

Evidence-to-Decision table 5.1.2

**In adults (including older persons) and adolescents with cancer-related pain are adjuvant steroids more effective than other steroids or placebo to achieve pain control?**

<b>POPULATION:</b>	Adults (including older persons) and adolescents with cancer-related pain	<p><b>Background:</b></p> <p>Steroids are among the most commonly used medications in palliative care, and are commonly used to relieve cancer pain<sup>76</sup>. They are particularly useful as adjuvant medications for management of metastatic bone pain, neuropathic pain, and visceral pain<sup>77</sup>.</p> <p><b>Current WHO recommendation:</b></p> <ul style="list-style-type: none"> <li>• Corticosteroids are indicated in the following general cases:             <ul style="list-style-type: none"> <li>○ To improve appetite</li> <li>○ To enhance sense of well-being</li> <li>○ To improve strength</li> <li>○ Hormone therapy                 <ul style="list-style-type: none"> <li>▪ Replacement</li> <li>▪ Anticancer</li> </ul> </li> <li>○ To relieve pain caused by                 <ul style="list-style-type: none"> <li>▪ Raised intracranial pressure</li> <li>▪ Nerve compression</li> <li>▪ Spinal cord compression</li> <li>▪ Metastatic arthralgia</li> <li>▪ Bone metastasis</li> </ul> </li> </ul> </li> <li>• Corticosteroids are indicated in the following specific cases:             <ul style="list-style-type: none"> <li>○ Spinal cord compression</li> <li>○ Nerve compression</li> <li>○ Dyspnoea:                 <ul style="list-style-type: none"> <li>▪ Pneumonitis (after radiotherapy)</li> <li>▪ Carcinomatous lymphangitis</li> </ul> </li> </ul> </li> </ul>
<b>INTERVENTION:</b>	Steroids	
<b>COMPARISON:</b>	Steroids	
<b>MAIN OUTCOMES:</b>	<ul style="list-style-type: none"> <li>• Pain relief</li> <li>• Pain relief speed</li> <li>• Pain relief maintenance</li> <li>• Quality of life (QoL)</li> <li>• Functional outcomes</li> <li>• Gastrointestinal bleed (adverse event)</li> <li>• Psychiatric effects (adverse event)</li> </ul>	
<b>STRATIFICATIONS:</b>	<ul style="list-style-type: none"> <li>• Age (adults, older persons, adolescents, children)</li> <li>• History of substance abuse</li> <li>• Refractory pain</li> </ul>	
<b>SETTING:</b>	All	
<b>PERSPECTIVE:</b>	Population	

		<ul style="list-style-type: none"> <li> <ul style="list-style-type: none"> <li>▪ Tracheal compression/stridor</li> </ul> </li> <li>○ Superior vena caval obstruction</li> <li>○ Pericardial effusion</li> <li>○ Haemoptysis</li> <li>○ Obstruction of hollow viscus           <ul style="list-style-type: none"> <li>▪ Bronchus</li> <li>▪ Ureter</li> <li>▪ Intestine</li> </ul> </li> <li>○ Hypercalcaemia (in lymphoma, myeloma)</li> <li>○ Radiation-induced inflammation</li> <li>○ Leukoerythroblastic anaemia</li> <li>○ Rectal discharge (give per rectum)</li> <li>○ Sweating</li> </ul> <ul style="list-style-type: none"> <li>• Either prednisolone or dexamethasone are recommended, the dose depending on clinical situation. 7mg of prednisolone is equivalent to 1mg of dexamethasone.</li> <li>• For nerve compression pain, prescribe 20-40mg prednisolone/4-6mg of dexamethasone per day. Reduce dose step by step to a maintenance dose after one week. The maintenance dose will depend on the amount necessary to relieve pain, but could be as low as 15mg prednisolone or 2mg dexamethasone. Occasionally, a higher dose may be necessary to achieve significant benefit.</li> <li>• In patients with raised intracranial pressure, an initial daily dose of 8-16mg dexamethasone is appropriate. It may be possible to begin to reduce this to a maintenance dose after one week. With spinal cord compression, even higher doses have been used in some centres – up to 100mg per day initially, reducing to 16mg during radiation therapy.</li> <li>• Adverse events include oedema, dyspeptic symptoms, and occasionally gastrointestinal bleeding. Proximal myopathy, agitation, hypomania, and opportunistic infections may also occur. The incidence of adverse gastrointestinal effects is increased if corticosteroids are used in conjunction with NSAIDs.</li> </ul>
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	CRITERIA	SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS
PROBLEM	Is the problem a priority?	<p><b><u>Research Evidence</u></b> Steroids are among the most commonly used medications in palliative care, and are commonly used to relieve cancer pain<sup>76</sup>.</p> <p><b><u>Additional considerations</u></b> The 1996 WHO cancer pain guidelines made recommendations on their use – so too should updated ones, which can make use of evidence developed since the formulation of the previous guidelines.</p>

<b>BENEFITS &amp; HARMS</b>	<p><b>Do the desirable effects outweigh the undesirable effects?</b></p> <p>Yes      No      Uncertain</p> <p><input type="checkbox"/>      <input type="checkbox"/>      <input type="checkbox"/> Yes</p>	<ul style="list-style-type: none"> <li>• <b>No randomized controlled trials</b> compared steroids to other steroids.</li> </ul> <p><b>BENEFITS and HARMS</b></p> <ul style="list-style-type: none"> <li>• <b>No trial</b> reported on <b>pain relief</b>.</li> <li>• <b>No trial</b> reported on <b>pain relief speed</b>.</li> <li>• <b>No trial</b> reported on <b>pain relief maintenance</b>.</li> <li>• <b>No trial</b> reported on <b>QoL</b>.</li> <li>• <b>No trial</b> reported on <b>functional outcomes</b>.</li> <li>• <b>No trial</b> reported on <b>gastrointestinal bleed</b>.</li> <li>• <b>No trial</b> reported on <b>psychiatric effects</b>.</li> </ul> <p><b>STRATIFICATIONS</b></p> <ul style="list-style-type: none"> <li>• Studies conducted in adults with a wide age range, without stratification into adolescent, non-older persons, and older persons.</li> <li>• Studies provide no data regarding history of substance abuse.</li> <li>• Studies provide no data regarding refractory pain.</li> </ul> <p><b>SUMMARY</b></p> <p>No eligible trials were found that address this sub-question.</p>
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<b>ACCEPTABILITY &amp; PREFERENCES</b>	<p><b>Is there important uncertainty or variability about how much people value the options?</b></p> <p>Major variability <input type="checkbox"/></p> <p>Minor variability <input type="checkbox"/></p> <p>Uncertain <input type="checkbox" value="Yes"/></p> <p><b>Is the option acceptable to key stakeholders?</b></p> <p>Yes    No    Uncertain  <input type="checkbox"/>    <input type="checkbox"/>    <input type="checkbox" value="Yes"/></p>	<p><b><u>Research Evidence</u></b> None</p> <p><b><u>Additional considerations</u></b> None</p>

<b>FEASIBILITY ./ RESOURCE USE</b>	<p><b>How large are the resource requirements?</b></p> <p>Major <input type="checkbox"/>    Minor <input type="checkbox"/>    Uncertain <input type="checkbox"/></p> <p>Yes <input type="checkbox"/>    No <input type="checkbox"/>    Uncertain <input type="checkbox"/></p>	<table border="1"> <thead> <tr> <th></th> <th>Price per 1mg</th> <th>Defined daily dose</th> </tr> </thead> <tbody> <tr> <td>Dexamethasone (Source:<sup>78</sup>)</td> <td>USD \$ 0.02475</td> <td>1.5mg</td> </tr> <tr> <td>Prednisolone (Source:<sup>79</sup>)</td> <td>USD \$ 0.00222</td> <td>10mg</td> </tr> <tr> <td>Methylprednisolone (Source:<sup>80</sup>)</td> <td>USD \$ 0.0104</td> <td>20mg</td> </tr> </tbody> </table>		Price per 1mg	Defined daily dose	Dexamethasone (Source: <sup>78</sup> )	USD \$ 0.02475	1.5mg	Prednisolone (Source: <sup>79</sup> )	USD \$ 0.00222	10mg	Methylprednisolone (Source: <sup>80</sup> )	USD \$ 0.0104	20mg
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<p><b>Is the option feasible to implement?</b></p> <p>Yes <input type="checkbox"/>    No <input type="checkbox"/>    Uncertain <input type="checkbox"/></p> <p>Yes <input type="checkbox"/>    No <input type="checkbox"/>    Uncertain <input type="checkbox"/></p>	<p><b>Would the option improve equity in health?</b></p> <p>Yes <input type="checkbox"/>    No <input type="checkbox"/>    Uncertain <input type="checkbox"/></p>	<p><u>Research Evidence</u> None</p> <p><u>Additional considerations</u> None</p>												

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**Recommendation****Current recommendation:**

- Corticosteroids are indicated in the following general cases:
    - To improve appetite
    - To enhance sense of well-being
    - To improve strength
    - Hormone therapy
      - Replacement
      - Anticancer
    - To relieve pain caused by
      - Raised intracranial pressure
      - Nerve compression
      - Spinal cord compression
      - Metastatic arthralgia
      - Bone metastasis
  - Corticosteroids are indicated in the following specific cases:
    - Spinal cord compression
    - Nerve compression
    - Dyspnoea:
      - Pneumonitis (after radiotherapy)
      - Carcinomatous lymphangitis
      - Tracheal compression/stridor
    - Superior vena caval obstruction
    - Pericardial effusion
    - Haemoptysis
    - Obstruction of hollow viscus
      - Bronchus
      - Ureter
      - Intestine
    - Hypercalcaemia (in lymphoma, myeloma)
    - Radiation-induced inflammation
    - Leukoerythroblastic anaemia
    - Rectal discharge (give per rectum)
    - Sweating
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- Either prednisolone or dexamethasone are recommended, the dose depending on clinical situation. 7mg of prednisolone is equivalent to 1mg of dexamethasone.
  - For nerve compression pain, prescribe 20-40mg prednisolone/4-6mg of dexamethasone per day. Reduce dose step by step to a maintenance dose after one week. The maintenance dose will depend on the amount necessary to relieve pain, but could be as low as 15mg prednisolone or 2mg dexamethasone. Occasionally, a higher dose may be necessary to achieve significant benefit.
  - In patients with raised intracranial pressure, an initial daily dose of 8-16mg dexamethasone is appropriate. It may be possible to begin to reduce this to a maintenance dose after one week. With spinal cord compression, even higher doses have been used in some centres – up to 100mg per day initially, reducing to 16mg during radiation therapy.
  - Adverse events include oedema, dyspeptic symptoms, and occasionally gastrointestinal bleeding. Proximal myopathy, agitation, hypomania, and opportunistic infections may also occur. The incidence of adverse gastrointestinal effects is increased if corticosteroids are used in conjunction with NSAIDs.

**New (draft) recommendation:**  
**None**

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**Strength of Recommendation**

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**Quality of Evidence**

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**Justification**

There were no trials that compared the effects of different steroids, only trials that compared the steroids with placebo. Therefore, the GDG could not make a recommendation for one steroid over others.

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**Subgroup considerations**

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**Implementation considerations**  
**[incl. M&E]**

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**Research priorities**

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