

# **Hyperparathyroidism (primary): diagnosis, assessment and initial management**

**Review questions**

*NICE guideline <number>*

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*This guideline was developed by the  
National Guideline Centre*



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# 1 Review questions

Evidence report	Type of review	Review questions	Outcomes
1.1 (a)	Diagnostic	What are the indications for diagnostic testing for primary hyperparathyroidism?	<p>Target condition: primary hyperparathyroidism</p> <ul style="list-style-type: none"> <li>• Specificity</li> <li>• Sensitivity</li> <li>• Positive and / or negative predictive value</li> <li>• ROC curve or area under curve</li> </ul>
1.1 (b)	Prognostic	In adults with fragility fracture, renal stones, and/or renal tract calcification what is the incidence of primary hyperparathyroidism?	Diagnosis of PHPT
1.2	Test and treat Diagnostic	Which biochemical test or combination of tests should be used for diagnosing primary hyperparathyroidism (for example, levels of parathyroid hormone, blood calcium and phosphate, alone or in combination)?	<p>Target condition: primary hyperparathyroidism</p> <p>Outcomes for test and treat review:</p> <ul style="list-style-type: none"> <li>• Mortality (dichotomous outcome)</li> <li>• Quality of life (continuous outcome)</li> <li>• Number of people receiving treatment, i.e., including people who may not have needed it such as those with false positive results (dichotomous outcome)</li> <li>• Repeat testing / additional testing (dichotomous outcome)</li> <li>• Adverse events related to test (as reported in the papers)</li> <li>• Adverse events related to treatment (as reported in the papers)</li> <li>• Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			<p>Outcomes for diagnostic accuracy review:</p> <ul style="list-style-type: none"> <li>• Specificity</li> <li>• Sensitivity</li> <li>• Positive and / or negative predictive value</li> <li>• ROC curve or area under curve</li> </ul>
2.1	Intervention	What is the clinical and cost effectiveness of surgery (parathyroidectomy) in people with primary hyperparathyroidism?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous outcome)</li> </ul> <p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Adverse events (to include voice change, hypoparathyroidism) (dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>
2.2	Intervention	What are the indications for surgery (parathyroidectomy) in people with primary hyperparathyroidism?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous outcome)</li> </ul> <p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Cardiovascular events (dichotomous outcome)</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			<ul style="list-style-type: none"> <li>• Adverse events (to include voice change, hypoparathyroidism; dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>
3.1	Test and treat Diagnostic	What is the clinical and cost effectiveness of using non-invasive imaging techniques (for example parathyroid ultrasound, sestamibi scanning, CT and MRI scanning) prior to surgery?	<p><b>For test-and-treat review:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Success (cure) / failure (dichotomous outcome)</li> <li>• Adverse events (dichotomous outcome)</li> <li>• BMD of the distal radius or the lumbar spine (continuous outcome)</li> <li>• Deterioration in renal function (dichotomous outcome)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Length of hospital stay (continuous outcome)</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia</li> <li>• Reoperation (dichotomous outcome)</li> <li>• Unnecessary neck exploration (dichotomous outcome)</li> </ul> <p><b>For diagnostic accuracy review:</b></p> <p>Target condition (for localisation studies): correct localisation of adenoma (correctly localises the region/quadrant from which an abnormal gland is removed [rather than just correctly identifies hyperactive tissue anywhere, or correctly lateralises the hyperactive gland]).</p> <p>Target condition (for intra-operative tests): correct prediction of removal of all abnormal tissue.</p>

Evidence report	Type of review	Review questions	Outcomes
			<p>Outcomes of interest: Specificity Sensitivity</p>
3.2	Test and treat Diagnostic	What is the clinical and cost effectiveness of using invasive imaging techniques (for example parathyroid venous sampling) prior to surgery?	<p><b>For test-and-treat review:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Success (cure) / failure (dichotomous outcome)</li> <li>• Adverse events (dichotomous outcome)</li> <li>• BMD of the distal radius or the lumbar spine (continuous outcome)</li> <li>• Deterioration in renal function (dichotomous outcome)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Length of hospital stay</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Reoperation (dichotomous outcome)</li> <li>• Unnecessary neck exploration (dichotomous outcome)</li> </ul> <p><b>For diagnostic accuracy review:</b> Target condition (for localisation studies): correct localisation of adenoma (correctly localises the region/quadrant from which an abnormal gland is removed [rather than just correctly identifies hyperactive tissue anywhere, or correctly lateralises the hyperactive gland]).</p> <p>Outcomes of interest: Specificity Sensitivity</p>
3.3	Test and treat Diagnostic	What is the clinical and cost effectiveness of using intraoperative parathyroid hormone assays, methylene blue and intraoperative frozen sections?	<p><b>For test-and-treat review:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> </ul>



Evidence report	Type of review	Review questions	Outcomes
			<ul style="list-style-type: none"> <li>• Success (cure) / failure (dichotomous outcome)</li> <li>• Adverse events (dichotomous outcome)</li> <li>• BMD of the distal radius or the lumbar spine (continuous outcome)</li> <li>• Deterioration in renal function (dichotomous outcome)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Length of hospital stay (continuous outcome)</li> <li>• Occurrence of kidney stones</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Reoperation (dichotomous outcome)</li> <li>• Unnecessary neck exploration (dichotomous outcome)</li> </ul> <p><b>For diagnostic accuracy review:</b></p> <p>Target condition (for intra-operative tests): correct prediction of removal of all abnormal tissue.</p> <p>Outcomes of interest: Specificity Sensitivity</p>
4.1	Intervention	What is the clinical and cost effectiveness of different types of surgical intervention, for example 4-gland exploration, compared with minimally invasive techniques?	<p><b>Critical outcomes</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Success (cure) / failure (dichotomous outcome)</li> </ul> <p><b>Important outcomes</b></p> <ul style="list-style-type: none"> <li>• Adverse events (bleeding (return to theatre), severe hypocalcaemia (as defined in the study), hypercalcaemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) (dichotomous outcome)</li> <li>• BMD of the distal radius or</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			<p>the lumbar spine (continuous)</p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous – study may also report renal replacement)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Length of hospital stay (continuous outcome)</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Reoperation (dichotomous outcome)</li> <li>• Unnecessary neck exploration (dichotomous outcome)</li> </ul>
4.2	Intervention	What are the management options for people in whom primary parathyroid surgery has failed?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> <li>• Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous)</li> </ul> <p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Adverse events (dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>
5.1	Intervention	What is the clinical and cost effectiveness of calcimimetics in people with primary hyperparathyroidism?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> </ul> <p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous - study may also report renal replacement)</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			<ul style="list-style-type: none"> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• BMD (continuous) of the distal radius or the lumbar spine</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Adverse events (to include discontinuation due to side effects; dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>
5.2	Intervention	What is the clinical and cost effectiveness of bisphosphonates in people with primary hyperparathyroidism?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> </ul> <p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (dichotomous – study may also report renal replacement)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• BMD (continuous) of the distal radius or the lumbar spine</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Adverse events (to include discontinuation due to side effects; dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> </ul>
6.1	Intervention	What is the optimum type and frequency of monitoring for people with primary hyperparathyroidism (for example, pre-operative, postoperative, non-surgical)?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• HRQOL (continuous outcome)</li> <li>• Mortality (dichotomous outcome)</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			<p><b>Important outcomes:</b></p> <ul style="list-style-type: none"> <li>• Deterioration in renal function (continuous outcome)</li> <li>• Fractures (vertebral or long bone) (dichotomous outcome)</li> <li>• Occurrence of kidney stones (dichotomous outcome)</li> <li>• Persistent hypercalcaemia (dichotomous outcome)</li> <li>• BMD of the distal radius or the lumbar spine (continuous outcome)</li> <li>• Cardiovascular events (dichotomous outcome)</li> <li>• Adverse events (to include voice change, hypoparathyroidism, hypothyroidism/hyperthyroidism) (dichotomous outcome)</li> <li>• Cancer incidence (dichotomous outcome)</li> <li>• Reoperation (for post-surgery stratum) (dichotomous outcome)</li> </ul>
6.2	Prognostic	What are the long-term outcomes in people with primary hyperparathyroidism?	<p><b>Critical outcomes:</b></p> <ul style="list-style-type: none"> <li>• Mortality (dichotomous outcome)</li> <li>• Fragility fracture (dichotomous outcome)</li> <li>• Renal stones (dichotomous outcome)</li> <li>• Renal tract calcification (dichotomous outcome)</li> <li>• Pancreatitis (dichotomous outcome)</li> <li>• Stroke (dichotomous outcome)</li> <li>• Hypertension (dichotomous outcome)</li> <li>• Myocardial infarction (dichotomous outcome)</li> <li>• Number of people who become eligible for surgery / meet the criteria for surgery (dichotomous)</li> <li>• Serum calcium (&gt;2.85 mmol/l) (dichotomous) (continuous if dichotomous not available)</li> <li>• 24-hour urine for calcium (&gt;10 mmol/dl) (dichotomous) (continuous if</li> </ul>

Evidence report	Type of review	Review questions	Outcomes
			dichotomous not available) <ul style="list-style-type: none"> <li>• BMD of proximal femur (T-score &lt;2.5; Z score &lt;2) (dichotomous) (continuous if dichotomous not available)</li> </ul>
7.1	Intervention	How should the management of primary hyperparathyroidism differ in pregnant women?	Outcomes follow those in the primary reviews for surgery, surgery interventions, calcimimetics, bisphosphonates, monitoring and patient information. <p>Additional pregnancy/neonatal outcomes:</p> <ul style="list-style-type: none"> <li>• Outcome of pregnancy – term/early/late (dichotomous outcome)</li> <li>• Congenital abnormalities (dichotomous outcome)</li> <li>• Early foetal loss (miscarriage) (dichotomous outcome)</li> <li>• Stillbirth (dichotomous outcome)</li> <li>• Admission for IV hydration (dichotomous outcome)</li> <li>• Complications during pregnancy (dichotomous outcome)</li> <li>• Eclampsia/pre-eclampsia</li> <li>• Complications post-partum – mother/baby – requirement for support for either (dichotomous outcome)</li> <li>• Apgar score baby (continuous outcome)</li> <li>• Calcium levels mother/baby at/around birth (continuous outcome)</li> <li>• Neonatal tetany or symptomatic hypocalcaemia (dichotomous outcome)</li> </ul>
8.1	Qualitative	What information is useful for people with primary hyperparathyroidism?	Any type of information described by studies. <ul style="list-style-type: none"> <li>• Content of information and how this information is delivered</li> <li>• Information to include pre- and post-surgery</li> <li>• Timing of information and support</li> </ul>