Evidence-to-Decision table 5.2.3		
In adults (including older persons) and adolescents with bone metastases, what is the evidence for the use of monoclonal antibodies (monoclonals) compared to no treatment in order to prevent and treat pain?		
POPULATION:	Adults (including older persons) and adolescents with cancer-related pain	**Background:** Bone pain is the most common type of pain from cancer and is present in approximately one out of three patients with bone metastases.[129,139] The pain is commonly a mixture of background pain and incident/episodic pain, which is commonly associated with weight bearing or movement.[130] Bone metastases can weaken bone sufficiently to greatly increase patients' risk of fracture. There are reports that monoclonal antibodies designed to target Nerve Growth Factor (NGF) and osteoclasts reduce pain scores in patients with metastatic bone pain[141] or fracture risk[142]. **Current WHO recommendation**: None.
INTERVENTION:	Monoclonals	
COMPARISON:	Placebo (no treatment)	
MAIN OUTCOMES:	• Pain relief • Pain relief speed • Pain relief maintenance • Quality of life (QoL) • Functional outcomes • Skeletal-related events • Osteonecrosis of the jaw (adverse event)	
STRATIFICATIONS:	• Age (adults, older persons, adolescents, children) • History of substance abuse • Refractory pain	
SETTING:	All	
PERSPECTIVE:	Population	

	CRITERIA	SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS
PROBLEM	**Is the problem a priority?** Yes	**Research evidence** None **Additional considerations** WHO does not have recommendations for treating bone pain and should investigate the various methods by which it might be treated, monoclonal antibodies being one of these methods.

BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable effects?** Yes: ☐ No: ☐ Uncertain: ☒ Yes	• **One randomized controlled trial** compared monoclonals to placebo, evaluating **tanezumab** in adults with prostate cancer, breast cancer, renal cell carcinoma, or multiple myeloma with painful bone metastases (mean age 56 years, range 32 to 77). **BENEFITS and HARMS** • **One trial** provided **very low strength of evidence** reported **no difference in average or worst pain between tanezumab and placebo** (between group differences -2.6 [95% CI -11.8, 6.6] and -0.1 [95% CI -9.3, 9.1], respectively), and in percentage of people who achieve pain relief (by at least 50%) (RR = 1.38 [95% CI 0.55, 3.49]). • **No trial** reported on **pain relief speed**. • **No trial** reported on **pain relief maintenance**. • **No trial** reported on **QoL**. • **No trial** reported on **functional outcomes**. • **One trial** provided **very low strength of evidence** of **increased skeletal-related events with monoclonals**, reporting only that 1 of 29 (3.4%) patients in the tanezumab arm had a femur **fracture** (RR = 3.1 [95% CI 0.13, 73.2]). • **No trial** reported on **osteonecrosis of the jaw**. **STRATIFICATIONS** • Studies conducted in adults with a wide age range, without stratification into adolescent, non-older persons, and older persons. • Studies provide no data regarding history of substance abuse. • Studies provide no data regarading refractory pain. **SUMMARY** We are uncertain whether monoclonals affect outcomes compared to placebo.

ACCEPTABILITY & PREFERENCES	**Is there important uncertainty or variability about how much people value the options?** Major variability [ ] Minor variability [ ] Uncertain [Yes] **Is the option acceptable to key stakeholders?** Yes [ ] No [ ] Uncertain [Yes]	**<u>Research evidence</u>** None **<u>Additional considerations</u>** None

FEASIBILITY ./ RESOURCE USE	**How large are the resource requirements?** Major Minor Uncertai [ ] [ ] [Yes] **Is the option feasible to implement?** Yes No Uncertain [ ] [ ] [Yes]	**Research evidence** The price of Tanezumab could not be found. **Additional considerations** None
	Would the option improve equity in health? Yes No Uncertai [ ] [ ] [Yes]	**Research evidence** None **Additional considerations** None

Recommendation	**Current recommendation:** None **New (draft) recommendation:** None
Strength of Recommendation	
Quality of Evidence	➢ **VERY LOW** [Pain (critical) = very low others omitted for no data or indeterminate findings]
Justification	The GDG did not feel it could make a recommendation on the basis of the eligible evidence. They noted that the paucity of trials probably derives from the preference to trial new therapies against the usual treatment rather than placebo.
Subgroup considerations	
Implementation considerations [incl. M&E]	
Research priorities	