Appendix D: Clinical evidence tables

Study	Bergenfelz 2005[4]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Germany; Setting: University Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: follow-up- 1 and 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Single parathyroid adenoma
Subgroup analysis within study	Not applicable
Inclusion criteria	Only patients with a single enlarged parathyroid gland were eligible for inclusion in the study.
Exclusion criteria	Patients with hereditary HPT (multiple endocrine neoplasia (MEN) 1 and 2, non-MEN-related familial HPT), suspicion of involvement of multiple parathyroid glands on sestamibi scanning, previous neck exploration for thyroid disorders, anticipated or planned simultaneous thyroid operations, and allergy to drugs used for local anaesthesia, as well as those who could not fully comprehend the information given or who rejected confirmation to participate, were excluded. Patients aged less than 18 years, those with a hypercalcaemic crisis and high-risk patients (American Society of Anaesthesiologists grade IV) were also excluded. For the entire group of patients the reasons for exclusion were: negative sestamibi scan, rejected participation, planned simultaneous operation, previous surgery for thyroid disorders, withdrawal of consent and suspicion of involvement of multiple parathyroid glands.
Recruitment/selection of patients	Between February 1999 and September 2002, 233 patients with biochemically proven PHPT and no previous surgery were operated on in the institution. There were 179 women and 54 men of median age 62 (range 16–84) years. The median serum level of calcium was 2.80 (range 2.50–4.80) mmol/L. Once informed consent had been given, patients had sestamibi scintigraphy for localisation of parathyroid adenomas. Only patients with a single enlarged parathyroid gland were eligible for inclusion in the study.
Age, gender and ethnicity	Age - Mean (SD): MIP- 57 (15); BCE- 62 (12). Gender (M:F): MIP- 5:20; BCE- 6:19. Ethnicity: not stated
Further population details	Not stated
Extra comments	Patients with a solitary parathyroid adenoma localised before surgery by sestamibi scintigraphy. Patients

Study	Bergenfelz 2005[4]
	had sestamibi scintigraphy for localisation of parathyroid adenomas. Only patients with single enlarged parathyroid gland were eligible for inclusion in the study. There was no difference in the symptoms and signs of PHPT between the groups (data not shown).
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Surgical techniques - Targeted/focused with localisation technique/s. Targeted Minimally invasive parathyroidectomy (MIP) via a 2cm incision using LA. The MIP procedure was an open targeted operation for parathyroid adenoma excision. Patients received midazolam 1–5 mg intravenously for sedation. The incision site was anaesthetized locally with 0.5 per cent bupivacaine and 1 per cent lignocaine (1: 1v/v). During the procedure additional intravenous analgesics (metamizol, pethricline) and repeated doses of midazolam were permitted. A 2 cm transverse incision was made at the site where the adenoma had been localised by sestamibi scanning. After mobilisation of the thyroid lobe, the parathyroid adenoma was localised, dissected, weighed and sent for frozen-section analysis. The ipsi- lateral parathyroid gland was not explored routinely. Duration not stated. Concurrent medication/care: Oral calcium was administered whenever a patient reported symptoms of hypocalcaemia and/or when the serum calcium was below 1.8 mmol/L. Vitamin D metabolites were given orally only when oral calcium supplementation did not result in complete resolution of hypocalcaemic symptoms. Indirectness: No indirectness Comments: Sestamibi scintigraphy- Scintigraphic evaluations of the neck and mediastinum used 450 MBq 99mTc-labelled sestamibi and a γ probe with a low-energy high-resolution collimator. Planar scans were obtained after 5, 15 and 120 min (128 × 128 matrix) and documented on multi format films. Single-photon emission computed tomography was used routinely. (n=25) Intervention 2: Surgical techniques - Non-targeted/non-focused without localisation technique/s. conventional bilateral cervical exploration (BCE) under GA. After induction of general anaesthesia, patients had a short Kocher incision. The straight muscles were opened in the midline, but not divided. To avoid any bias, the study protocol required the surgeon always to start a BCE on the left side of the neck and to aim to identify all 4 parathyroid glands. Enlarged glands were excised, weighed and sent for frozen-section analysis to confirm their parathyroid origin. The wound was closed, but the patient was kept under anaesthesia until the results of the frozen section examination had been received. Intraoperative PTH levels were not monitored during BCE. Duration not stated. Concurrent medication/care: Oral calcium was administered whenever a patient reported symptoms of hypocalcaemia and/or when the serum calcium was below 1.8 mmol/L. Vitamin D metabolites were given orally only when oral calcium supplementation did not result in complete resolution of hypocalcaemic symptoms. Indirectness: No indirectness

Study	Bergenfelz 2005[4]
	Comments: The study protocol defined conversion from MIP to BCE in the following situations: intraoperative demonstration of two normal parathyroid glands on the side where the scan had suggested the adenoma; inadequate decrease in PTH concentration after adenoma excision; no confirmation of parathyroid tissue by frozen-section analysis; and intraoperative suspicion of multiple gland disease. Conversion was also allowed for safety reasons and the patient's well-being, for example when there was a technical problem or the patient felt uncomfortable during the procedure. Conversion to BCE was necessary in three patients who had been randomised to undergo MIP under local anaesthesia-In two of these patients the parathyroid adenoma was not found through the 2-cm incision in spite of a true-positive preoperative localisation. Another patient felt unable to continue the procedure under local anaesthesia. One patient in the MIP group had raised postoperative levels of serum calcium and PTH despite an adequate decrease in PTH concentration at 5 and 15 min after resection of a parathyroid adenoma. The patient underwent a BCE during the same hospital stay; three hyperplastic glands were found, of which two and a half were resected.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TARGETED/FOCUSED WITH LOCALISATION TECHNIQUE/S versus NON-TARGETED/NON-FOCUSED/4-GLAND EXPLORATION WITHOUT LOCALISATION TECHNIQUE/S

Protocol outcome 1: Adverse events (bleeding [return to theatre], severe hypocalcaemia, hypercalcemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) at end of follow-up
- Actual outcome: vocal cord palsy at post-operative; Group 1: 1/25, Group 2: 0/25
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness
- Actual outcome: Hypocalcaemia at 1 month; Group 1: 0/25, Group 2: 3/25
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness
- Actual outcome: Drainage of wound seroma at post-operative; Group 1: 0/25, Group 2: 1/25
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Reoperation at end of follow-up
- Actual outcome: Re-operation at end of follow-up; Group 1: 1/25, Group 2: 0/25
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study	Bergenfelz 2005[4]
Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at end of follow-up; Deterioration in renal function at end of follow-up; Fractures (vertebral or long bone) at end of follow-up; Occurrence of kidney stones at end of follow-up; Persistent hypercalcaemia at end of follow-up; BMD of the distal radius or the lumbar spine at end of follow-up; Length of hospital stay at end of follow-up; Unnecessary neck exploration at end of follow-up; Mortality at end of follow-up

Study	Miccoli 1999[17]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=38)
Countries and setting	Conducted in Italy; Setting: Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: follow-up- 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Single parathyroid adenoma
Subgroup analysis within study	Not applicable
Inclusion criteria	Sporadic form of PHPT, no prior neck surgery, absence of thyroid nodules, and pre-operative ultrasonography suggestive for solitary parathyroid adenoma.
Exclusion criteria	Not stated
Recruitment/selection of patients	From March to November 1998, 47 patients with PHPT were referred to the unit for parathyroidectomy.
Age, gender and ethnicity	Age - Mean (SD): bilateral- 60 (14); VAP- 48 (13). Gender (M:F): bilateral - 11/6; VAP- 13/7. Ethnicity: not stated
Further population details	Not stated
Extra comments	Patients with PHPT. The patients' eligibility for VAP was considered on the basis of clinical history and ultrasound findings. Those considered eligible for VAP were then randomly divided to bilateral or VAP. serum calcium (mg/dL) : bilateral 10.8; VAP 11.1 serum iPTH: bilateral 195; VAP 221 Pre-operative localisation studies was ordered by the referring physician, ultrasound examination of the neck

Study	Miccoli 1999[17]
	was performed by an expert radiologist using a linear transducer with colour Doppler capability. The patient's eligibility for VAP was considered on the basis of both clinical history and ultrasound findings.
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Surgical techniques - Targeted/focused with localisation technique/s. Video assisted parathyroidectomy (VAP) (one of the options of minimal access parathyroidectomy). VAP procedures under general endotracheal anaesthesia or bilateral superficial cervical block in association with laryngeal mask. The procedure was carried out through a 15 mm incision at the notch level. The cervical midline was opened, and a conventional 12 mm trocar was inserted between the strap muscles and the thyroid on the side of the suspected lesion. Under endoscopic vision, a 3-4 minute carbon dioxide insufflation allowed a gentle and anatomic dissection of the thyrotraceal groove. The trocar was then removed, and the operative space was maintained with small external retractors. A 30 degree 5 mm endoscope allowed optimal visualisation of the operative field. Needle-scopic instruments (2mm) were used to identify and prepare the parathyroid adenoma. Conventional titanium vascular clips were used for the ligation of the thyroid middle vein and the hylus of the adenoma. Pre-operative localisation for all patients (both groups) was done by referring physician. Ultrasound examination of the neck performed by an expert radiologist using a linear transducer with colour Doppler capability for only VAP group. Duration not stated. Concurrent medication/care: not stated. Indirectness: No indirectness (n=18) Intervention 2: Surgical techniques - Non-targeted/non-focused without localisation technique/s. Bilateral neck exploration - Patients underwent a bilateral exploration of the neck under endotracheal GA. Through a traditional cervicotomy, the thyro tracheal groove was exposed; the laryngeal recurrent nerve was identified and carefully preserved, and an attempt was made to identify 4 parathyroid glands. Macroscopically enlarged parathyroid glands were then removed. Frozen section was used for tissue confirmation. No biopsy specimens of normal parathyroid glands were obtained. Intraoperative quick parathyroid hormone assay (qPTHa) was not used. Duration not stated. Concurrent medication/care: not stated. Indirectness: No indirectness Extra comment: Two patients had multiglandular disease that was discovered during the surgery and were excluded from the study. In one of these 2 patients (conventional group), a second enlarged gland was found on the same side of the adenoma that was localised before the operation. The other patient underwent VAP (focused) but did not show the expected parathyroid hormone drop after the removal of the adenoma; operation was converted to a traditional approach, and a second cystic adenoma was found in the contralateral side of the neck.
Funding	Funding not stated

Study	Miccoli 1999[17]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TARGETED/FOCUSED WITH LOCALISATION TECHNIQUE/S versus NON-TARGETED/NON-FOCUSED/4-GLAND EXPLORATION WITHOUT LOCALISATION TECHNIQUE/S Protocol outcome 1: Adverse events (bleeding [return to theatre], severe hypocalcaemia, hypercalcemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) at end of follow-up - Actual outcome: Temporary hypocalcaemia at Post-operative; Group 1: 1/20, Group 2: 3/18 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome: wound infection at Post-operative; Group 1: 0/20, Group 2: 1/18 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome: laryngeal nerve palsy at 6 months; Group 1: 3/20, Group 2: 0/18 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at end of follow-up; Deterioration in renal function at end of follow-up; Fractures (vertebral or long bone) at end of follow-up; Occurrence of kidney stones at end of follow-up; Persistent hypercalcaemia at end of follow-up; BMD of the distal radius or the lumbar spine at end of follow-up; Length of hospital stay at end of follow-up; Reoperation at end of follow-up; Unnecessary neck exploration at end of follow-up; Mortality at end of follow-up

Study	Russell 2006[23]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in United Kingdom; Setting: Royal Victoria Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: follow-up- 23 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Single parathyroid adenoma
Subgroup analysis within study	Not applicable

Study	Russell 2006[23]
Inclusion criteria	With the exception of five individuals, all patients with proven HPT during the study interval underwent dual-isotope subtraction scanning using 99mTc and Tc-labelled sestamibi. The decision to advise operation in individual patients was taken on clinical and biochemical grounds, and was not influenced by the outcome of the parathyroid scinti scan. Patients with a positive scan, defined as one residual focus of radioactivity following subtraction, were deemed suitable for scan-directed unilateral neck exploration. In each patient the neck was explored via a short 'collar' incision and the side and site of the parathyroid tumour, as suggested by the isotope scan, was exposed. If the adenoma was identified and considered to be in a position in keeping with the scan report, an attempt was made to identify the ipsilateral normal parathyroid. If there was no evidence of a second enlarged gland on the side initially explored, the patient was randomised to unilateral or bilateral operation by means of a consecutively numbered sealed envelope system. For individuals randomised to unilateral exploration the operation was terminated and the neck closed. The contralateral side of the neck was exposed in those randomised to bilateral operation and an attempt made to identify the two parathyroids on the second side.
Exclusion criteria	Exclusion criteria for unilateral parathyroid exploration Negative isotope scan; more than one focus of activity on isotope scan; tumour not located on side suggested by isotope scan; two enlarged parathyroids found on first side explored; history of familial HPT or multiple endocrine neoplasia.
Recruitment/selection of patients	Between 1 April 1998 and 31 December 2003, a total of 196 patients had cervical exploration for HPT. Six of these were undergoing reoperation for persistent or recurrent hypercalcaemia following initial operation. Thus 190 individuals were submitted to first-time neck exploration for HPT. Of these, 100 patients were deemed suitable for randomisation and the remaining 90 patients were excluded from the study for a variety of reasons.
Age, gender and ethnicity	Age - Mean (range): Focused unilateral: 61.5 (range 35–82) years; Standard bilateral- 62.5 (range 18–81) years). Gender (M: F): Focused unilateral-12/42; Standard bilateral- 10/36. Ethnicity: not stated
Further population details	Not stated
Extra comments	Patients were diagnosed with HPT on the basis of persistent hypercalcaemia with a concomitant increased or inappropriate level of serum parathyroid hormone (intact molecule assay).
Indirectness of population	No
Interventions	(n=54) Intervention 1: Surgical techniques - Targeted/focused with localisation technique/s. Focused unilateral cervical exploration. No further details. Duration 65.6 mins. Concurrent medication/care: not stated. Indirectness: No indirectness (n=46) Intervention 2: Surgical techniques - Non-targeted/non-focused with localisation technique/s. standard bilateral neck exploration. No further details. Duration 79.7 mins. Concurrent medication/care: not

Study	Russell 2006[23]
	stated. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TARGETED/FOCUSED WITH LOCALISATION TECHNIQUE/S versus NON-TARGETED/NON-FOCUSED/4-GLAND EXPLORATION WITH LOCALISATION TECHNIQUE/S Protocol outcome 1: Adverse events (bleeding (return to theatre), severe hypocalcaemia, hypercalcemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) at end of follow-up - Actual outcome: Permanent unilateral vocal cord paralysis at end of follow-up; Group 1: 0/54, Group 2: 2/46 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Indirectness of outcome: No indirectness - Actual outcome: Symptomatic hypocalcaemia at post-operative period; Group 1: 0/54, Group 2: 0/46 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at end of follow-up; Deterioration in renal function at end of follow-up; Fractures (vertebral or long bone) at end of follow-up; Occurrence of kidney stones at end of follow-up; Persistent hypercalcaemia at end of follow-up; BMD of the distal radius or the lumbar spine at end of follow-up; Length of hospital stay at end of follow-up; Reoperation at end of follow-up; Unnecessary neck exploration at end of follow-up; Mortality at end of follow-up

Study	Sadik 2011[24]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in Irish Republic; Setting: Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: follow-up- 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Single parathyroid adenoma
Subgroup analysis within study	Not applicable

Study	Sadik 2011[24]
Inclusion criteria	Not stated
Exclusion criteria	Not stated
Recruitment/selection of patients	All patients presenting with a bio-chemical diagnosis of primary hyperparathyroidism between July 2003 and May 2005 were studied. Twenty patients underwent MIPUSS and 10 patients were selected for open procedure (OP). One patient with 4-gland hyperplasia on Sestamibi and ultra-sonographic studies was excluded.
Age, gender and ethnicity	Age - Mean (SD): open procedure- 61.5 +/- 10.46; MIPUSS-65.0 +/-14.59. Gender (M:F): open procedure- 3/7 ; MIPUSS- 5/15. Ethnicity: not stated
Further population details	Not stated
Extra comments	Patients presenting with a bio-chemical diagnosis of primary hyperparathyroidism. Average pre-op serum: OP 2.90 +/- 0.35; MIPUSS 2.96 +/- 0.26
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Surgical techniques - Targeted/focused with localisation technique/s. Minimally invasive parathyroidectomy using surgical sonography (MIPUSS) Pre-operative management: All thirty selected patients underwent pre-admission investigative imaging using 99mTc-sestamibi. Injection of 20 to 25 mCi 99mTc-sestamibi was performed and views were acquired at 15, 60, and 180 minutes utilising identical acquisition parameters. A consultant radiologist and surgeon reviewed all scans. Operative procedure-patients underwent general anaesthesia with endotracheal intubation Once positioned, a surgeon trained in ultrasonography used a 10MHz linear array ultrasound probe (Sonosite, USA) to localise the lesion. The adenoma was identified as a hypoechoic area close to the thyroid. The site was localised percutaneously and the neck marked over the maximum transverse and longitudinal planes. Where these two lines intersected a 3 cm transverse mark was placed on the neck. Following skin preparation, the area of incision was infiltrated with 10cc of local anaesthetic (xylocaine 0.5% with 1:10,000 adrenaline) and the incision made. Sub-platysmal planes were created and the strap muscles were mobilised. The thyroid plane was then entered between the strap muscles and the sternocleidomastoid muscle. The plane was then continued down to the adenoma. Once visualised, the adenoma was not immediately mobilised, instead a 14-gauge needle was placed through the wound onto the adenoma. Once the lesion was concordant with ultrasound findings and the recurrent laryngeal nerve identified and avoided, the adenoma was then excised and confirmed on frozen section. The neck was closed with interrupted absorbable sutures and interrupted non-absorbable sutures to the skin which were removed at 48 hours and

Study	Sadik 2011[24]
	replaced with adhesive strips. No drain was used. Duration not stated. Concurrent medication/care: not stated. Indirectness: No indirectness (n=10) Intervention 2: Surgical techniques - Non-targeted/non-focused without localisation technique/s. Conventional unilateral open procedure (OP) without sonography. All patients underwent pre-admission investigative imaging using 99m Tc-sestamibi. Injection of 20 to 25 mCi 99mTc-sestamibi was performed and views were acquired at 15, 60, and 180 minutes utilising identical acquisition parameters. No ultrasound was used intraoperatively in these cases. After administration of general anaesthesia and intubation the patient was similarly positioned as MIPUSS. A 6 cm unilateral incision was made in order to allow exploration of superior and inferior parathyroids on the side localised by preoperative sestamibi scan. The anatomic approach and closure are as same as for MIPUSS. Duration not stated. Concurrent medication/care: not stated. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TARGETED/FOCUSED WITH LOCALISATION TECHNIQUE/S versus NON-TARGETED/NON-FOCUSED/4-GLAND EXPLORATION WITHOUT LOCALISATION TECHNIQUE/S Protocol outcome 1: Adverse events (bleeding [return to theatre], severe hypocalcaemia, hypercalcemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) at end of follow-up - Actual outcome: Temporary hypocalcaemia at 30 days; Group 1: 2/20, Group 2: 3/10 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome: Temporary recurrent laryngeal nerve palsy at 30 days; Group 1: 1/20, Group 2: 0/10 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Length of hospital stay at end of follow-up - Actual outcome: Hospital stay at hours; Group 1: mean 22.64 (SD 4.13); n=20, Group 2: mean 47.5 (SD 9.81); n=10 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at end of follow-up; Deterioration in renal function at end of follow-up; Fractures (vertebral or long bone) at end of follow-up; Occurrence of kidney stones at end of follow-up; Persistent hypercalcaemia at end of follow-up; BMD of the distal radius or the lumbar spine at end of follow-up; Reoperation at end of

Study	Sadik 2011[24]
	follow-up; Unnecessary neck exploration at end of follow-up; Mortality at end of follow-up

Study	Slepavicius 2008[27]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in Lithuania; Setting: University hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: follow-up: 1 month, 6 months and 1 year after surgery
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Single parathyroid adenoma
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients from 18 to 90 years of age with diagnosis of primary hyperparathyroidism and having indications for surgical treatment.
Exclusion criteria	Family history of PHPT, relapse of PHPT, previous neck surgery, patients with indications for partial or complete removal of thyroid gland, severe concomitant pathology, making surgical treatment impossible, patients that due to psychical disorders cannot evaluate adequately their health status, pregnancy and breast feeding, patients with symptoms of hypercalcaemic crisis, patients refusing to participate during the study.
Recruitment/selection of patients	Fifty seven patients were referred to the department of abdominal and endocrine surgery of Klaipeda University Hospital and second department of abdominal surgery of Vilnius University Hospital. For the first surgery for PHPT between February 2005 and February 2008. Before surgery patients with diagnosis of PHPT determined clinically and with lab tests were divided into 2 groups.
Age, gender and ethnicity	Age - Range: 18-90 years. Gender (M:F): not stated. Ethnicity: not stated
Further population details	Not stated
Extra comments	Patients with diagnosis of primary hyperparathyroidism. All patients were symptomatic.
Indirectness of population	No indirectness
Interventions	(n=24) Intervention 1: Surgical techniques - Targeted/focused with localisation technique/s. Focused parathyroidectomy (FP) group patients were those for which focused parathyroidectomy was performed. For those patients' pre-operative localisation studies before operation as well as intraoperative IPTH monitoring and frozen sections were performed.

Study	Slepavicius 2008[27]
	All patients underwent parathyroidectomy under GA. For FP a 2-2.5 cm transverse incision placed on the side of the abnormal gland, medial to the medial margin of the sternocleidomastoid muscle. The incision presumed inferior gland was placed 2 cm above the clavicle, whereas that one for presumed superior gland was placed somewhat higher. The platysma was transected and the sternocleidomastoid muscle was retracted laterally to expose the strap muscles. These were retracted exposing a space of thyroid and parathyroid glands. Parathyroid scintigraphy was performed with 99mTc99m-sestamibi for pre-operative dual-phase sestamibi parathyroid scan of the neck and chest with planar images. A true positive result was defined as a single abnormal focal accumulation or suspected adenoma on sestamibi or ultrasound scanning that corresponded anatomically to a surgically proven parathyroid adenoma. All parathyroidectomies were guided by intact parathyroid hormone (IIPTH) monitoring. Duration surgery (day 1) and discharge (day 2). Concurrent medication/care: Calcium and vitamin D preparations after surgery were administered only in case of occurrence of symptoms of post-surgery hypocalcaemia. Indirectness: No indirectness (n=23) Intervention 2: Surgical techniques - Non-targeted/non-focused without localisation technique/s. Conventional surgery group patients were those for which parathyroidectomy was performed with traditional Kocher incision and revision of all parathyroid glands and frozen section examination. Localisation examination before surgery was not carried out. For traditional group of patients surgery was performed through a 6-8 cm standard Kocher incision. Wound drainage was not used for both patient groups. Neither intact parathyroid hormone (IIPTH) monitoring nor pre-operative localisation performed. Duration surgery (day 1) and discharge (day 2). Concurrent medication/care: Calcium and vitamin D preparations after surgery were administered only in case of occurrence of symptoms of post-surgery hypocalcaemia. Indirectness: No indirectness Comments: For patients of both groups, the following blood tests were performed: general blood, electrolytes, creatinine, IPTH, alkaline phosphatase. Bone density was determined by DXA method. For all patients kidney echoscopy was performed. If hyperplasia of parathyroid glands was found during the surgery, those patients were excluded from the study. The diagnosis of parathyroid adenoma and hyperplasia was established by conventional histologic criteria supported by gross morphology in both groups and by the intra-operative decrease of IIPTH concentration in the FP group. Solitary parathyroid gland adenoma was confirmed by pathological examination in all 21/24 patients in the

Study	Slepavicius 2008[27]
	focused group. In 3 focused group patients, IIPTH level 15 min after resection of parathyroid gland did not drop more than 50% from the baseline. Operation was converted to conventional and hyperplasia of all parathyroid glands was found. From 23 patients operated by conventional method, two patients had hyperplasia.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TARGETED/FOCUSED WITH LOCALISATION TECHNIQUE/S versus NON-TARGETED/NON-FOCUSED/4-GLAND EXPLORATION WITHOUT LOCALISATION TECHNIQUE/S Protocol outcome 1: Adverse events (bleeding [return to theatre], severe hypocalcaemia, hypercalcaemia, laryngeal nerve injury, vocal cord paralysis/laryngeal nerve injury, haematoma, infection) at end of follow-up - Actual outcome: Temporary recurrent laryngeal nerve palsy at post-operative follow-up; Group 1: 1/21, Group 2: 1/21; Comments: Palsy disappeared in both patients during 1 month after surgery. Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome: Hypocalcaemia at 30 days after surgery; Group 1: 0/21, Group 2: 1/21 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at end of follow-up; Deterioration in renal function at end of follow-up; Fractures (vertebral or long bone) at end of follow-up; Occurrence of kidney stones at end of follow-up; Persistent hypercalcaemia at end of follow-up; BMD of the distal radius or the lumbar spine at end of follow-up; Length of hospital stay at end of follow-up; Reoperation at end of follow-up; Unnecessary neck exploration at end of follow-up; Mortality at end of follow-up