

<b>Author(s)</b> <b>Country</b> <b>Date included in the review</b> <b>AMSTAR score</b> <b>Number of articles</b>	<b>Method:</b> <b>Level of evidence</b> <b>Questions</b>	<b>Conclusions</b>
<p>Yolcu et al. 2020b USA Review and meta-analysis of published articles until December 20, 2018 N=5</p>	<p><b>Method:</b> Comprehensive literature search of English RCT and observational studies directly comparing prophylactic medication to a placebo for prevention of HO following SCI in adult age group (<math>\geq 18</math> yr). A meta-analysis comparing the incidence of HO between the two groups was conducted, with a subgroup analysis of non-steroidal anti-inflammatory drugs (NSAIDs) and non-NSAIDs. <b>Databases:</b> EBM, Embase, Ovid Medline, Scopus, Web of Science <b>Level of Evidence:</b> According to the Cochrane Collaboration for assessing risk, the two RCTs showed low risk. The observational studies scored between 7–8 on the Newcastle-Ottawa Scale (NOS), indicating high quality of evidence. Confidence in estimates was high for both overall HO and NSAIDs subgroup, while non-NSAIDs was ranked low due to inconsistency in reporting as well as the large CI. <b>Questions/measures/hypothesis:</b> Assess the preventive efficacy of prophylactic medications on heterotopic ossification after SCI compared to placebo.</p>	<ol style="list-style-type: none"> <li>1. Overall incidence of HO was 9.73 % in the medication group versus 16.5 % in the placebo group, although the difference is not statistically significant (<math>p=0.21</math>).</li> <li>2. In the subgroup analysis for NSAIDs, those who received prophylactic treatment with NSAIDs had a lower incidence of HO compared to those who received placebo (<math>p=0.003</math>).</li> <li>3. As for studies that used bisphosphonates, a significant difference in incidence of HO was not found (<math>p=0.58</math>) and the overall evidence was inconclusive.</li> </ol>
<p>Aubut et al. 2011 Canada Review of published articles between 1980-2010 AMSTAR=8 N=26</p>	<p><b>Method:</b> Comprehensive literature search of English RCT, Cohort studies, case series, and review articles of traumatic SCI in adult age group (<math>\geq 18</math> yr). <b>Databases:</b> MEDLINE, EMBASE, CINAHL, PsycInfo. <b>Level of evidence:</b> <i>Moderate quality:</i> Downgraded high quality studies, non-randomized trials, prospective cohort studies; <i>Low quality:</i> Retrospective observational, retrospective cohort and case-control studies; <i>Very low quality:</i> Case series, case reports, reviews and others. <b>Questions/measures/hypothesis:</b> 1. Examine the effectiveness of pharmacological, non-pharmacological and surgical management of HO after ABI</p>	<ol style="list-style-type: none"> <li>1. ABI population usually required multicomponent treatments compared to the SCI population.</li> <li>2. There are more level 1 and level 2 evidence for the SCI literature in supporting HO treatment, while the literature for the ABI population is weaker with mainly level 4 evidence.</li> <li>3. HO in SCI patients was mostly seen in the hip while the ABI patients had more varied location of HO including hip, knee and elbow.</li> <li>4. Etidronate and indomethacin post-surgery suggested for both populations to reduce the risk for HO.</li> </ol>

	and SCI.	
<p>Teasell et al. 2010 Canada Review of published articles between 1980- 2009 AMSTAR=8 N=13</p>	<p><b>Method:</b> Comprehensive literature search of English RCT, Cohort studies, case series, and review articles of traumatic SCI in adult age group (<math>\geq 18</math>yr). <b>Databases:</b> MEDLINE, EMBASE, CINAHL, PsycInfo. <b>Level of evidence:</b> <i>Moderate quality:</i> Downgraded high quality studies, non-randomized trials, prospective cohort studies; <i>Low quality:</i> Retrospective observational, retrospective cohort and case-control studies; <i>Very low quality:</i> Case series, case reports, reviews and others. <b>Questions/measures/hypothesis:</b> Examine the effectiveness of pharmacological, non-pharmacological and surgical management of HO after SCI.</p>	<ol style="list-style-type: none"> <li>1. There was strong evidence that early prophylactic treatment was efficacious in preventing HO, in which NSAIDs showed greatest effectiveness (level 1 evidence).</li> <li>2. Bisphosphonates had the strongest evidence for treatment of HO (level)</li> <li>3. There is some evidence for the use of Pulse low intensity electromagnetic field therapy (PLIMF), however, further research is needed.</li> </ol>