<td>47</td>
<td>Urgent endoscopy (1-12 hours) compared with later endoscopy (&gt;12 h to 48 h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EGD within 48 h</td>
<td>46</td>
<td>1) Main outcome:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lin 1996 (84)</td>
<td>EGD &lt; 12 h</td>
<td>162</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EGD &gt; 12 h</td>
<td>163</td>
<td>2) Secondary outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lee 1999 (85)</td>
<td>Urgent endoscopy ≤1-2 h in emergency</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Elective endoscopy ≤1-2 days of admission</td>
<td>54</td>
<td>Mortality: OR 0.70 (95%CI 0.14, 3.57)</td>
</tr>
</tbody>
</table>

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therapy having undergone with high mortality in patients should be used to proton continuous followed by intravenous bolus C3: High

B11: Routine 2nd-look endoscopy is not recommended

6 RCTs (23)

- 2nd-look endoscopy + INJ (epi) + HP ≤16-24 h after initial endoscopy
- Observation

Messman 1998 (111)

- 2nd-look endoscopy + INJ (epi) q 16-24 h until Forrest IIc/III
- No 2nd-look endoscopy

Villanueva 1994 (112)

- 2nd-look endoscopy + INJ (epi) ≤18-24 h after initial endoscopy
- No 2nd-look endoscopy

Saeed 1996 (113)

- 2nd-look endoscopy + HP (+/-) INJ (epi) 24 hours after initial endoscopy
- No 2nd-look endoscopy

Chiu 2003 (110)

- 2nd-look endoscopy + INJ (epi) + HP ≤16-24 h after initial endoscopy
- Observation

Messman 1998 (111)

- 2nd-look endoscopy + INJ (epi) q 16-24 h until Forrest IIc/III
- No 2nd-look endoscopy

Villanueva 1994 (112)

- 2nd-look endoscopy + INJ (epi) ≤18-24 h after initial endoscopy
- No 2nd-look endoscopy

Saeed 1996 (113)

- 2nd-look endoscopy + HP (+/-) INJ (epi) 24 hours after initial endoscopy
- No 2nd-look endoscopy

Chiu 2006 (abstract) (115)

- 2nd-look endoscopy + treatment (not specified) 16–24 h after initial endoscopy
- IV OME CI (not further specified)

Lee 2005 (abstract) (116)

- 2nd-look endoscopy + INJ (epi) + clips 24 h after initial endoscopy
- Observation

C3: High-dose PPI An intravenous bolus followed by continuous-infusion proton-pump inhibitor should be used to decrease rebleeding and mortality in patients with high-risk stigmata having undergone successful endoscopic therapy

31 RCTs (24)

Update of previous meta-analysis (24 trials) (124)

Sung 2009 (125)

- IV ESO 80 mg bolus, over 30 min then 8 mg/h for 71.5 h
- Placebo

Wei 2007 (126)

- PO ESO 40 mg BID for 3 days
- Placebo

Naumovski-Mihalic 2005 (abstract) (127)

- IV PAN 3×40 mg (not further specified)
- IV RAN 3×50 mg (not further specified)

Lin 2006 (128)

- IV OME 40 mg q 6 h for 3 days, then PO OME 20 mg/d for 2 mo

Total 750

Routine 2nd-look endoscopy compared to observation or no retreatment

1) Main outcome:
Rebleeding: OR 0.59 (95%CI 0.38, 0.91)
2) Secondary outcomes:
Surgery: OR 0.43 (95%CI 0.19, 0.96)
Mortality: OR 0.65 (95%CI 0.26, 1.62)
3) Routine 2nd look demonstrated a significant reduction in rebleeding and surgery. Comments: Clinical trial heterogeneity was noted across studies with regards to patient selection, choice of hemostatic method, and choice of control therapy, especially high-dose IV PPI. The robustness of the results was poor in sensitivity analyses. The statement was not recommended (“probably don’t do it”) because: a) Existing published data do not favour the use of routine 2nd-look endoscopy, especially in the era of high dose IV PPI; and b) potential absolute risk reductions are likely to be low after initial endoscopic treatment with hemoclips or combination therapy. There exists a potential benefit when 2nd-look is applied to a subgroup of patients, such as those with particularly high-risk presentations, but this hypothesis requires further study.

Total 5792

PPI treatment with or without endoscopic therapy compared with placebo or H2RA

1) Main outcome:
Rebleeding: OR 0.45 (95%CI 0.36, 0.57)
2) Secondary outcome:
Surgery: OR 0.56 (95%CI 0.45, 0.70)
Mortality: OR 0.90 (95%CI 0.67, 1.19)
3) In this meta-analysis, overall, PPI treatment reduces rebleeding and surgery. Comments: The statement was recommended (“do it”) because strong evidence demonstrates the efficacy of high-dose IV PPI therapy after successful endoscopy therapy, with regard to improvements in rebleeding, surgery, and mortality. It is not possible to make definitive conclusion regarding the efficacy of either lower IV doses or high-dose oral compared to high-dose IV. However, lower IV doses or high-dose oral PPI (at doses equivalent to high-dose IV) are also effective (especially in Asian populations) and can be considered when high-dose IV is not available or not feasible.
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Details</th>
<th>Hex Ref</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Zargar 2006 (129) | - IV OME 40 mg q 12 h for 3 days, then PO OME 20 mg/d for 2 months  
- IV CIM 400 mg q 12 h for 3 days  
- IV PAN 80 mg bolus + CI 8 mg/h for 72 h  
- Placebo | 66 | |
| Khoshbaten 2006 (130) | - IV CIM 200 mg q 6 h until endoscopy (≤12-24 h) then PO OME 40 mg/d until day 14  
- IV CIM 200 mg q 6 h until endoscopy (≤12-24 h) then IV CIM 200 mg q 6 h for 3 days followed by PO CIM 400 mg q 12 h until day 14  
- IV PAN 40 mg q 12 h for 3 days, then PO PAN 40 mg/d for 8 wks  
- IV RAN 50 mg q 8 h for 3 days, then PO RAN 150 mg q 12 h for 8 wks | 67 | |
| Hsu 2004 (131) | - IV PAN 40 mg q 12 h for 3 days, then PO PAN 40 mg/d for 8 wks  
- IV RAN 50 mg q 8 h for 3 days, then PO RAN 150 mg q 12 h for 8 wks | 102 | |
| E4: | In a patient with a prior ulcer bleed who requires cardiovascular prophylaxis, it should be recognized that clopidogrel alone has a higher risk of rebleeding compared to ASA combined with a PPI |  | |
| Chan 2005 (211) | - PO ESO 20 BID + ASA 80 mg/d for 12 mos  
- Clopidogrel 75 mg/d for 12 mos  
- PO ESO 20 mg/d + ASA 1000 mg/d for 12 mos  
- Clopidogrel 75 mg/d for 12 mos | 159 | ASA plus a PPI compared to clopidogrel therapy  
1) Main Outcome:  
Rebleeding: OR 0.06 (95%CI 0.01, 0.32)  
2) Secondary outcome:  
Mortality: OR 0.63 (95%CI 0.24, 1.64)  
Comments: In this meta-analysis, ASA plus PPI significantly reduced rebleeding. |
| Lai 2006 (212) | Total 490 | 161 |

ASA=acetylsalicylic acid, CIM=cimetidine, CI=confidence interval, epi=epinephrine, ESO=esomeprazole, HP=heater probe, H2RA=histamine 2-receptor antagonist, INJ=intravenous, IV=intravenous, MD=mean difference, OR=odds ratio, OME=omeprazole, PAN=pantoprazole, PO=oral, PPI=proton pump inhibitor, RCT=randomized controlled trial, RAN=ranitidine