National Institute for Health and Care Excellence

Final

Hyperparathyroidism (primary): diagnosis, assessment and initial management

[F] Evidence review for management options in failed primary surgery

NICE guideline NG132

Intervention evidence review

May 2019

Final

This evidence review was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN: 978-1-4731-3415-7

Contents

1 Management options in failed primary surgery

1.1 Review question: What are the management options for people in whom primary parathyroid surgery has failed?

1.2 Introduction

Approximately 4–5% of people are not cured after the first parathyroid surgery. Surgery may fail to normalise serum calcium for a number of reasons including not removing the adenoma(s) or missing a diagnosis of familial hypocalciuric hypercalcaemia (FHH). In the former scenario there is variation in the application of further diagnostic tests and differing views about the type of second surgery, if any, to be offered. If no surgery is offered then a decision has to be made as to whether to offer medical treatments.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults (18 years or over) with primary hyperparathyroidism in whom primary surgery has failed.
Interventions	• Re-operation • Calcimimetics • Bisphosphonates • Monitoring
Comparisons	All interventions compared to each other
Outcomes	Critical outcomes: • HRQOL (continuous outcome) • Mortality (dichotomous outcome) • Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous) Important outcomes: • Deterioration in renal function (dichotomous) • Persistent hypercalcaemia (dichotomous outcome) • Cardiovascular events (dichotomous outcome) • Adverse events (dichotomous outcome) • Cancer incidence (dichotomous outcome)
Study design	RCTs and systematic reviews of RCTs In absence of RCT evidence, NRSs will be included Cohort/cross-sectional studies for diagnostic accuracy and RCTs for test and treat for surgical localisation.

1.4 Clinical evidence

1.4.1 Included studies

No specific search was conducted for this review. We looked for relevant studies in patients with failed primary surgery from the evidence reviews on bisphosphonates, calcimimetics, monitoring, surgical indications, surgical interventions, surgical localisation and monitoring. Three studies were included from the calcimimetics and surgical localisation reviews. No relevant clinical studies including this group were identified in the bisphosphonates, surgical indications, surgical interventions or monitoring evidence reviews.

One study [482] in the calcimimetics evidence review included a subgroup of patients who previously had failed parathyroidectomy and was included in this review. The study compared oral cinacalcet tablets with placebo for treatment of people with primary hyperparathyroidism. The proportion of participants achieving normocalcaemia (serum calcium ≤2.57 mmol/litre) with a minimum of 0.12 mmol/litre reduction from baseline was reported separately for the subgroup of patients with failed primary surgery (n=18) and is presented in this review. Evidence on lumbar and distal radius BMDs and withdrawals due to adverse events that were also measured in the study was not available for the aforementioned subgroup. There were 8 diagnostic accuracy studies in the surgical localisation review that included a re-operation stratum. Of those, 2 studies reported results of participants with re-operation separately and were included in the present review.[84, 526] These were assessing the diagnostic accuracy of imaging techniques: sestamibi scanning (MIBI) and intra-operative localisation techniques: intra-operative parathyroid hormone monitoring (IOPTH), to aid parathyroid surgery.

These are summarised in Table 2 and Table 3 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 4,

Table **5** and Table 6). See also the study selection flow chart in appendix C, forest plot in appendix E, study evidence tables in appendix D, GRADE tables in appendix F and excluded studies list in appendix I.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of the calcimimetics study included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Peacock 2005 [482]	Cinacalcet versus placebo	n=18 Mild to moderate PHPT with disease severity ranging from asymptomatic to symptomatic Serum calcium 2.57–3.12 mmol/L	Proportion of participants achieving normocalcaemia (serum calcium ≤2.57 mmol/L) with a minimum of 0.12 mmol/L reduction from baseline (follow-up 24 & 52 weeks)	Calcimimetics review Outcome for previous surgery is reported at 52 weeks. It is unclear to which time period patients achieving normocalcaemia were observed – but mean serum Ca for re-operation strata is reported at 52 weeks.

Table 3: Summary of diagnostic accuracy studies from surgical localisation included in the evidence review

Study	Population (number of participants; 1st/re-operation strata; any preselection)	Index test(s)	IOPTH results after 1st gland / all glands excised	IOPTH threshold & timepoint
Bonjer 1997 [84]	n=27 (n=25 with PHPT) 16% re-operation (results reported separately)	MIBI	N/A	N/A
Rossi 2000 [526]	n=11 73% re-operation (analysed in mixed 1st and re-operation; except for IOPTH can subgroup into 1st operation and re-operation)	IOPTH	IOPTH results after all glands excised (all had solitary adenoma)	>50% drop at 5 or 10 minutes from baseline (unclear if pre-incision or pre-excision)

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 4: Clinical evidence summary: Cinacalcet versus placebo in patients who had re-operation

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Cinacalcet (95% CI)
Normocalcaemia (serum Ca ≤ 2.57 mmol/L) cases	18 (1 study) 24 & 52 weeks	VERY LOW [a,b] due to risk of bias, imprecision	RR 7 (1.07 to 45.9)	Moderate	
				111 per 1000	666 more per 1000 (from 8 more to 1000 more)

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 5: Clinical evidence summary: Diagnostic accuracy of imaging localisation test – Re-operation stratum

Index Test (Threshold)	Number of studies	N	Quality	Sensitivity % (95% CI)	Specificity % (95% CI)
MIBI					
MIBI	1	4	LOW[a] due to imprecision	100% (40 to100%)	Not estimable

a. Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. The evidence was downgraded by 1 increment when the confidence interval around the point estimate crossed 1 clinical decision threshold: 50% or 90%. The evidence was downgraded by 2 increments when the confidence interval around the point estimate crossed 2 clinical decision thresholds (50% and 90%).

Table 6: Clinical evidence summary: Diagnostic accuracy of intra-operative tests - Re-operation stratum

Index Test (Threshold)	Number of studies	N	Quality	Sensitivity % (95% CI)	Specificity % (95% CI)
IOPTH					
>50% drop at ≤10 minutes	1	3	VERY LOW[a,b] due to risk of bias, imprecision	100% (29 to 100%)	Not estimable
>50% drop at >10 minutes	0	-	-	-	-
>50% drop at 10 minutes, plus 20 minute sample in people without a drop at 10 minutes	0	-	-	-	-
Frozen Section					
Frozen section	0	-	-	-	-

The committee deemed the sensitivity and specificity as equally important for decision-making. The assessment of the evidence quality was conducted with equal emphasis on both the sensitivity and specificity (if there was no inconsistency or imprecision in either measure then no downgrade was made, but if there was inconsistency or imprecision in either the sensitivity or specificity then appropriate downgrades were made for inconsistency/imprecision).
a. Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
b. Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. The evidence was downgraded by 1 increment when the confidence interval around the point estimate crossed 1 clinical decision threshold: 50% or 90%. The evidence was downgraded by 2 increments when the confidence interval around the point estimate crossed 2 clinical decision thresholds (50% and 90%).

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.5.3 Unit costs

The committee discussed that there were multiple possible management pathways for people where surgery has failed including reoperation, pharmacological management, and monitoring. The unit costs potentially associated with each of these are presented below for consideration.

Table 7: Costs associated with reoperation

Description	Cost	Notes	Source
Pre-operative imaging techniques			
Ultrasound scan	£52	Ultrasound Scan with duration of less than 20 minutes, without contrast	NHS Reference Costs 2016/17[174]
Sestamibi scan	£189	Nuclear Medicine Parathyroid scan	NHS Reference Costs 2016/17[174]
SPECT/CT	£284	Single Photon Emission Computed Tomography with Computed Tomography (SPECT-CT) of One Area, 19 years and over	NHS Reference Costs 2016/17[174]
CT	£121	Computerised Tomography Scan of One Area, with Pre- and Post-Contrast	NHS Reference Costs 2016/17[174]
MRI	£162	Magnetic Resonance Imaging Scan of One Area, with Post-Contrast Only, 19 years and over	NHS Reference Costs 2016/17[174]
Parathyroid angiography and venous sampling	£1,320		Hospital trust of committee member
Consultations			
Outpatient appointment	£158	Endocrinology outpatient consultation	NHS Reference Costs 2016/17[174]
Re-operation			
Parathyroidectomy[(a)]	£3,417	Parathyroid Procedures with CC Score 2+	NHS Reference Costs 2016/17[174]

(a) Assumed to be a complex case and therefore higher CC score to reflect higher cost of re-intervention

Table 8: Cost of pharmacological treatment for people where surgery has failed

Drug	Dose	Cost – month	Cost – annual
Calcimimetics			
Cinacalcet	60 mg (30 mg twice daily)	£273	£3,278
Bisphosphonates			

Drug	Dose	Cost – month	Cost – annual
Alendronic acid (tablet)	70 mg weekly	£0.78	£9.39
Zoledronic acid (IV)	50 mcg/ml once a year	-	£13.24 [+ £260 for delivery (day case)]

Source: BNF – September 2017[313], NHS Drug Tariff 2017[451] eMIT[153]

Table 9: Monitoring costs

Description	Cost	Notes	Source
GP consultation	£37	Assumed average duration of 9.22 minutes	PSSRU 2017[159]
Blood tests (adjusted serum calcium, serum creatinine, renal function, lipids)	£1.13	Clinical biochemistry test	NHS Reference Costs 2016/17[174]
PTH	£8		Average of three NHS hospitals sought by the committee
Blood test for vitamin D	£16.50	Average of two NHS hospitals[(a)]	Filby 2014[213]
DXA scan	£83	In outpatient setting	NHS Reference Costs 2016/17[174]
Ultrasound scan	£52	Ultrasound scan with duration of less than 20 minutes, without contrast	NHS Reference Costs 2016/17[174]
X-ray	£30	Direct access plain film	NHS Reference Costs year[173]
Blood pressure	£6	Assume cost of 15 minute contact with community or hospital based nurse	PSSRU 2017[159]
ECG	£37		NHS Reference costs 10/11[175]

1.6 Resource costs

The recommendations made by the committee based on this review are not expected to have a substantial impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

1.7.1.1 Calcimimetics versus placebo

There was clinically important benefit of a calcimimetic (cinacalcet) for normocalcaemia – serum calcium ≤2.57 mmol/L (1 study, n=18; follow up 52 weeks; Very Low quality).

No evidence was identified for the outcomes of health-related quality of life; mortality; preservation of end organ function (bone mineral density, fractures, renal stones and renal function); deterioration of renal function; cardiovascular events; adverse events; cancer incidence.

1.7.1.2 Diagnostic accuracy of localisation tests

One study showed that MIBI had 100% (40 to 100%) sensitivity in people with failed primary surgery (n=4; Low quality). Specificity was not estimable.

One study showed that IOPTH had 100% (29 to 100%) sensitivity in people with failed primary surgery (n=3; Very Low quality). Specificity was not estimable.

No evidence was identified for the specificity; sensitivity of US imaging; SPECT; SPECT-CT; MRI; 4DCT; CT; Parathyroid venous sampling; Methylene blue; Intra-operative frozen sections.

1.7.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

The committee considered the outcomes of health-related quality of life, mortality and preservation of end organ function (bone mineral density, fractures, renal stones and renal function) as critical outcomes for decision making. Other important outcomes included deterioration in renal function, persistent hypercalcaemia, cardiovascular events, adverse events and cancer incidence for the intervention studies. Sensitivity and specificity were considered outcomes of interest for the diagnostic accuracy of index tests (localisation and intra-operative techniques).

No evidence was identified for the critical outcomes for participants with previous failed surgery in any of the primary evidence reviews on bisphosphonates, surgical indications, surgical interventions (focused surgery versus 4-gland exploration) and monitoring.

No evidence was identified for the outcomes of lumbar and distal radius BMDs and withdrawals due to adverse events reported in the calcimimetics review for participants with previous failed surgery. No evidence was identified for the specificity of localisation tests in participants having re-operation in the surgical localisation review.

1.8.1.2 The quality of the evidence

The quality of the evidence comparing the use of cinacalcet with placebo in terms of normocalcaemia included in this review was Very Low due to risk of bias and imprecision. The evidence was available from only one study with a short-term follow-up of 52 weeks, limiting our confidence in the estimate of the effect of cinacalcet and our ability to draw conclusions about their long-term impact on normocalcaemia.

The evidence regarding the diagnostic accuracy of sestamibi (MIBI) was available from one study. The evidence was of Low quality and was downgraded for imprecision. Evidence on the sensitivity of IOPTH was only available from one study and only for the ≤10 minute time point drop for re-operation patients. The quality of the evidence was Very Low and was downgraded for risk of bias and imprecision. Overall, the diagnostic accuracy studies included in this review had a small number of participants with re-operation which could explain the absence of data with regards to the specificity of the tests.

1.8.1.3 Benefits and harms

Surgery

There was no evidence available on repeat surgery for people with previous failed surgery. The committee from their experience stated that repeat parathyroid surgery is relatively uncommon and failure rates are higher than primary surgery, and hence felt that consideration should be given to these operations being directed to centres with the relevant experience.

The committee discussed that when there is a failure to bring about normocalcaemia after primary parathyroid surgery, a confirmation of the underlying diagnosis of primary hyperparathyroidism, together with a review of the indications for surgery, should be made. The committee noted that two main causes of failure to restore normocalcaemia after primary surgery are: identification and removal of an enlarged parathyroid gland in the presence of unrecognised underlying multigland disease (this situation is most commonly encountered after an initial focused surgical strategy); and primary failure to identify pathological parathyroid gland at surgical exploration (this situation is often in the presence of negative pre-operative imaging and can be related to surgical experience or parathyroid glands being in an ectopic position within the neck or lying in a true ectopic position outside of the surgical field altogether).

The committee highlighted that consideration of second surgical exploration needs to be carefully reviewed by a multidisciplinary team taking into account the likely underlying pathology, findings of the initial investigations and surgical exploration and the clinical and biochemical indications for repeat surgery. The committee noted that whilst a more thorough 4-gland exploration may reveal the true parathyroid pathology, second surgical explorations are more difficult and more prone to failure and complications. Hence the committee agreed that further surgery if indicated should be performed at a centre with expertise in re-operative parathyroid surgery.

The committee agreed that if second surgical exploration is deemed inappropriate or declined, medical strategies should be considered to reduce the ongoing risk of end organ damage.

Pre-operative localisation

Evidence for pre-operative localisation in people undergoing repeat surgery was available for sestamibi scanning and intra-operative parathyroid hormone monitoring (IOPTH). The results for both tests showed a very high sensitivity for patients undergoing re-operation. The committee noted that the sensitivity evidence was based on a very limited sample of people having re-operation and that the lack of evidence on the specificity of the diagnostic tests was due to this very small number of patients. No evidence relevant to participants undergoing re-operation was available for any other index tests including US imaging, SPECT, MRI, CT and intra-operative frozen sections.

The committee discussed the usefulness of pre-operative localisation to inform surgical approach. The committee discussed various pre-operative localisation techniques including sestamibi scanning, US of the neck, SPECT/CT, 4DCT, venous sampling and PET scanning options. Due to lack of sufficient evidence, the committee did not make a specific recommendation for the type of pre-localisation technique. The committee agreed that further localisation for patients with failed surgery should take place at a specialised centre with expertise and should be the result of a decision made by a multi-disciplinary team at the centre. They felt that the choice of imaging should depend on the preference of the surgeon and the local availability and expertise. The committee considered that pre-operative localisation needs to be determined in the context of review of previous localisation findings.

Calcimimetics

Evidence from one study including a sub-group of patients who had previous failed surgery showed that for treatment with cinacalcet there was a clinical benefit of achieving normocalcaemia (serum Ca ≤2.57 mmol/litre) compared to placebo for those patients. The committee noted that the cut-off point used to define normocalcaemia did not reflect the 2.6 mmol/litre cut-off most commonly used in UK current practice. This discrepancy may limit the usefulness of the outcome in evaluating the effect of cinacalcet on normocalcaemia. In addition, the committee noted that the 52 week follow-up of the study and the small sample size of people with re-operation included in the study limit the ability to draw conclusions with regards to the use of calcimimetics for renal stones.

The committee discussed the cut-off values for hypercalcaemia and use of cinacalcet. The clinical benefit in quality of life in this review was judged to be in people with an adjusted serum calcium level above 2.85 mmol/litre. Therefore, the cut-off was set at 2.85 mmol/litre for people with symptoms of hypercalcaemia. For the cut-off to define hypercalcaemia in the presence or absence of symptoms, the committee agreed from clinical experience that this should be set at above 3.0 mmol/litre, largely due to the increased risk of hypercalcaemic crises that may be seen with this degree of hypercalcaemia. Based on the evidence and their clinical experience, the committee agreed that in people eligible for surgery and who have calcium levels above 2.85 mmol/litre, treatment with cinacalcet would help in reduction of symptoms. The committee also agreed that people with a calcium level above 3.0 mmol/litre would be likely to benefit from a reduced risk of hypercalcaemic crisis with cinacalcet, irrespective of whether they had symptoms or not.

The committee discussed that for people with an initial albumin-adjusted serum calcium level below 3.0 mmol/litre, continuation of treatment should be based on reduction in symptoms and for people with initial albumin-adjusted serum calcium level 3.0 mmol/litre or above, continuation of treatment should be based on either reduction in serum calcium or reduction in symptoms.

The committee agreed that albumin-adjusted serum calcium level should be measured before initiation of cinacalcet treatment and within 1 week after starting treatment or adjusting the dose. They also agreed that albumin-adjusted serum calcium level should be measured every 2–3 months to manage treatment related changes in serum calcium. This is in accordance with the British National Formulary.

The committee agreed to make recommendations specifically for cinacalcet as the evidence was available only for this type of calcimimetic and they also felt that if another calcimimetic was to be available in the future for use in primary hyperparathyroidism, the criteria for its use would be different. Hence they agreed that these recommendations should be applicable to cinacalcet only.

Bisphosphonates

No evidence was identified for the use of bisphosphonates in primary hyperparathyroidism patients with previous failed surgery. Based on the evidence for people with primary hyperparathyroidism and bone end organ effects (see evidence report H) and their experience, the committee agreed that bisphosphonate treatment should be considered in people with failed primary surgery as a means of improving bone mineral density to reduce fracture risk in line with NICE guideline on osteoporosis: assessing the risk of fragility fracture. This may be particularly relevant for people where there is a significant delay in offering re-operative surgical cure.

Monitoring

No evidence was available for monitoring people with failed surgery. Based on their experience, the committee agreed that monitoring in people with failed surgery would be in line with those who have not had previous surgery (see evidence report I), in order to assess progression of disease and/or meeting eligibility criteria for re-surgery. Monitoring should be considered to bridge the gap between first surgery and MDT review and re-assessment in a specialist centre. The committee agreed that symptoms and comorbidities should be assessed annually or at presentation and albumin-adjusted serum calcium and eGFR or serum creatinine annually; DXA scan should be considered at diagnosis and every 2 to 3 years (as bone mineral changes take a long time to manifest on DXA scan) and ultrasound of the renal tract should be performed in cases where renal stones are suspected, to help determine the optimal management pathway. The committee considered that monitoring serum calcium level and symptoms of hypercalcaemia would support discussion of the most appropriate treatment strategy, including repeat surgery. Ultrasound of the kidneys would help in identifying cause for specific interventions or appropriate referral, and DXA scan would help in assessing fracture risk and/or the need for bisphosphonates.

1.8.2 Cost effectiveness and resource use

No relevant health economic evaluations were identified for this question.

Unit costs were presented to the committee to aid their consideration of cost-effectiveness. These included unit costs of measures covered in other parts of this guideline, including surgery, calcimimetics, bisphosphonates, and monitoring. However, as mentioned above there was little clinical evidence available for treatment options in this population, and therefore it was difficult for the committee to formally assess the cost effectiveness of treatment options. The recommendations made were primarily consensus based.

The British Association of Endocrine and Thyroid Surgeons (BAETs) audit data suggests that in current practice the failure rate for first-time surgery in people with primary hyperparathyroidism is 4.4%, and therefore this population is small.

The committee discussed that people with failed first surgery will not have received any quality of life improvements from treatment, and potentially some disutility as a result of the surgery and scarring of the neck.

As the only definitive cure for primary hyperparathyroidism is to remove adenomas, the committee considered it important that surgery be reconsidered in this population. Due to the greater risks associated with repeat surgery, the committee considered that such a decision should be discussed with multiple professionals involved with the person's care to this point to determine whether repeat surgery is suitable. This would include the surgeon who performed the original operation, an endocrinologist, and the imaging clinician. Furthermore, the committee agreed that if repeat surgery is to be undertaken, further pre-operative imaging would be required. This will vary from case to case depending on the person's original imaging results and what was seen and noted during surgery, and therefore the committee considered it most appropriate that this be decided by the specialist centre performing the surgery after review with the MDT mentioned above. The committee noted that it is more likely that some of the more expensive imaging modalities are used in this scenario. This is because these cases are often much more complex and it is considered that these are likely to provide further detailed imaging to inform further surgery.

The committee acknowledged that repeat surgery would incur a high cost when considering the cost of clinician time in the multidisciplinary discussion, pre-op imaging and repeat surgery, which is often longer compared to first surgery. However, they discussed that although repeat surgery is likely to have a higher failure rate than first time surgery (current practice according to BAETS audit suggests 12.8%), the majority of people having repeat surgery will be cured (normocalcaemic) and likely to receive a quality of life improvement due to improvement in symptoms as well as potential reduced risk of end organ disease such as fragility fracture and renal stones. The remaining people who still have failed surgery after two operations are rare and are likely to have complex disease such as ectopic, greater than 4-gland disease or rare syndromes.

The committee discussed that the only alternative treatment to repeat surgery to treat the resultant hypercalcaemia would be to prescribe calcimimetics. This incurs a very high drug cost of around £3,300 per patient per year. The clinical review suggests there is a clinical benefit of calcimimetics in achieving normocalcaemia, but the committee noted that to maintain effectiveness continuous treatment is required. Assuming that repeat surgery and calcimimetics have the same effect in achieving normocalcaemia, the committee highlighted that surgery would be more cost effective as it requires a one-off high cost with sustained benefit due to cure, whereas calcimimetics requires continuous high cost to maintain a similar benefit without providing a definitive cure of the primary hyperparathyroidism. In addition, calcimimetics can also result in unpleasant adverse events which will incur further cost and a disutility in quality of life. Therefore overall, the committee considered that repeat surgery would be more cost effective than calcimimetics and should be offered to patients after an initial failed surgery. However, if the person declines further surgery, calcimimetics should be considered in certain populations as it is the only alternative treatment to control symptoms of, and reduce the likelihood of, end organ damage as a result of hypercalcaemia.

The committee also discussed the impact on costs and quality of life for no further treatment after failed first surgery and instead only monitoring the person. The committee considered that the cost of monitoring would be the same as that for those who have not had parathyroid surgery as they are considered to be at the same risk of end organ damage. However, there is no potential improvement in quality of life from this management option compared to surgery and calcimimetics, and in most cases is inappropriate. The committee discussed that this is unlikely to be a common option unless alternative treatment options are turned down by the person.

Taking all of the above into consideration the committee considered that repeat surgery would be the most cost effective treatment for those where first surgery has failed, and therefore made an offer recommendation for repeat surgery. However, they considered that if this was not considered suitable or was declined by the person then calcimimetics should be considered.

Overall, the committee considered that this was current practice in many areas, and therefore did not consider these recommendations would lead to a substantial resource impact.

1.8.3 Other factors the committee took into account

The committee was aware of data from the Fifth National Audit Report 2017 of The British Association of Endocrine and Thyroid Surgeons, which were discussed within the consideration of the evidence for the management options for people with failed surgery[129].

It has been reported that most patients undergoing re-operation have only had one previous exploration; however the extent of previous surgery (for example targeted/focused or bilateral exploration/4-gland exploration) was not established. The small number of reported re-operative parathyroidectomies being performed supported the need for greater sub-specialisation in cases of re-operation.

In most cases of re-operation, a single gland was removed, which implied that the reason leading to re-operation was largely due to missed solitary adenomas or a missed second adenoma. The location of the majority of glands removed at re-operation being in the neck, which is a typical anatomical location, also implied that these may be the consequence of inadequate exploration in the first operation or failure of pre-operative imaging to detect the presence of a multigland disease leading to the failure of a previous targeted operation. The next most common location of removed parathyroid glands was the ectopic neck (including lesions in the carotid sheath or intra-thyroidal parathyroid adenomas). In cases where no parathyroid gland was removed at re-operation, it was difficult to understand how the location of the tumour could have been determined with certainty.

The majority of re-operative surgeries (approximately 94%) were performed by consultants, with registrars being the main assistants, involved in approximately 30% of re-operations. Overall, the reported involvement of consultants in re-operations was 98.4%.

Persistent hypercalcaemia is a key outcome measure following re-operation as it indicates failure to cure the disease. The rate of persistent hypercalcaemia reported after re-operation was 12.8%. Cure in re-operative surgery was also linked to the number of glands removed at re-operation. The highest rate of persisting hypercalcaemia (77.8%) was noted when no glands were removed. This was followed by the removal of 3.5 glands (33.3% rate of persisting hypercalcaemia) and 3 glands (20%). Total parathyroidectomy, involving the removal of four glands, was associated with the lowest rate of persistent hypercalcaemia (0.0%), indicating a higher cure rate. The audit reported that use of intra-operative PTH assay although to a small extent did significantly improve cure rate.

References

1. Aarum S, Nordenstrom J, Reihner E, Zedenius J, Jacobsson H, Danielsson R et al. Operation for primary hyperparathyroidism: the new versus the old order. A randomised controlled trial of preoperative localisation. Scandinavian Journal of Surgery. 2007; 96(1):26-30

2. Abboud B, Sleilaty G, Ayoub S, Hachem K, Smayra T, Ghorra C et al. Intrathyroid parathyroid adenoma in primary hyperparathyroidism: Can it be predicted preoperatively? World Journal of Surgery. 2007; 31(4):817-23

3. Abdulkader R, Dharmapalaiah C, Stephenson S, Clunie G. The incidence of previously undiagnosed conditions in patients attending fracture liaison service. Annals of the Rheumatic Disease. 2012; 71(Suppl 3):AB1040

4. Adler JT, Chen H, Schaefer S, Sippel RS. What is the added benefit of cervical ultrasound to 99mTc-sestamibi scanning in primary hyperparathyroidism? Annals of Surgical Oncology. 2011; 18(10):2907-11

5. Adler JT, Sippel RS, Chen H. The influence of surgical approach on quality of life after parathyroid surgery. Annals of Surgical Oncology. 2008; 15(6):1559-65

6. Agarwal A, George RK, Gupta SK, Mishra SK. Pancreatitis in patients with primary hyperparathyroidism. Indian Journal of Gastroenterology. 2003; 22(6):224-5

7. Agarwal G, Sadacharan D, Ramakant P, Shukla M, Mishra SK. The impact of vitamin D status and tumor size on the intraoperative parathyroid hormone dynamics in patients with symptomatic primary hyperparathyroidism. Surgery Today. 2012; 42(12):1183-8

8. Agha A, Hornung M, Rennert J, Uller W, Lighvani H, Schlitt HJ et al. Contrast-enhanced ultrasonography for localization of pathologic glands in patients with primary hyperparathyroidism. Surgery. 2012; 151(4):580-6

9. Agha A, Hornung M, Stroszczynski C, Schlitt HJ, Jung EM. Highly efficient localization of pathological glands in primary hyperparathyroidism using contrast-enhanced ultrasonography (CEUS) in comparison with conventional ultrasonography. Journal of Clinical Endocrinology and Metabolism. 2013; 98(5):2019-25

10. Agha A, Scherer MN, Mantouvalou K, Woenckhaus M, Froehlich D, Barlage S et al. Effectiveness of parathyroid-hormone measurement in detecting patients with multiple gland disease causing primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2007; 392(6):703-8

11. Agus ZS. Conservative vs surgical treatment of hyperparathyroidism: which to choose, and when? Cleveland Clinic Journal of Medicine. 1993; 60(3):191-2

12. Ahmed K, Alhefdhi A, Schneider DF, Ojomo KA, Sippel RS, Chen H et al. Minimal benefit to subsequent intraoperative parathyroid hormone testing after all four glands have been identified. Annals of Surgical Oncology. 2013; 20(13):4200-4

13. Ahsan T, Erum U, Inam Pal KM, Jabeen R, Qureeshi SG, Rehman UL et al. The many guises of primary hyperparathyroidism: An unchanged scenario. Journal of the Pakistan Medical Association. 2017; 67(4):580-5

14. Akbaba G, Berker D, Isik S, Aydin Y, Ciliz D, Peksoy I et al. A comparative study of pre-operative imagingmethods in patients with primary hyperparathyroidism: Ultrasonography, Tc-99m sestamibi, single photon emission computed tomography,

and magnetic resonance imaging. Journal of Endocrinological Investigation. 2012; 35(4):359-64

15. Akbaba G, Isik S, Ates Tutuncu Y, Ozuguz U, Berker D, Guler S. Comparison of alendronate and raloxifene for the management of primary hyperparathyroidism. Journal of Endocrinological Investigation. 2013; 36(11):1076-82

16. Akin M, Atasever T, Kurukahvecioglu O, Dogan M, Gokaslan D, Poyraz A et al. Preoperative detection of parathyroid adenomas with Tc-99m MIBI and Tc-99m pertechnetate scintigraphy: histopathological and biochemical correlation with Tc-99m MIBI uptake. Bratislavske Lekarske Listy. 2009; 110(3):166-9

17. Al-Askari M, Gough J, Stringer KM, Gough IR. Surgeon-performed ultrasound in primary hyperparathyroidism: A prospective study of 204 consecutive patients. World Journal of Endocrine Surgery. 2012; 4(1):8-12

18. Alabdulkarim Y, Nassif E. Sestamibi (99mTc) scan as a single localization modality in primary hyperparathyroidism and factors impacting its accuracy. Indian Journal of Nuclear Medicine. 2010; 25(1):6-9

19. Albuja-Cruz MB, Allan BJ, Parikh PPS, Lew JI. Efficacy of localization studies and intraoperative parathormone monitoring in the surgical management of hyperfunctioning ectopic parathyroid glands. Surgery. 2013; 154(3):453-60

20. Alexandrides TK, Kouloubi K, Vagenakis AG, Yarmenitis S, Spyridonidis T, Vassilakos P et al. The value of scintigraphy and ultrasonography in the preoperative localization of parathyroid glands in patients with primary hyperparathyroidism and concomitant thyroid disease. Hormones. 2006; 5(1):42-51

21. Alhava EM, Karjalainen P, Paakkonen M. Bone mineral density and surgical treatment of primary hyperparathyroidism. Acta Chirurgica Scandinavica. 1988; 154(5-6):345-7

22. Alhefdhi A, Pinchot SN, Davis R, Sippel RS, Chen H. The necessity and reliability of intraoperative parathyroid hormone (PTH) testing in patients with mild hyperparathyroidism and PTH levels in the normal range. World Journal of Surgery. 2011; 35(9):2006-9

23. Aliyev S, Agcaoglu O, Aksoy E, Birsen O, Milas M, Mitchell J et al. An analysis of whether surgeon-performed neck ultrasound can be used as the main localizing study in primary hyperparathyroidism. Surgery. 2014; 156(5):1127-31

24. Almqvist EG, Becker C, Bondeson AG, Bondeson L, Svensson J. Early parathyroidectomy increases bone mineral density in patients with mild primary hyperparathyroidism: a prospective and randomized study. Surgery. 2004; 136(6):1281-8

25. Almqvist EG, Bondeson AG, Bondeson L, Nissborg A, Smedgård P, Svensson SE. Cardiac dysfunction in mild primary hyperparathyroidism assessed by radionuclide angiography and echocardiography before and after parathyroidectomy. Surgery. 2002; 132(6):1126-32; discussion 1132

26. Alvarez-Allende CR, Pascual Marrero AM, Castillo CA, Mendez-Latalladi W. Parathyroidectomy outcomes in normocalcemic primary hyperparathyroidism. Journal of the American College of Surgeons. 2014; 219(4 Suppl):e12

27. Amaral LM, Queiroz DC, Marques TF, Mendes M, Bandeira F. Normocalcemic versus hypercalcemic primary hyperparathyroidism: More stone than bone? Journal of Osteoporosis. 2012; 2012:128352

28. Ambrogini E, Cetani F, Cianferotti L, Vignali E, Banti C, Viccica G et al. Surgery or surveillance for mild asymptomatic primary hyperparathyroidism: a prospective, randomized clinical trial. Journal of Clinical Endocrinology and Metabolism. 2007; 92(8):3114-21

29. Ammori BJ, Madan M, Gopichandran TD, Price JJ, Whittaker M, Ausobsky JR et al. Ultrasound-guided unilateral neck exploration for sporadic primary hyperparathyroidism: Is it worthwhile? Annals of the Royal College of Surgeons of England. 1998; 80(6):433-7

30. Anderson SR, Vaughn A, Karakla D, Wadsworth JT. Effectiveness of surgeon interpretation of technetium Tc 99m sestamibi scans in localizing parathyroid adenomas. Archives of Otolaryngology - Head and Neck Surgery. 2008; 134(9):953-7

31. Anonymous. Erratum: A 10-year prospective study of primary hyperparathyroidision with or without parathyroid surgery (New England Journal of Medicine (October 21, 1999) 341 (1249-1255)). New England Journal of Medicine. 2000; 342(2):144

32. Anonymous. Surgery reduces risk of fracture in primary hyperparathyroidism. BMJ. 2000; 321(7261):C

33. Ansquer C, Mirallie E, Carlier T, Abbey-Huguenin H, Aubron F, Kraeber-Bodere F. Preoperative localization of parathyroid lesions. Value of 99mTc-MIBI tomography and factors influencing detection. Nuclear-Medizin. 2008; 47(4):158-62

34. Antonelli R, Falcone S, Scillitani A, Salcuni AS, Carnevale V, Battista C et al. Normocalcemic hyperparathyroidism: Studies on bone loss over a ten-year follow-up time. Endocrine Reviews. 2011; 32(3 Suppl):P3-105

35. Apostolopoulos DJ, Houstoulaki E, Giannakenas C, Alexandrides T, Spiliotis J, Nikiforidis G et al. Technetium-99m-tetrofosmin for parathyroid scintigraphy: Comparison to thallium-technetium scanning. Journal of Nuclear Medicine. 1998; 39(8 Suppl.):1433-41

36. Arciero CA, Peoples GE, Stojadinovic A, Shriver CD. The utility of a rapid parathyroid assay for uniglandular, multiglandular, and recurrent parathyroid disease. American Surgeon. 2004; 70(7):588-92

37. Arici C, Cheah WK, Ituarte PHG, Morita E, Lynch TC, Siperstein AE et al. Can localization studies be used to direct focused parathyroid operations? Surgery. 2001; 129(6):720-9

38. Aspinall SR, Nicholson S, Bliss RD, Lennard TWJ. The impact of surgeon-based ultrasonography for parathyroid disease on a British endocrine surgical practice. Annals of the Royal College of Surgeons of England. 2012; 94(1):17-22

39. Attie JN, Khan A, Rumancik WM, Moskowitz GW, Hirsch MA, Herman PG. Preoperative localization of parathyroid adenomas. American Journal of Surgery. 1988; 156(4):323-6

40. Babey M, Arampatzis S, Popp A, Schuematschek-Kainth J, Kopp PA, Lippuner K. Normocalcemic primary hyperparathyroidism in patients with low bone mass: Biochemical and clinical characteristics. Journal of Bone and Mineral Research. 2010; 25(S1):S259

41. Bachar G, Mizrachi A, Hadar T, Feinmesser R, Shpitzer T. Role of parathyroid hormone monitoring during parathyroidectomy. Head and Neck. 2011; 33(12):1754-7

42. Badii B, Staderini F, Foppa C, Tofani L, Skalamera I, Fiorenza G et al. Cost-benefit analysis of the intraoperative parathyroid hormone assay in primary hyperparathyroidism. Head and Neck. 2017; 39(2):241-6

43. Bai HX, Giefer M, Patel M, Orabi AI, Husain SZ. The association of primary hyperparathyroidism with pancreatitis. Journal of Clinical Gastroenterology. 2012; 46(8):656-61

44. Bailey RR, Dann E, Greenslade NF, Little PJ, McRae CU, Utley WL. Urinary stones: a prospective study of 350 patients. New Zealand Medical Journal. 1974; 79(516):961-5

45. Bambach CP, Reeve TS. Parathyroid identification by methylene blue infusion. Australian and New Zealand Journal of Surgery. 1978; 48(3):314-7

46. Bandeira F, Griz LH, Bandeira C, Pinho J, Lucena CS, Alencar C et al. Prevalence of cortical osteoporosis in mild and severe primary hyperparathyroidism and its relationship with bone markers and vitamin D status. Journal of Clinical Densitometry. 2009; 12(2):195-9

47. Bandeira FA, Oliveira RI, Griz LH, Caldas G, Bandeira C. Differences in accuracy of 99mTc-sestamibi scanning between severe and mild forms of primary hyperparathyroidism. Journal of Nuclear Medicine Technology. 2008; 36(1):30-5

48. Bandeira L, Cozadd D, Bucovsky M, McMahon DJ, Lee JA, Silverberg SJ et al. Occult nephrolithiasis in primary hyperparathyroidism. Endocrine Reviews. 2016; 37(2 Suppl 1):FRI-333

49. Bao L, Li Y, Lin H. Effect of parathyroidectomy and pharmacotherapy in primary hyperthyroidism on bone metabolism. Osteoporosis International. 2013; 24(Suppl 1):S125

50. Barber B, Moher C, Cote D, Fung E, O'Connell D, Dziegielewski P et al. Comparison of single photon emission CT (SPECT) with SPECT/CT imaging in preoperative localization of parathyroid adenomas: A cost-effectiveness analysis. Head and Neck. 2016; 38 (Suppl 1):E2062-5

51. Barczynski M, Cicho S, Konturek A, Cicho W. Minimally invasive video-assisted parathyroidectomy versus open minimally invasive parathyroidectomy for a solitary parathyroid adenoma: a prospective, randomized, blinded trial World Journal of Surgery. 2006; 30(5):721-31

52. Barczynski M, Golkowski F, Konturek A, Buziak-Bereza M, Cichon S, Hubalewska-Dydejczyk A et al. Technetium-99m-sestamibi subtraction scintigraphy vs. ultrasonography combined with a rapid parathyroid hormone assay in parathyroid aspirates in preoperative localization of parathyroid adenomas and in directing surgical approach. Clinical Endocrinology. 2006; 65(1):106-13

53. Barczynski M, Konturek A, Cichon S, Hubalewska-Dydejczyk A, Golkowski F, Huszno B. Intraoperative parathyroid hormone assay improves outcomes of minimally invasive parathyroidectomy mainly in patients with a presumed solitary parathyroid adenoma and missing concordance of preoperative imaging. Clinical Endocrinology. 2007; 66(6):878-85

54. Barczynski M, Konturek A, Hubalewska-Dydejczyk A, Cichon S, Nowak W. Evaluation of Halle, Miami, Rome, and Vienna intraoperative iPTH assay criteria in guiding minimally invasive parathyroidectomy. Langenbeck's Archives of Surgery. 2009; 394(5):843-9

55. Barczynski M, Konturek A, Hubalewska-Dydejczyk A, Cichon S, Nowak W. Utility of intraoperative bilateral internal jugular venous sampling with rapid parathyroid hormone testing in guiding patients with a negative sestamibi scan for minimally invasive parathyroidectomy--a randomized controlled trial. Langenbeck's Archives of Surgery. 2009; 394(5):827-35

56. Barkun J, Duh QY, Wiseman S, McKenzie M. Canadian Association of General Surgeons and American College of Surgeons Evidence Based Reviews in Surgery. 16. Randomized trial of parathyroidectomy in mild asymptomatic primary hyperparathyroidism. Canadian Journal of Surgery. 2006; 49(1):59-61

57. Barraclough BH, Reeve TS, Duffy PJ, Picker RH. The localization of parathyroid tissue by ultrasound scanning prior to surgery in patients with hyperparathyroidism. World Journal of Surgery. 1981; 5(1):91-5

58. Battersby C, Burnett W, Winch J. Pancreatitis associated with hyperparathyroidism. Medical Journal of Australia. 1969; 2(25):1268-70

59. Beard DE, Goodyear WE. Hyperparathyroidism and urolithiasis. Journal of Urology. 1950; 64(5):638-42

60. Berczi C, Mezosi E, Galuska L, Varga J, Bajnok L, Lukacs G et al. Technetium-99m-sestamibi/pertechnetate subtraction scintigraphy vs ultrasonography for preoperative localization in primary hyperparathyroidism. European Radiology. 2002; 12(3):605-9

61. Bergenfelz A, Algotsson L, Roth B, Isaksson A, Tibblin S, Irvin IGL. Side localization of parathyroid adenomas by simplified intraoperative venous sampling for parathyroid hormone. World Journal of Surgery. 1996; 20(3):358-60

62. Bergenfelz A, Isaksson A, Ahren B. Intraoperative monitoring of intact PTH during surgery for primary hyperparathyroidism. Langenbecks Archiv für Chirurgie. 1994; 379(1):50-3

63. Bergenfelz A, Isaksson A, Lindblom P, Westerdahl J, Tibblin S. Measurement of parathyroid hormone in patients with primary hyperparathyroidism undergoing first and reoperative surgery. British Journal of Surgery. 1998; 85(8):1129-32

64. Bergenfelz A, Jansson S, Martensson H, Reihner E, Wallin G, Kristoffersson A et al. Scandinavian quality register for thyroid and parathyroid surgery: Audit of surgery for primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2007; 392(4):445-51

65. Bergenfelz A, Kanngiesser V, Zielke A, Nies C, Rothmund M. Conventional bilateral cervical exploration versus open minimally invasive parathyroidectomy under local anaesthesia for primary hyperparathyroidism. British Journal of Surgery. 2005; 92(2):190-7

66. Bergenfelz A, Lindblom P, Tibblin S, Westerdahl J. Unilateral versus bilateral neck exploration for primary hyperparathyroidism: A prospective randomized controlled trial. Annals of Surgery. 2002; 236(5):543-51

67. Bergenfelz A, Tennvall J, Valdermarsson S, Lindblom P, Tibblin S. Sestamibi versus thallium subtraction scintigraphy in parathyroid localization: A prospective comparative study in patients with predominantly mild primary hyperparathyroidism. Surgery. 1997; 121(6):601-5

68. Bergenfelz AOJ, Jansson SKG, Wallin GK, Martensson HG, Rasmussen L, Eriksson HLO et al. Impact of modern techniques on short-term outcome after surgery for primary hyperparathyroidism: A multicenter study comprising 2,708 patients. Langenbeck's Archives of Surgery. 2009; 394(5):851-60

69. Bergenfelz AOJ, Wallin G, Jansson S, Eriksson H, Martensson H, Christiansen P et al. Results of surgery for sporadic primary hyperparathyroidism in patients with preoperatively negative sestamibi scintigraphy and ultrasound. Langenbeck's Archives of Surgery. 2011; 396(1):83-90

70. Bewick J, Pfleiderer A. The value and role of low dose methylene blue in the surgical management of hyperparathyroidism. Annals of the Royal College of Surgeons of England. 2014; 96(7):526-29

71. Bhadada SK, Arya AK, Mukhopadhyay S, Khadgawat R, Sukumar S, Lodha S et al. Primary hyperparathyroidism: insights from the Indian PHPT registry. Journal of Bone and Mineral Metabolism. 2018; 36(2):238-45

72. Bhansali A, Masoodi SR, Bhadada S, Mittal BR, Behra A, Singh P. Ultrasonography in detection of single and multiple abnormal parathyroid glands in primary hyperparathyroidism: Comparison with radionuclide scintigraphy and surgery. Clinical Endocrinology. 2006; 65(3):340-5

73. Bhatnagar A, Vezza PR, Bryan JA, Atkins FB, Ziessman HA. Technetium-99m-sestamibi parathyroid scintigraphy: Effect of P- glycoprotein, histology and tumor size on detectability. Journal of Nuclear Medicine. 1998; 39(9):1617-20

74. Biertho L, Chu C, Inabnet WB. Image-directed parathyroidectomy under local anaesthesia in the elderly. British Journal of Surgery. 2003; 90(6):738-42

75. Bilezikian JP, Doppman JL, Shimkin PM. Preoperative localization of abnormal parathyroid tissue. Cumulative experience with venous sampling and arteriography. American Journal of Medicine. 1973; 55(4):505-14

76. Billotey C, Sarfati E, Aurengo A, Duet M, Mundler O, Toubert ME et al. Advantages of SPECT in technetium-99m-sestamibi parathyroid scintigraphy. Journal of Nuclear Medicine. 1996; 37(11):1773-8

77. Bishop B, Wang B, Parikh PP, Lew JI. Intraoperative parathormone monitoring mitigates age-related variability in targeted parathyroidectomy for patients with primary hyperparathyroidism. Annals of Surgical Oncology. 2015; 22:655-61

78. Blanchard C, Mathonnet M, Sebag F, Caillard C, Kubis C, Drui D et al. Quality of life is modestly improved in older patients with mild primary hyperparathyroidism postoperatively: Results of a prospective multicenter study. Annals of Surgical Oncology. 2014; 21(11):3534-40

79. Blower PJ, Kettle AG, O'Doherty MJ, Collins RE, Coakley AJ. 123I-methylene blue: an unsatisfactory parathyroid imaging agent. Nuclear Medicine Communications. 1992; 13(7):522-7

80. Bobanga ID, McHenry CR. Is intraoperative parathyroid hormone monitoring necessary for primary hyperparathyroidism with concordant preoperative imaging? American Journal of Surgery. 2017; 213(3):484-8

81. Boggs JE, Irvin GL, III, Molinari AS, Deriso GT, Shaha AR, Watson CG et al. Intraoperative parathyroid hormone monitoring as an adjunct to parathyroidectomy. Surgery. 1996; 120(6):954-8

82. Bollerslev J, Jansson S, Mollerup CL, Nordenström J, Lundgren E, Tørring O et al. Medical observation, compared with parathyroidectomy, for asymptomatic primary hyperparathyroidism: a prospective, randomized trial. Journal of Clinical Endocrinology and Metabolism. 2007; 92(5):1687-92

83. Bollerslev J, Rosen T, Mollerup CL, Nordenström J, Baranowski M, Franco C et al. Effect of surgery on cardiovascular risk factors in mild primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2009; 94(7):2255-61

84. Bonjer HJ, Bruining HA, Valkema R, Lameris JS, de Herder WW, van der Harst E et al. Single radionuclide scintigraphy with 99mtechnetium-sestamibi and ultrasonography in hyperparathyroidism. European Journal of Surgery. 1997; 163(1):27-32

85. Bonzelaar LB, Salapatas AM, Hwang MS, Friedman M. Parathyroidectomy for hyperparathyroidism: Morbidity and mortality. Otolaryngology - Head and Neck Surgery. 2016; 155(1):P57

86. Borel Rinkes IH, Smit PC, Thijssen JH, van Vroonhoven TJ. Peroperative measurement of PTH in the management of primary hyperparathyroidism. Acta Oto-Rhino-Laryngologica Belgica. 2001; 55(2):147-152

87. Bradford Carter W, Sarfati MR, Fox KA, Patton DD. Preoperative detection of sporadic parathyroid adenomas using technetium-99m-sestamibi: What role in clinical practice? American Surgeon. 1997; 63(4):317-21

88. Bradley SJ, Knodle KF. Ultrasound based focused neck exploration for primary hyperparathyroidism. American Journal of Surgery. 2016; 213(3):452-5

89. Brardi S, Cevenini G, Verdacchi T, Romano G, Ponchietti R. Use of cinacalcet in nephrolithiasis associated with normocalcemic or hypercalcemic primary hyperparathyroidism: results of a prospective randomized pilot study. Archivio Italiano di Urologia, Andrologia. 2015; 87(1):66-71

90. Brennan MF, Doppman JL, Kurdy AG. Assessment of techniques for preoperative parathyroid gland localization in patients undergoing reoperation for hyperparathyroidism. Surgery. 1982; 91(1):6-11

91. Britton DC, Thompson MH, Johnston ID, Fleming LB. Renal function following parathyroid surgery in primary hyperparathyroidism. Lancet. 1971; 2(7715):74-75

92. Brothers TE, Thompson NW. Surgical treatment of primary hyperparathyroidism in elderly patients. Acta Chirurgica Scandinavica. 1987; 153(3):175-8

93. Broulik PD, Broulikova A, Adamek S, Libansky P, Tvrdon J, Broulikova K et al. Improvement of hypertension after parathyroidectomy of patients suffering from primary hyperparathyroidism. International Journal of Endocrinology. 2011; 2011:309068

94. Brown SJ, Lee JC, Christie J, Maher R, Sidhu SB, Sywak MS et al. Four-dimensional computed tomography for parathyroid localization: a new imaging modality. ANZ Journal of Surgery. 2015; 85(6):483-7

95. Bruining HA, Van Houten H, Juttmann JR. Results of operative treatment of 615 patients with primary hyperparathyroidism. World Journal of Surgery. 1981; 5(1):85-90

96. Bruno I, Collarino A, Perotti G, Di Giuda D, Cannarile A, Negri M et al. Diagnostic accuracy of 99mTc-Sestamibi dual-phase parathyroid scintigraphy and integrated imaging of thyroid in patients submitted to video-assisted minimally invasive parathyroidectomy. European Journal of Nuclear Medicine and Molecular Imaging. 2010; 37(2 Suppl):S446-7

97. Bugis SP, Berno E, Rusnak CH, Chu D. Technetium99m-sestamibi scanning before initial neck exploration in patients with primary hyperparathyroidism. European Archives of Oto-Rhino-Laryngology. 1995; 252(3):149-52

98. Bumpous JM, Goldstein RL, Flynn MB. Surgical and calcium outcomes in 427 patients treated prospectively in an image-guided and intraoperative PTH (IOPTH) supplemented protocol for primary hyperparathyroidism: Outcomes and opportunities. Laryngoscope. 2009; 119(2):300-6

99. Burke JF, Naraharisetty K, Schneider DF, Sippel RS, Chen H. Early-phase technetium-99m sestamibi scintigraphy can improve preoperative localization in primary hyperparathyroidism. American Journal of Surgery. 2013; 205(3):269-73

100. Burney RE, Jones KR, Coon JW, Blewitt DK, Herm AM. Assessment of patient outcomes after operation for primary hyperparathyroidism. Surgery. 1996; 120(6):1013-9

101. Burney RE, Jones KR, Peterson M, Christy B, Thompson NW, Cady B et al. Surgical correction of primary hyperparathyroidism improves quality of life. Surgery. 1998; 124(6):987-92

102. Butt HZ, Husainy MA, Bolia A, London NJ. Ultrasonography alone can reliably locate parathyroid tumours and facilitates minimally invasive parathyroidectomy. Annals of the Royal College of Surgeons of England. 2015; 97(6):420-4

103. Caixas A, Berna L, Hernandez A, Tebar FJ, Madariaga P, Vegazo O et al. Efficacy of preoperative diagnostic imaging localization of technetium 99m-sestamibi scintigraphy in hyperparathyroidism. Surgery. 1997; 121(5):535-541

104. Cakal E, Cakir E, Dilli A, Colak N, Unsal I, Aslan MS et al. Parathyroid adenoma screening efficacies of different imaging tools and factors affecting the success rates. Clinical Imaging. 2012; 36(6):688-694

105. Calo PG, Medas F, Loi G, Pisano G, Sorrenti S, Erdas E et al. Parathyroidectomy for primary hyperparathyroidism in the elderly: experience of a single endocrine surgery center. Aging Clinical and Experimental Research. 2016; 29(S1):15-21

106. Calo PG, Pisano G, Loi G, Medas F, Barca L, Atzeni M et al. Intraoperative parathyroid hormone assay during focused parathyroidectomy: the importance of 20 minutes measurement. BMC Surgery. 2013; 13:36

107. Calo PG, Pisano G, Loi G, Medas F, Tatti A, Piras S et al. Surgery for primary hyperparathyroidism in patients with preoperatively negative sestamibi scan and discordant imaging studies: The usefulness of intraoperative parathyroid hormone monitoring. Clinical Medicine Insights: Endocrinology and Diabetes. 2013; 6:63-7

108. Calo PG, Pisano G, Tatti A, Medas F, Boi F, Mariotti S et al. Intraoperative parathyroid hormone assay during focused parathyroidectomy for primary hyperparathyroidism: Is it really mandatory? Minerva Chirurgica. 2012; 67(4):337-42

109. Campbell MJ, Sicuro P, Alseidi A, Blackmore CC, Ryan JA. Two-phase (low-dose) computed tomography is as effective as 4D-CT for identifying enlarged parathyroid glands. International Journal of Surgery. 2015; 14:80-4

110. Cannon J, Lew JI, Solorzano CC. Parathyroidectomy for hypercalcemic crisis: 40 years' experience and long-term outcomes. Surgery. 2010; 148(4):807-12; discussion 812-3

111. Carlier T, Oudoux A, Mirallie E, Seret A, Daumy I, Leux C et al. 99mTc-MIBI pinhole SPECT in primary hyperparathyroidism: Comparison with conventional SPECT,

planar scintigraphy and ultrasonography European Journal of Nuclear Medicine and Molecular Imaging. 2008; 35(3):637-643

112. Carnaille B, Oudar C, Pattou F, Combemale F, Rocha J, Proye C. Pancreatitis and primary hyperparathyroidism: forty cases. Australian and New Zealand Journal of Surgery. 1998; 68(2):117-9

113. Carnaille B, Oudar C, Pattou F, Quievreux J, Proye C. Improvements in parathyroid surgery in the intact 1-84 PTH assay era. Australian and New Zealand Journal of Surgery. 1998; 68(2):112-6

114. Carneiro-Pla D. Effectiveness of "office"-based, ultrasound-guided differential jugular venous sampling (DJVS) of parathormone in patients with primary hyperparathyroidism. Surgery. 2009; 146(6):1014-20

115. Carneiro-Pla DM, Irvin GL, III, Chen H. Consequences of parathyroidectomy in patients with "mild" sporadic primary hyperparathyroidism. Surgery. 2007; 142(6):795-9

116. Carneiro-Pla DM, Solorzano CC, Irvin IGL. Consequences of targeted parathyroidectomy guided by localization studies without intraoperative parathyroid hormone monitoring. Journal of the American College of Surgeons. 2006; 202(5):715-22

117. Carneiro DM, Solorzano CC, Nader MC, Ramirez M, Irvin IGL, Udelsman R et al. Comparison of intraoperative iPTH assay (QPTH) criteria in guiding parathyroidectomy: Which criterion is the most accurate? Surgery. 2003; 134(6):973-81

118. Casara D, Rubello D, Pelizzo M, Shapiro B. Clinical role of $^{99m}TcO_4$/MIBI scan, ultrasound and intra-operative gamma probe in the performance of unilateral and minimally invasive surgery in primary hyperparathyroidism. European Journal of Nuclear Medicine. 2001; 28(9):1351-9

119. Casas AT, Burke GJ, Mansberger AR, Wei JP. Impact of technetium-99m-sestamibi localization on operative time and success of operations for primary hyperparathyroidism. American Surgeon. 1994; 60(1):12-6; discussion 16-7

120. Casas AT, Burke GJ, Sathyanarayana, Mansberger AR, Jr, Wei JP. Prospective comparison of technetium-99m-sestamibi/iodine-123 radionuclide scan versus high-resolution ultrasonography for the preoperative localization of abnormal parathyroid glands in patients with previously unoperated primary hyperparathyroidism. American Journal of Surgery. 1993; 166(4):369-73

121. Casez JP, Tschopp P, Sandberg Tschopp A, Lippuner K, Zingg E, Jaeger P. Effects of nasal calcitonin on bone mineral density following parathyroidectomy in patients with primary hyperparathyroidism. Hormone Research. 2003; 59(6):263-9

122. Cassibba S, Pellegrino M, Gianotti L, Baffoni C, Baralis E, Attanasio R et al. Silent renal stones in primary hyperparathyroidism: prevalence and clinical features. Endocrine Practice. 2014; 20(11):1137-42

123. Catania A, Sorrenti S, Falvo L, Santulli M, Berni A, De Antoni E. Validity and limits of intraoperative rapid parathyroid hormone assay in primary hyperparathyroidism treated by traditional and mini-invasive surgery. International Surgery. 2002; 87(4):226-32

124. Catargi B, Raymond JM, Lafarge-Gense V, Leccia F, Roger P, Tabarin A. Localization of parathyroid tumors using endoscopic ultrasonography in primary hyperparathyroidism. Journal of Endocrinological Investigation. 1999; 22(9):688-92

125. Caudle AS, Brier SE, Calvo BF, Hong JK, Meyers MO, Ollila DW. Experienced radio-guided surgery teams can successfully perform minimally invasive radio-guided parathyroidectomy without intraoperative parathyroid hormone assays. American Surgeon. 2006; 72(9):785-9

126. Caveny SA, Klingensmith WC, 3rd, Martin WE, Sage-El A, McIntyre RC, Jr., Raeburn C et al. Parathyroid imaging: the importance of dual-radiopharmaceutical simultaneous acquisition with 99mTc-sestamibi and 123I. Journal of Nuclear Medicine Technology. 2012; 40(2):104-10

127. Cayo AK, Sippel RS, Schaefer S, Chen H. Utility of intraoperative PTH for primary hyperparathyroidism due to multigland disease. Annals of Surgical Oncology. 2009; 16(12):3450-4

128. Cesareo R, Stasio E, Vescini F, Campagna G, Cianni R, Pasqualini V et al. Effects of alendronate and vitamin D in patients with normocalcemic primary hyperparathyroidism. Osteoporosis International. 2017; 26(4):1295-302

129. Chadwick D, Kinsman R, Walton P. Fifth national audit report. The British Association of Endocrine & Thyroid Surgeons, 2017. Available from: http://www.baets.org.uk/wp-content/uploads/BAETS-Audit-National-Report-2017.pdf

130. Cham S, Sepahdari AR, Hall KE, Yeh MW, Harari A. Dynamic parathyroid computed tomography (4dct) facilitates reoperative parathyroidectomy and enables cure of missed hyperplasia. Annals of Surgical Oncology. 2015; 22(11):3537-42

131. Chan RK, Ibrahim SI, Pil P, Tanasijevic M, Moore FD, Jr. Validation of a method to replace frozen section during parathyroid exploration by using the rapid parathyroid hormone assay on parathyroid aspirates. Archives of Surgery. 2005; 140(4):371-3

132. Chapuis Y, Fulla Y, Bonnichon P, Tarla E, Abboud B, Pitre J et al. Values of ultrasonography, sestamibi scintigraphy, and intraoperative measurement of 1-84 PTH for unilateral neck exploration of primary hyperparathyroidism. World Journal of Surgery. 1996; 20(7):835-40

133. Chatterton BE, Wycherley AG, Muecke TS, Hoare LL, Malycha P. Thallium-201-technetium-99m subtraction scanning: its value in 50 cases of hyperparathyroidism submitted to surgery. Australian and New Zealand Journal of Surgery. 1987; 57(5):289-94

134. Chen CC, Holder LE, Scovill WA, Tehan AM, Gann DS. Comparison of parathyroid imaging with technetium-99m- pertechnetate/sestamibi subtraction, double-phase technetium-99m-sestamibi and technetium-99m-sestamibi SPECT. Journal of Nuclear Medicine. 1997; 38(6):834-9

135. Chen H, Mack E, Starling JR, Irvin GL, III, Clark OH, Prinz RA et al. A comprehensive evaluation of perioperative adjuncts during minimally invasive parathyroidectomy: Which is most reliable? Annals of Surgery. 2005; 242(3):375-83

136. Chen H, Parkerson S, Udelsman R. Parathyroidectomy in the elderly: Do the benefits outweigh the risks? World Journal of Surgery. 1998; 22(6):531-6

137. Chen H, Pruhs Z, Starling JR, Mack E. Intraoperative parathyroid hormone testing improves cure rates in patients undergoing minimally invasive parathyroidectomy. Surgery. 2005; 138(4):583-90

138. Chen H, Sokoll LJ, Udelsman R. Outpatient minimally invasive parathyroidectomy: A combination of sestamibi-SPECT localization, cervical block anesthesia, and intraoperative parathyroid hormone assay. Surgery. 1999; 126(6):1016-22

139. Cheng SP, Lee JJ, Liu TP, Yang PS, Liu SC, Hsu YC et al. Quality of life after surgery or surveillance for asymptomatic primary hyperparathyroidism: A meta-analysis of randomized controlled trials. Medicine. 2015; 94(23):e931

140. Cheung K, Wang TS, Farrokhyar F, Roman SA, Sosa JA. A meta-analysis of preoperative localization techniques for patients with primary hyperparathyroidism Annals of Surgical Oncology. 2012; 19(2):577-83

141. Chick WK, Tai DKC, Shek ACC, Tang PLF. Use of intraoperative parathyroid hormone assay in primary hyperparathyroidism: A selective approach. Surgical Practice. 2017; 21(1):42-9

142. Chigot JP, Menegaux F, Achrafi H. Should primary hyperparathyroidism be treated surgically in elderly patients older than 75 years? Surgery. 1995; 117(4):397-401

143. Chiu B, Sturgeon C, Angelos P, Talpos GB, Grant CS, Snyder S et al. Which intraoperative parathyroid hormone assay criterion best predicts operative success? A study of 352 consecutive patients. Archives of Surgery. 2006; 141(5):483-8

144. Cho E, Chang JM, Yoon SY, Lee GT, Ku YH, Kim HI et al. Preoperative localization and intraoperative parathyroid hormone assay in korean patients with primary hyperparathyroidism. Endocrinology and Metabolism. 2014; 29(4):464-9

145. Chou FF, Wang PW, Sheen-Chen SM. Preoperative localisation of parathyroid glands in primary hyperparathyroidism. European Journal of Surgery. 1997; 163(12):889-95

146. Chow CC, Chan WB, Li JK, Chan NN, Chan MH, Ko GT et al. Oral alendronate increases bone mineral density in postmenopausal women with primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2003; 88(2):581-7

147. Chun IK, Cheon GJ, Paeng JC, Kang KW, Chung JK, Lee DS. Detection and characterization of parathyroid adenoma/hyperplasia for preoperative localization: Comparison between ^{11}C-Methionine PET/CT and ^{99m}Tc-Sestamibi scintigraphy. Nuclear Medicine and Molecular Imaging. 2013; 47(3):166-72

148. Ciappuccini R, Morera J, Pascal P, Rame JP, Heutte N, Aide N et al. Dual-phase 99mTc sestamibi scintigraphy with neck and thorax SPECT/CT in primary hyperparathyroidism: A single-institution experience. Clinical Nuclear Medicine. 2012; 37(3):223-8

149. Civelek AC, Ozalp E, Donovan P, Udelsman R. Prospective evaluation of delayed technetium-99m sestamibi SPECT scintigraphy for preoperative localization of primary hyperparathyroidism. Surgery. 2002; 131(2):149-57

150. Clark OH, Stark DD, Gooding GAW. Localization procedures in patients requiring reoperation for hyperparathyroidism. World Journal of Surgery. 1984; 8(4):509-21

151. Clark PB, Case D, Watson NE, Morton KA, Perrier ND. Experienced scintigraphers contribute to success of minimally invasive parathyroidectomy by skilled endocrine surgeons. American Surgeon. 2003; 69(6):478-83; discussion 483-84

152. Clifton-Bligh PB, Nery ML, Supramaniam R, Reeve TS, Delbridge L, Stiel JN et al. Mortality associated with primary hyperparathyroidism. Bone. 2015; 74:121-4

153. Commercial Medicines Unit (CMU), Department of Health. Electronic market information tool (EMIT) [Last updated 5 January 2018]. 2011. Available from: http://cmu.dh.gov.uk/electronic-market-information-tool-emit/ Last accessed: 05/10/2018.

154. Cook GJR, Wong JCH, Smellie WJB, Young AE, Maisey MN, Fogelman I. [^{11}C]Methionine positron emission tomography for patients with persistent or recurrent hyperparathyroidism after surgery. European Journal of Endocrinology. 1998; 139(2):195-7

155. Cook MR, Pitt SC, Schaefer S, Sippel R, Chen H. A rising IoPTH level immediately after parathyroid resection: Are additional hyperfunctioning glands always present? an application of the wisconsin criteria. Annals of Surgery. 2010; 251(6):1127-30

156. Corlew DS, Bryda SL, Bradley EL, 3rd, DiGirolamo M. Observations on the course of untreated primary hyperparathyroidism. Surgery. 1985; 98(6):1064-71

157. Cowie AGA. Morbidity in adult parathyroid surgery. Journal of the Royal Society of Medicine. 1982; 75(12):942-5

158. Csupor E, Toth E, Meszaros S, Ferencz V, Szucs J, Lakatos P et al. Is there any connection between the presence of kidney stones in primary hyperparathyroidism and the location of an underlying adenoma? Experimental and Clinical Endocrinology and Diabetes. 2005; 113(5):257-61

159. Curtis L, Burns A. Unit costs of health and social care 2017. Canterbury. Personal Social Services Research Unit University of Kent, 2017. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/

160. Czerniak A, Zwas ST, Shustik O, Avigad I, Ayalon A, Dolev E. The use of radioiodinated toluidine blue for preoperative localization of parathyroid pathology. Surgery. 1991; 110(5):832-8

161. D'Agostino J, Diana M, Vix M, Nicolau S, Soler L, Bourhala K et al. Three-dimensional metabolic and radiologic gathered evaluation using VR-RENDER fusion: a novel tool to enhance accuracy in the localization of parathyroid adenomas. World Journal of Surgery. 2013; 37(7):1618-25

162. D'Agostino J, Wall J, Soler L, Vix M, Duh QY, Marescaux J. Virtual neck exploration for parathyroid adenomas: A first step toward minimally invasive image-guided surgery. JAMA Surgery. 2013; 148(3):232-8

163. D'Andrea V, Biancari F, Catania A, Chiarini S, Lippolis G, Falvo L et al. Surgical treatment for hyperparathyroidism. Italian Journal of Mineral and Electrolyte Metabolism. 1996; 10(1):39-43

164. Danzi JT, Farmer RG, Esselstyn CB, Jr. Recurrent pancreatitis associated with normocalcemia, parathyroid hyperplasia, and increased serum parathormone. Cleveland Clinic Quarterly. 1974; 41(1):39-43

165. Davis DD, Tee MC, Kowal J, Holmes DT, Wiseman SM. Streamlining of intra-operative parathyroid hormone measurements for cure during parathyroidectomy. American Journal of Surgery. 2013; 205(5):597-601

166. Day KM, Elsayed M, Beland MD, Monchik JM. The utility of 4-dimensional computed tomography for preoperative localization of primary hyperparathyroidism in patients not localized by sestamibi or ultrasonography. Surgery. 2015; 157(3):534-9

167. De Geronimo S, Romagnoli E, Diacinti D, D'Erasmo E, Minisola S. The risk of fractures in postmenopausal women with primary hyperparathyroidism. European Journal of Endocrinology. 2006; 155(3):415-20

168. De Simone B, Del Rio P, Catena F, Fallani G, Bendinelli C, Napoli JA et al. Preoperative localization of parathyroid adenoma in video-assisted era: is cervical

ultrasound or 99mTc Sesta MIBI scintigraphy better? Minerva Chirurgica. 2017; 72(5):375-82

169. Deaconson TF, Wilson SD, Lemann J, Jr. The effect of parathyroidectomy on the recurrence of nephrolithiasis. Surgery. 1987; 102(6):910-3

170. Del Rio P, Cataldo S, Sommaruga L, Arcuri MF, Massa M, Sianesi M. Localization of pathological gland's site in primary hyperparathyroidism: ten years experience with MIBI scintigraphy. Il Giornale di Chirurgia. 2008; 29(4):186-9

171. Demirkurek CH, Adalet I, Terzioglu T, Ozarmagan S, Bozbora A, Ozbey N et al. Efficiency of gamma probe and dual-phase Tc-99m sestamibi scintigraphy in surgery for patients with primary hyperparathyroidism. Clinical Nuclear Medicine. 2003; 28(3):186-91

172. Denham DW, Norman J. Cost-effectiveness of preoperative sestamibi scan for primary hyperparathyroidism is dependent solely upon the surgeon's choice of operative procedure. Journal of the American College of Surgeons. 1998; 186(3):293-304

173. Department of Health. NHS reference costs 2015-16. Available from: https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016 Last accessed: 17/01/2018.

174. Department of Health. NHS reference costs 2016/2017. Available from: https://improvement.nhs.uk/resources/reference-costs/ Last accessed: 17/01/2018.

175. Department of Health. NHS reference costs 2010-11. 2012. Available from: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131140 Last accessed: 05/10/2018.

176. Derom A, Wallaert P, Janzing H, Van den Brande F, Derom F. Intraoperative identification of parathyroids by means of methylene blue. Acta Chirurgica Belgica. 1994; 94(2):97-100

177. Derom AF, Wallaert PC, Janzing HM, Derom FE. Intraoperative identification of parathyroid glands with methylene blue infusion. American Journal of Surgery. 1993; 165(3):380-2

178. Deutmeyer C, Weingarten M, Doyle M, Carneiro-Pla D. Case series of targeted parathyroidectomy with surgeon-performed ultrasonography as the only preoperative imaging study. Surgery. 2011; 150(6):1153-60

179. Diaz-Guerra GM, Guadalix S, Garcia F, Melon N, Martinez-Pueyo JI, Ferrero E et al. Parathyroidectomy in primary hyperparathyroidism (PHPT): Retrospective study of 272 patients. Endocrine Reviews. 2015; 36(2 Suppl):SAT-266

180. Diaz De La Guardia FV, Martin MA, Arrabal Polo MA, Flores SQ, Ortiz JLM, Gomez AZ. Renal lithiasis in patients with primary hyperparathyroidism. Evolution and treatment. Archivos Españoles de Urología. 2010; 63(1):32-40

181. Dillavou ED, Jenoff JS, Intenzo CM, Cohn HE. The utility of sestamibi scanning in the operative management of patients with primary hyperparathyroidism. Journal of the American College of Surgeons. 2000; 190(5):540-45

182. Dimkovic NB, Wallele AA, Oreopoulos DG. Renal stone disease, elevated iPTH level and normocalcemia. International Urology and Nephrology. 2002; 34(1):135-41

183. Dolgin C, Lo Gerfo P, LiVolsi V, Feind C. Twenty-five year experience with primary hyperparathyroidism at Columbia Presbyterian Medical Center. Head and Neck Surgery. 1979; 2(2):92-8

184. Doppman JL, Skarulis MC, Chang R, Alexander HR, Bartlett D, Libutti SK et al. Hypocalcemic stimulation and nonselective venous sampling for localizing parathyroid adenomas: Work in progress. Radiology. 1998; 208(1):145-51

185. Drews M, Paszkowski J, Stawny B, Banasiewicz T, Hermann J, Meczynski M et al. Comparison of parathyroid gland localization techniques in patients treated due to gland hyperfunction. Polski Przeglad Chirurgiczny. 2003; 75(9):821-8

186. Dudek MK, Jenkins BJ, Goode AW, Newell MS, Boucher BJ. The accuracy of conventional and three-dimensional thallium-technetium scans in patients with hyperparathyroidism resulting from multiglandular hyperplasia. British Journal of Radiology. 1994; 67(796):325-7

187. Dumitrescu B, van Helden S, ten Broeke R, Nieuwenhuijzen-Kruseman A, Wyers C, Udrea G et al. Evaluation of patients with a recent clinical fracture and osteoporosis, a multidisciplinary approach. BMC Musculoskeletal Disorders. 2008; 9:109

188. Dunlop DAB, Papapoulos SE, Lodge RW. Parathyroid venous sampling: anatomic considerations and results in 95 patients with primary hyperparathyroidism. British Journal of Radiology. 1980; 53(627):183-91

189. Dwarakanathan AA, Saclarides TJ, Witt TR. The role of ultrasonography in the evaluation of primary hyperparathyroidism. Surgery Gynecology and Obstetrics. 1986; 163(6):504-8

190. Dy BM, Grant CS, Wermers RA, Kearns AE, Huebner M, Harmsen WS et al. Changes in bone mineral density after surgical intervention for primary hyperparathyroidism. Surgery. 2012; 152(6):1051-8

191. Dy BM, Richards ML, Vazquez BJ, Thompson GB, Farley DR, Grant CS. Primary hyperparathyroidism and negative Tc99 sestamibi imaging: To operate or not? Annals of Surgical Oncology. 2012; 19(7):2272-8

192. Ebisuno S, Inagaki T, Yoshida T, Yamamoto M, Tabuse Y, Kohjimoto Y et al. Preoperative localization of parathyroid adenomas using 99mTc-MIBI scintigraphy in patients with hyperparathyroidism. International Journal of Urology. 1997; 4(2):126-9

193. Edwards ME, Rotramel A, Beyer T, Gaffud MJ, Djuricin G, Loviscek K et al. Improvement in the health-related quality-of-life symptoms of hyperparathyroidism is durable on long-term follow-up. Surgery. 2006; 140(4):655-64

194. Eichhorn-Wharry LI, Carlin AM, Talpos GB. Mild hypercalcemia: An indication to select 4-dimensional computed tomography scan for preoperative localization of parathyroid adenomas. American Journal of Surgery. 2011; 201(3):334-8

195. Eisenberg H, Pallotta J, Sherwood LM. Selective arteriography, venography and venous hormone assay in diagnosis and localization of parathyroid lesions. American Journal of Medicine. 1974; 56(6):810-20

196. Elaraj DM, Sippel RS, Lindsay S, Sansano I, Duh QY, Clark OH et al. Are additional localization studies and referral indicated for patients with primary hyperparathyroidism who have negative sestamibi scan results? Archives of Surgery. 2010; 145(6):578-81

197. Eloy JA, Mitty H, Genden EM. Preoperative selective venous sampling for nonlocalizing parathyroid adenomas. Thyroid. 2006; 16(8):787-90

198. Elvius M, Lagrelius A, Nygren A, Alveryd A, Christensson TA, Nordenström J. Seventeen year follow-up study of bone mass in patients with mild asymptomatic hyperparathyroidism some of whom were operated on. European Journal of Surgery. 1995; 161(12):863-9

199. Emmolo I, Dal Corso H, Borretta G, Visconti G, Piovesan A, Cesario F et al. Unexpected results using rapid intraoperative parathyroid hormone monitoring during parathyroidectomy for primary hyperparathyroidism. World Journal of Surgery. 2005; 29(6):785-8

200. Erdman WA, Breslau NA, Weinreb JC, Weatherall P, Setiawan H, Harrell R et al. Noninvasive localization of parathyroid adenomas: A comparison of X-ray computerized tomography, ultrasound, scintigraphy and MRI. Magnetic Resonance Imaging. 1989; 7(2):187-94

201. Ersoy R, Ersoy O, Evranos Ogmen B, Polat SB, Kilic M, Yildirim N et al. Diagnostic value of endoscopic ultrasonography for preoperative localization of parathyroid adenomas. Endocrine. 2014; 47(1):221-6

202. Espiritu RP, Kearns AE, Vickers KS, Grant C, Ryu E, Wermers RA. Depression in primary hyperparathyroidism: Prevalence and benefit of surgery. Journal of Clinical Endocrinology and Metabolism. 2011; 96(11):E1737-E1745

203. Estella E, Leong MSZ, Bennett I, Hartley L, Wetzig N, Archibald CA et al. Parathyroid hormone venous sampling prior to reoperation for primary hyperparathyroidism. ANZ Journal of Surgery. 2003; 73(10):800-5

204. Eufrazino C, Veras A, Bandeira F. Epidemiology of primary hyperparathyroidism and its non-classical manifestations in the city of Recife, Brazil. Clinical Medicine Insights: Endocrinology and Diabetes. 2013; 6:69-74

205. Ezzat AHH, El. Baradie T, Attia A, Kotb M, Zaher A, Gouda I. Surgical management of primary hyperparathyroidism guided by double-phase Tc-99m-MIBI scintigraphy. Chinese-German Journal of Clinical Oncology. 2012; 11(1):24-32

206. Ezzat WF, Fathey H, Fawaz S, El-Ashri A, Youssef T, Othman HB. Intraoperative parathyroid hormone as an indicator for parathyroid gland preservation in thyroid surgery. Swiss Medical Weekly. 2011; 141:w13299

207. Falkheden T, Ohlsson L, Sjogren B. Renal function in primary hyperparathyroidism. A follow-up study two to eleven years after surgery comprising 139 patients. Scandinavian Journal of Urology and Nephrology. 1980; 14(2):167-75

208. Falko JM, Maeder MC, Conway C, Mazzaferri EL, Skillman TG. Primary hyperparathyroidism: Analysis of 220 patients with special emphasis on familial hypocalciuric hypercalcemia. Heart and Lung. 1984; 13(2):124-31

209. Fang WL, Tseng LM, Chen JY, Chiou SY, Chou YH, Wu CW et al. The management of high-risk patients with primary hyperparathyroidism - Minimally invasive parathyroidectomy vs. medical treatment. Clinical Endocrinology. 2008; 68(4):520-8

210. Farnebo LO, Trigonis C, Forsgren L. Surgery for primary hyperparathyroidism. Experience with 400 patients during 10 years (1972-1981). Acta Chirurgica Scandinavica. 1984; 150(Suppl. 520):11-6

211. Fayet P, Hoeffel C, Fulla Y, Legmann P, Hazebroucq V, Luton JP et al. Technetium-99m sestamibi scintigraphy, magnetic resonance imaging and venous blood sampling in persistent and recurrent hyperparathyroidism. British Journal of Radiology. 1997; 70(833):459-64

212. Feingold DL, Alexander HR, Chen CC, Libutti SK, Shawker TH, Simonds WF et al. Ultrasound and sestamibi scan as the only preoperative imaging tests in reoperation for parathyroid adenomas. Surgery. 2000; 128(6):1103-10

213. Filby A, Lewis L, Taylor M. An economic evaluation of interventions to improve the uptake of vitamin D supplements in England and Wales. London. National Institute for Health and Care Excellence, 2014. Available from: https://www.nice.org.uk/guidance/ph56/documents/economic-evaluation-report2

214. Fogelman I, McKillop JH, Bessent RG. Successful localisation of parathyroid adenomata by thallium-201 and technetium-99m substraction scintigraphy: Description of an improved technique. European Journal of Nuclear Medicine. 1984; 9(12):545-7

215. Foster GS, Bekerman C, Blend MJ, Byrom E, Pinsky SM. Preoperative imaging in primary hyperparathyroidism. Role of thallium-technetium subtraction scintigraphy. Archives of Otolaryngology - Head and Neck Surgery. 1989; 115(10):1197-202

216. Freaney R, Casey OM, Muldowney FP. The long-term effect of parathyroidectomy on renal function. Irish Journal of Medical Science. 1978; 147(6):205-9

217. Freudenberg LS, Frilling A, Sheu SY, Gorges R. Optimizing preoperative imaging in primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2006; 391(6):551-6

218. Gallacher SJ, Kelly P, Shand J, Logue FC, Cooke T, Boyle IT et al. A comparison of 10 MHz ultrasound and 201-thallium/99m-technetium subtraction scanning in primary hyperparathyroidism. Postgraduate Medical Journal. 1993; 69(811):376-80

219. Gallowitsch HJ, Mikosch P, Kresnik E, Gomez I, Lind P. Technetium 99m tetrofosmin parathyroid imaging: Results with double- phase study and SPECT in primary and secondary hyperparathyroidism. Investigative Radiology. 1997; 32(8):459-65

220. Gallowitsch HJ, Mikosch P, Kresnik E, Unterweger O, Lind P. Comparison between 99mTc-tetrofosmin/pertechnetate subtraction scintigraphy and 99mTc-tetrofosmin SPECT for preoperative localization of parathyroid adenoma in an endemic goiter area. Investigative Radiology. 2000; 35(8):453-9

221. Garcia-Santos EP, Martin-Fernandez J, Gil-Rendo A, Menchen-Trujillo B, Martinez de Paz F, Manzanares-Campillo MC et al. Rapid intraoperative determination of intact parathyroid hormone during surgery for primary hyperparathyroidism. Experience at our center. Endocrinologia y Nutricion. 2014; 61(1):3-8

222. Garcia-Talavera P, Diaz-Soto G, Montes AA, Villanueva JG, Cobo A, Gamazo C et al. Contribution of early SPECT/CT to 99mTc-MIBI double phase scintigraphy in primary hyperparathyroidism: Diagnostic value and correlation between uptake and biological parameters. Revista Espanola de Medicina Nuclear e Imagen Molecular. 2016; 35(6):351-7

223. Garcia-Talavera P, Garcia-Talavera JR, Gonzalez C, Martin E, Martin M, Gomez A. Efficacy of in-vivo counting in parathyroid radioguided surgery and usefulness of its association with scintigraphy and intraoperative PTHi. Nuclear Medicine Communications. 2011; 32(9):847-52

224. Garcia-Talavera P, Gonzalez C, Garcia-Talavera JR, Martin E, Martin M, Gomez A. Radioguided surgery of primary hyperparathyroidism in a population with a high prevalence of thyroid pathology. European Journal of Nuclear Medicine and Molecular Imaging. 2010; 37(11):2060-7

225. Garner SC, Leight GS, Jr. Initial experience with intraoperative PTH determinations in the surgical management of 130 consecutive cases of primary hyperparathyroidism. Surgery. 1999; 126(6):1132-8

226. Gauger PG, Agarwal G, England BG, Delbridge LW, Matz KA, Wilkinson M et al. Intraoperative parathyroid hormone monitoring fails to detect double parathyroid adenomas: A 2-institution experience. Surgery. 2001; 130(6):1005-10

227. Gawande AA, Monchik JM, Abbruzzese TA, Iannuccilli JD, Ibrahim SI, Moore FD, Jr et al. Reassessment of parathyroid hormone monitoring during parathyroidectomy for primary hyperparathyroidism after 2 preoperative localization studies. Archives of Surgery. 2006; 141(4):381-4

228. Gedik GK, Sari O. Influence of single photon emission computed tomography (SPECT) reconstruction algorithm on diagnostic accuracy of parathyroid scintigraphy: Comparison of iterative reconstruction with filtered backprojection. Indian Journal of Medical Research. 2017; 145(4):479-87

229. Gergel M, Brychta I, Vician M, Olejnik J. Primary hyperparathyreosis: is concordant sonography and scintigraphy really so important? Bratislavske Lekarske Listy. 2014; 115(10):649-52

230. Ghemigian A, Buruiana A, Olaru M, Dumitru N, Goldstein A, Hortopan D et al. Parathyroid adenoma imaging-preoperative localization. ARS Medica Tomitana. 2015; 21(3):116-23

231. Ghose RR, Morgan WD. Improvement in renal function in primary hyperparathyroidism following parathyroidectomy. Postgraduate Medical Journal. 1981; 57(663):28-30

232. Gil-Cardenas A, Gamino R, Reza A, Pantoja JP, Herrera MF. Is intraoperative parathyroid hormone assay mandatory for the success of targeted parathyroidectomy? Journal of the American College of Surgeons. 2007; 204(2):286-90

233. Gilat H, Cohen M, Feinmesser R, Benzion J, Shvero J, Segal K et al. Minimally invasive procedure for resection of a parathyroid adenoma: The role of preoperative high-resolution ultrasonography. Journal of Clinical Ultrasound. 2005; 33(6):283-7

234. Gill MT, Dean M, Karr J, Aultman DF, Nathan CO. Intraoperative parathyroid hormone assay: a necessary tool for multiglandular disease. Otolaryngology - Head & Neck Surgery. 2011; 144(5):691-7

235. Gimm O, Arnesson LG, Olofsson P, Morales O, Juhlin C. Super-selective venous sampling in conjunction with quickPTH for patients with persistent primary hyperparathyroidism: Report of five cases. Surgery Today. 2012; 42(6):570-6

236. Giraldez-Rodriguez LA, Giraldez-Casasnovas LJ. Minimally invasive parathyroidectomy as treatment for primary hyperparathyroidism. Boletin de la Asociacion Medica de Puerto Rico. 2008; 100(1):27-32

237. Glynn N, Lynn N, Donagh C, Crowley RK, Smith D, Thompson CJ et al. The utility of 99mTc-sestamibi scintigraphy in the localisation of parathyroid adenomas in primary hyperparathyroidism. Irish Journal of Medical Science. 2011; 180(1):191-4

238. Gofrit ON, Lebensart PD, Pikarsky A, Lackstein D, Gross DJ, Shiloni E. High-resolution ultrasonography: Highly sensitive, specific technique for preoperative localization of parathyroid adenoma in the absence of multinodular thyroid disease. World Journal of Surgery. 1997; 21(3):287-91

239. Gogas J, Kouskos E, Mantas D, Markopoulos C, Kyriaki D, Tseleni-Balafouta S et al. Pre-operative Tc-99m-sestamibi scanning and intra-operative nuclear mapping : Are they accurate in localizing parathyroid adenomas? Acta Chirurgica Belgica. 2003; 103(6):626-30

240. Goldstein RE, Carter IWM, Fleming M, Bumpous J, Lentsch E, Rice M et al. Unilateral cervical surgical exploration aided by intraoperative parathyroid hormone monitoring in patients with primary hyperparathyroidism and equivocal sestamibi scan results. Archives of Surgery. 2006; 141(6):552-7

241. Gooding GA, Okerlund MD, Stark DD, Clark OH. Parathyroid imaging: comparison of double-tracer (T1-201, Tc-99m) scintigraphy and high-resolution US. Radiology. 1986; 161(1):57-64

242. Gracie D, Hussain SSM. Use of minimally invasive parathyroidectomy techniques in sporadic primary hyperparathyroidism: Systematic review. Journal of Laryngology and Otology. 2012; 126(3):221-7

243. Grant CS, Thompson G, Farley D, Van Heerden J, Prinz R, Ryan J et al. Primary hyperparathyroidism surgical management since the introduction of minimally invasive parathyroidectorny: Mayo clinic experience. Archives of Surgery. 2005; 140(5):472-9

244. Grayev AM, Gentry LR, Hartman MJ, Chen H, Perlman SB, Reeder SB. Presurgical localization of parathyroid adenomas with magnetic resonance imaging at 3.0 T: An adjunct method to supplement traditional imaging. Annals of Surgical Oncology. 2012; 19(3):981-9

245. Griffith B, Chaudhary H, Mahmood G, Carlin AM, Peterson E, Singer M et al. Accuracy of 2-phase parathyroid CT for the preoperative localization of parathyroid adenomas in primary hyperparathyroidism. American Journal of Neuroradiology. 2015; 36(12):2373-9

246. Gross ND, Weissman JL, Veenker E, Cohen JI. The diagnostic utility of computed tomography for preoperative localization in surgery for hyperparathyroidism. Laryngoscope. 2004; 114(2):227-31

247. Grosso I, Sargiotto A, D'Amelio P, Tamone C, Gasparri G, De Filippi PG et al. Preoperative localization of parathyroid adenoma with sonography and 99mTc-sestamibi scintigraphy in primary hyperparathyroidism. Journal of Clinical Ultrasound. 2007; 35(4):186-90

248. Guerin C, Lowery A, Gabriel S, Castinetti F, Philippon M, Vaillant-Lombard J et al. Preoperative imaging for focused parathyroidectomy: Making a good strategy even better. European Journal of Endocrinology. 2015; 172(5):519-26

249. Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with ^{99m}technetium sestamibi scintigraphy Clinical Endocrinology. 2002; 57(2):241-9

250. Habibollahi P, Shin B, Shamchi SP, Wachtel H, Fraker DL, Trerotola SO. Eleven-year retrospective report of super-selective venous sampling for the evaluation of recurrent or persistent hyperparathyroidism in 32 patients. Cardiovascular and Interventional Radiology. 2018; 41(1):63-72

251. Haciyanli M, Lal G, Morita E, Duh QY, Kebebew E, Clark OH. Accuracy of preoperative localization studies and intraoperative parathyroid hormone assay in patients with primary hyperparathyroidism and double adenoma. Journal of the American College of Surgeons. 2003; 197(5):739-46

252. Hagstrom E, Lundgren E, Mallmin H, Rastad J, Hellman P. Positive effect of parathyroidectomy on bone mineral density in mild asymptomatic primary hyperparathyroidism. Journal of Internal Medicine. 2006; 259(2):191-8

253. Halvorson DJ, Burke GJ, Mansberger AR, Jr, Wei JP. Use of technetium Tc 99m sestamibi and iodine 123 radionuclide scan for preoperative localization of abnormal parathyroid glands in primary hyperparathyroidism. Southern Medical Journal. 1994; 87(3):336-9

254. Hamamci EO, Piyade R, Bostanoglu S, Sakcak I, Avsar MF, Cosgu E. Preoperative localization in primary hyperparathyroidism surgery. Turkiye Klinikleri Journal of Medical Sciences. 2011; 31(3):686-90

255. Hamdy NAT, Gray RES, McCloskey E, Galloway J, Rattenbury JM, Brown CB et al. Clodronate in the medical management of hyperparathyroidism. Bone. 1987; 8(Suppl. 1):S69-S77

256. Hamilton R, Greenberg BM, Gefter W, Kressel H, Spritzer C. Successful localization of parathyroid adenomas by magnetic resonance imaging. American Journal of Surgery. 1988; 155(3):370-3

257. Hammonds JC, Williams JL, Harvey L. Primary hyperparathyroidism - a review of cases in the Sheffield area. British Journal of Urology. 1976; 48(7):539-48

258. Hanif F, Coffey JC, Romics L, Jr, O'Sullivan K, Aftab F, Redmond HP. Rapid intraoperative parathyroid hormone assay - More than just a comfort measure. World Journal of Surgery. 2006; 30(2):156-61

259. Hanninen EL, Vogl TJ, Steinmuller T, Ricke J, Neuhaus P, Felix R. Preoperative contrast-enhanced MRI of the parathyroid glands in hyperparathyroidism. Investigative Radiology. 2000; 35(7):426-30

260. Hara N, Takayama T, Onoguchi M, Obane N, Miyati T, Yoshioka T et al. Subtraction SPECT for parathyroid scintigraphy based on maximization of mutual information. Journal of Nuclear Medicine Technology. 2007; 35(2):84-90

261. Harris L, Yoo J, Driedger A, Fung K, Franklin J, Gray D et al. Accuracy of technetium-99M SPECT-CT hybrid images in predicting the precise intraoperative anatomical location of parathyroid adenomas. Head and Neck. 2008; 30(4):509-17

262. Hassani S, Braunstein GD, Seibel MJ, Brickman AS, Geola F, Pekary AE et al. Alendronate therapy of primary hyperparathyroidism. Endocrinologist. 2001; 11(6):459-64

263. Hasselgren PO, Fidler JP. Further evidence against the routine use of parathyroid ultrasonography prior to initial neck exploration for hyperparathyroidism. American Journal of Surgery. 1992; 164(4):337-40

264. Hassler S, Ben-Sellem D, Hubele F, Constantinesco A, Goetz C. Dual-isotope 99mTc-MIBI/123I parathyroid scintigraphy in primary hyperparathyroidism: comparison of subtraction SPECT/CT and pinhole planar scan. Clinical Nuclear Medicine. 2014; 39(1):32-6

265. Hathaway TD, Jones G, Stechman M, Scott-Coombes D. The value of intraoperative PTH measurements in patients with mild primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2013; 398(5):723-7

266. Hayakawa N, Nakamoto Y, Kurihara K, Yasoda A, Kanamoto N, Miura M et al. A comparison between 11C-methionine PET/CT and MIBI SPECT/CT for localization of

parathyroid adenomas/hyperplasia. Nuclear Medicine Communications. 2015; 36(1):53-59

267. Heath H, 3rd. Clinical spectrum of primary hyperparathyroidism: evolution with changes in medical practice and technology. Journal of Bone and Mineral Research. 1991; 6 (Suppl 2):S63-70; discussion S83-4

268. Hedback G, Oden A. Increased risk of death from primary hyperparathyroidism--an update. European Journal of Clinical Investigation. 1998; 28(4):271-6

269. Hedback G, Oden A, Tisell LE. The influence of surgery on the risk of death in patients with primary hyperparathyroidism. World Journal of Surgery. 1991; 15(3):399-407

270. Hedback G, Tisell LE, Bengtsson BA, Hedman I, Oden A. Premature death in patients operated on for primary hyperparathyroidism. World Journal of Surgery. 1990; 14(6):829-36

271. Hedback GM, Oden AS. Cardiovascular disease, hypertension and renal function in primary hyperparathyroidism. Journal of Internal Medicine. 2002; 251(6):476-83

272. Heiba SI, Jiang M, Rivera J, Genden E, Inabnet W, Machac J et al. Direct comparison of neck pinhole dual-tracer and dual-phase MIBI accuracies with and without SPECT/CT for parathyroid adenoma detection and localization. Clinical Nuclear Medicine. 2015; 40(6):476-82

273. Heineman TE, Kutler DI, Cohen MA, Kuhel WI. Is Intraoperative Parathyroid Hormone Monitoring Warranted in Cases of 4D-CT/Ultrasound Localized Single Adenomas? Otolaryngology - Head & Neck Surgery. 2015; 153(2):183-8

274. Heizmann O, Viehl CT, Schmid R, Muller-Brand J, Muller B, Oertli D. Impact of concomitant thyroid pathology on preoperative workup for primary hyperparathyroidism. European Journal of Medical Research. 2009; 14(1):37-41

275. Heller KS, Attie JN, Dubner S. Parathyroid localization: Inability to predict multiple gland involvement. American Journal of Surgery. 1993; 166(4):357-9

276. Hessman O, Westerdahl J, Al-Suliman N, Christiansen P, Hellman P, Bergenfelz A. Randomized clinical trial comparing open with video-assisted minimally invasive parathyroid surgery for primary hyperparathyroidism. British Journal of Surgery. 2010; 97(2):177-84

277. Hewin DF, Brammar TJ, Kabala J, Farndon JR. Role of preoperative localization in the management of primary hyperparathyroidism. British Journal of Surgery. 1997; 84(10):1377-80

278. Hindie E, Melliere D, Jeanguillaume C, Perlemuter L, Chehade F, Galle P. Parathyroid imaging using simultaneous double-window recording of technetium-99m-sestamibi and iodine-123. Journal of Nuclear Medicine. 1998; 39(6):1100-5

279. Hindie E, Melliere D, Perlemuter L, Jeanguillaume C, Galle P. Primary hyperparathyroidism: Higher success rate of first surgery after preoperative Tc-99m sestamibi-I-123 subtraction scanning. Radiology. 1997; 204(1):221-8

280. Hindie E, Melliere D, Simon D, Perlemuter L, Galle P. Primary hyperparathyroidism: Is technetium 99m-Sestamibi/iodine-123 subtraction scanning the best procedure to locate enlarged glands before surgery? Journal of Clinical Endocrinology and Metabolism. 1995; 80(1):302-7

281. Hinson AM, Lee DR, Hobbs BA, Fitzgerald RT, Bodenner DL, Stack BC, Jr. Preoperative 4D CT localization of nonlocalizing parathyroid adenomas by ultrasound and SPECT-CT. Otolaryngology - Head & Neck Surgery. 2015; 153(5):775-8

282. Hjern B, Almqvist S, Granberg PO, Lindvall N, Wasthed B. Pre operative localization of parathyroid tissue by selective neck vein catheterization and radioimmunoassay of parathyroid hormone. Acta Chirurgica Scandinavica. 1975; 141(1):31-9

283. Ho Shon IA, Roach PJ, Bernard EJ, Delbridge LW. Optimal pinhole techniques for preoperative localization with tc-99m MIBI for primary hyperparathyroidism. Clinical Nuclear Medicine. 2001; 26(12):1002-9

284. Ho Shon IA, Yan W, Roach PJ, Bernard EJ, Shields M, Sywak M et al. Comparison of pinhole and SPECT 99mTc-MIBI imaging in primary hyperparathyroidism. Nuclear Medicine Communications. 2008; 29(11):949-55

285. Hoda NE, Phillips P, Ahmed N. Recommendations after non-localizing sestamibi and ultrasound scans in primary hyperparathyroid disease: order more scans or explore surgically? Journal of the Mississippi State Medical Association. 2013; 54(2):36-41

286. Horanyi J, Duffek L, Szlavik R, Takacs I, Toth M, Romics L, Jr. Intraoperative determination of pth concentrations in fine needle tissue aspirates to identify parathyroid tissue during parathyroidectomy. World Journal of Surgery. 2010; 34(3):538-43

287. Horiuchi T, Onouchi T, Inoue J, Shionoiri A, Hosoi T, Orimo H. A strategy for the management of elderly women with primary hyperparathyroidism: a comparison of etidronate therapy with parathyroidectomy. Gerontology. 2002; 48(2):103-8

288. Hornung M, Jung EM, Stroszczynski C, Schlitt HJ, Agha A. Contrast-enhanced ultrasonography (CEUS) using early dynamic in microcirculation for localization of pathological parathyroid glands: First-line or complimentary diagnostic modality? Clinical Hemorheology and Microcirculation. 2011; 49(1-4):83-90

289. Hughes DT, Miller BS, Doherty GM, Gauger PG. Intraoperative parathyroid hormone monitoring in patients with recognized multiglandular primary hyperparathyroidism. World Journal of Surgery. 2011; 35(2):336-41

290. Hunter GJ, Schellingerhout D, Vu TH, Perrier ND, Hamberg LM. Accuracy of four-dimensional CT for the localization of abnormal parathyroid glands in patients with primary hyperparathyroidism. Radiology. 2012; 264(3):789-95

291. Hwang RS, Morris LF, Ro K, Park S, Ituarte PHG, Hong JC et al. A selective, bayesian approach to intraoperative PTH monitoring. Annals of Surgery. 2010; 251(6):1122-6

292. Iacobone M, Scarpa M, Lumachi F, Favia G, Grant C, Rosen IB et al. Are frozen sections useful and cost-effective in the era of intraoperative qPTH assays? . Surgery. 2005; 138(6):1159-65

293. Ibrahim EAG, Elsadawy ME. Combined Tc-99m sesta MIBI scin tigraphy and Ultrasonography in preoperative detection and localization of parathyroid adenoma. Egyptian Journal of Radiology and Nuclear Medicine. 2015; 46(4):937-41

294. Inabnet WB, Fulla Y, Richard B, Bonnichon P, Icard P, Chapuis Y. Unilateral neck exploration under local anesthesia: The approach of choice of asymptomatic primary hyperparathyroidism. Surgery. 1999; 126(6):1004-10

295. Irvin GL, III , Dembrow VD, Prudhomme DL, Proye C, Thomas CG, Jr, Gaz RD et al. Clinical usefulness of an intraoperative 'quick parathyroid hormone' assay. Surgery. 1993; 114(6):1019-23

296. Irvin GL, III, Prudhomme DL, Deriso GT, Sfakianakis G, Chandarlapaty SKC. A new approach to parathyroidectomy. Annals of Surgery. 1994; 219(5):574-81

297. Isidori AM, Cantisani V, Giannetta E, Diacinti D, David E, Forte V et al. Multiparametric ultrasonography and ultrasound elastographyin the differentiation of parathyroid lesions from ectopicthyroid lesions or lymphadenopathies. Endocrine. 2017; 57(2):335-43

298. Ito F, Sippel R, Lederman J, Chen H. The utility of intraoperative bilateral internal jugular venous sampling with rapid parathyroid hormone testing. Annals of Surgery. 2007; 245(6):959-63

299. Itoh K, Ishizuka R. Tc-99m-MIBI scintigraphy for recurrent hyperparathyroidism after total parathyroidectomy with autograft. Annals of Nuclear Medicine. 2003; 17(4):315-20

300. Jabiev AA, Lew JI, Solorzano CC. Surgeon-performed ultrasound: A single institution experience in parathyroid localization. Surgery. 2009; 146(4):569-77

301. James BC, Nagar S, Tracy M, Kaplan EL, Angelos P, Scherberg NH et al. A novel, ultrarapid parathyroid hormone assay to distinguish parathyroid from nonparathyroid tissue. Surgery. 2014; 156(6):1638-43

302. Jansson S, Mollerup C, Nordenstrom J, Varhaug JE, Isaksen G, Bollerslev J. The SIPH study: surgery vs. medical observation in mild, asymptomatic phpt preliminary results from a prospective, randomized study. Langenbeck's Archives of Surgery. 2006; 391(3):242

303. Jarhult J, Kristoffersson A, Lundstrom B, Oberg L. Comparison of ultrasonography and computed tomography in preoperative location of parathyroid adenomas. Acta Chirurgica Scandinavica. 1985; 151(7):583-7

304. Jaskowiak N, Norton JA, Richard Alexander H, Doppman JL, Shawker T, Skarulis M et al. A prospective trial evaluating a standard approach to reoperation for missed parathyroid adenoma. Annals of Surgery. 1996; 224(3):308-22

305. Jaskowiak NT, Sugg SL, Helke J, Koka MR, Kaplan EL. Pitfalls of intraoperative quick parathyroid hormone monitoring and gamma probe localization in surgery for primary hyperparathyroidism. Archives of Surgery. 2002; 137(6):659-69

306. Javaid A, Arfaj AA. Technetium-99m sestamibi scintigraphy and bone densitometry in primary hyperparathyroidism. Endocrine Practice. 1999; 5(4):169-73

307. Jha S, Jayaraman M, Jha A, Jha R, Modi KD, Kelwadee JV. Primary hyperparathyroidism: A changing scenario in India. Indian Journal of Endocrinology and Metabolism. 2016; 20(1):80-3

308. Jinih M, O'Connell E, O'Leary D P, Liew A, Redmond HP. Focused parathyroidectomy versus open parathyroidectomy for primary hyperparathyroidism: A meta-analysis. Irish Journal of Medical Science. 2016; 185(Suppl 2):S85

309. Jinih M, O'Connell E, O'Leary DP, Liew A, Redmond HP. Focused versus bilateral parathyroid exploration for primary hyperparathyroidism: A systematic review and meta-analysis. Annals of Surgical Oncology. 2017; 24(7):1924-34

310. Johnson LR, Doherty G, Lairmore T, Moley JF, Brunt LM, Koenig J et al. Evaluation of the performance and clinical impact of a rapid intraoperative parathyroid hormone assay in conjunction with preoperative imaging and concise parathyroidectomy. Clinical Chemistry. 2001; 47(5):919-25

311. Johnson NA, Yip L, Tublin ME. Cystic parathyroid adenoma: sonographic features and correlation with 99mTc-sestamibi SPECT findings. American Journal of Roentgenology. 2010; 195(6):1385-90

312. Johnston LB, Carroll MJ, Britton KE, Lowe DG, Shand W, Besser GM et al. The accuracy of parathyroid gland localization in primary hyperparathyroidism using sestamibi radionuclide imaging. Journal of Clinical Endocrinology and Metabolism. 1996; 81(1):346-52

313. Joint Formulary Committee. British National Formulary (BNF) September 2017. 2017. Available from: http://www.bnf.org.uk Last accessed: 18/09/2018.

314. Joliat GR, Demartines N, Portmann L, Boubaker A, Matter M. Successful minimally invasive surgery for primary hyperparathyroidism: influence of preoperative imaging and intraoperative parathyroid hormone levels. Langenbeck's Archives of Surgery. 2015; 400(8):937-44

315. Jones JJ, Brunaud L, Dowd CF, Duh QY, Morita E, Clark OH. Accuracy of selective venous sampling for intact parathyroid hormone in difficult patients with recurrent or persistent hyperparathyroidism. Surgery. 2002; 132(6):944-51

316. Jones JM, Russell CFJ, Ferguson WR, Laird JD. Pre-operative sestamibi-technetium subtraction scintigraphy in primary hyperparathyroidism: Experience with 156 consecutive patients. Clinical Radiology. 2001; 56(7):556-9

317. Jorna FH, Jager PL, Que TH, Lemstra C, Plukker JT. Value of 123I-subtraction and single-photon emission computed tomography in addition to planar 99mTc-MIBI scintigraphy before parathyroid surgery. Surgery Today. 2007; 37(12):1033-41

318. Kairaluoma MV, Kellosalo J, Makarainen H, Haukipuro K, Kairaluoma MI. Parathyroid re-exploration in patients with primary hyperparathyroidism. Annales Chirurgiae et Gynaecologiae. 1994; 83(3):202-6

319. Kairaluoma MV, Kellosalo J, Mäkäräinen H, Haukipuro K, Kairaluoma MI. Cost effectiveness of preoperative ultrasound in primary parathyroid surgery. Annales Chirurgiae et Gynaecologiae. 1994; 83(4):279-83

320. Kairaluoma MV, Makarainen H, Kellosalo J, Haukipuro K, Pirttiaho H, Kairaluoma MI. Preoperative ultrasound in patients undergoing initial neck exploration for primary hyperparathyroidism. Annales Chirurgiae et Gynaecologiae. 1993; 82(3):171-6

321. Kairys JC, Daskalakis C, Weigel RJ. Surgeon-performed ultrasound for preoperative localization of abnormal parathyroid glands in patients with primary hyperparathyroidism. World Journal of Surgery. 2006; 30(9):1658-63

322. Kandil E, Malazai AJ, Alrasheedi S, Tufano RP. Minimally invasive/focused parathyroidectomy in patients with negative sestamibi scan results. Archives of Otolaryngology - Head and Neck Surgery. 2012; 138(3):223-5

323. Kang YS, Rosen K, Clark OH, Higgins CB. Localization of abnormal parathyroid glands of the mediastinum with MR imaging. Radiology. 1993; 189(1):137-41

324. Karakas E, Kann S, Hoffken H, Bartsch DK, Celik I, Gorg C et al. Does contrast-enhanced cervical ultrasonography improve preoperative localization results in

patients with sporadic primary hyperparathyroidism? Journal of Clinical Imaging Science. 2012; 2:64

325. Katayama Y, Katagiri A, Saito K, Obara K, Komeyama T, Sato S et al. Localizing methods of primary hyperparathyroidism and those results. Japanese Journal of Urology. 1990; 81(5):707-12

326. Kaur P, Gattani R, Singhal AA, Sarin D, Arora SK, Mithal A. Impact of preoperative imaging on surgical approach for primary hyperparathyroidism: Data from single institution in India. Indian Journal of Endocrinology and Metabolism. 2016; 20(5):625-30

327. Keane DF, Roberts G, Smith R, Martin J, Peacey S, Bem C et al. Planar parathyroid localization scintigraphy: A comparison of subtraction and 1-, 2- and 3-h washout protocols. Nuclear Medicine Communications. 2013; 34(6):582-9

328. Kebapci M, Entok E, Kebapci N, Adapinar B. Preoperative evaluation of parathyroid lesions in patients with concomitant thyroid disease: Role of high resolution ultrasonography and dual phase technetium 99m sestamibi scintigraphy. Journal of Endocrinological Investigation. 2004; 27(1):24-30

329. Keidar Z, Solomonov E, Karry R, Frenkel A, Israel O, Mekel M. Preoperative [99mTc]MIBI SPECT/CT interpretation criteria for localization of parathyroid adenomas-correlation with surgical findings. Molecular Imaging and Biology. 2017; 19(2):265-70

330. Kelly HR, Hamberg LM, Hunter GJ. 4D-CT for preoperative localization of abnormal parathyroid glands in patients with hyperparathyroidism: Accuracy and ability to stratify patients by unilateral versus bilateral disease in surgery-naive and re-exploration patients. American Journal of Neuroradiology. 2014; 35(1):176-81

331. Kenny AM, MacGillivray DC, Pilbeam CC, Crombie HD, Raisz LG. Fracture incidence in postmenopausal women with primary hyperparathyroidism. Surgery. 1995; 118(1):109-14

332. Khaliq T, Khawar A, Shah SA, Mehboob A, Farooqui A. Unilateral exploration for primary hyperparathyroidism. Journal of the College of Physicians and Surgeons Pakistan. 2003; 13(10):588-91

333. Khan A, Bilezikian J, Bone H, Gurevich A, Lakatos P, Misiorowski W et al. Cinacalcet normalizes serum calcium in a double-blind randomized, placebo-controlled study in patients with primary hyperparathyroidism with contraindications to surgery. European Journal of Endocrinology. 2015; 172(5):527-35

334. Khan A, Samtani S, Varma VM, Frost A, Cohen J. Preoperative parathyroid localization: Prospective evaluation of technetium 99m sestamibi. Otolaryngology - Head and Neck Surgery. 1994; 111(4):467-72

335. Khan AA, Bilezikian JP, Bone HG, Gurevich A, Lakatos P, Misiorowski W et al. Cinacalcet normalizes serum calcium in a randomized, placebocontrolled clinical study in patients with primary hyperparathyroidism unable to undergo parathyroidectomy. Endocrine Reviews. 2014; 35(4 Suppl):MON-0196

336. Khan AA, Bilezikian JP, Kung A, Dubois SJ, Standish TI, Syed ZA. Alendronate therapy in men with primary hyperparathyroidism. Endocrine Practice. 2009; 15(7):705-13

337. Khan AA, Bilezikian JP, Kung AW, Ahmed MM, Dubois SJ, Ho AY et al. Alendronate in primary hyperparathyroidism: a double-blind, randomized, placebo-controlled trial. Journal of Clinical Endocrinology and Metabolism. 2004; 89(7):3319-25

338. Khan AA, Khatun Y, Walker A, Jimeno J, Hubbard JG. Role of intraoperative PTH monitoring and surgical approach in primary hyperparathyroidism. Annals of Medicine and Surgery. 2015; 4(3):301-5

339. Khorasani N, Mohammadi A. Effective factors on the sensitivity of preoperative sestamibi scanning for primary hyperparathyroidism. International Journal of Clinical and Experimental Medicine. 2014; 7(9):2639-44

340. Khosla S, Melton LJ, III, Wermers RA, Crowson CS, O'Fallon WM, Riggs BL. Primary hyperparathyroidism and the risk of fracture: A population-based study. Journal of Bone and Mineral Research. 1999; 14(10):1700-7

341. Kim HG, Kim WY, Woo SU, Lee JB, Lee YM. Minimally invasive parathyroidectomy with or without intraoperative parathyroid hormone for primary hyperparathyroidism. Annals of Surgical Treatment and Research. 2015; 89(3):111-6

342. Kim WW, Rhee Y, Ban EJ, Lee CR, Kang SW, Jeong JJ et al. Is focused parathyroidectomy appropriate for patients with primary hyperparathyroidism? Annals of Surgical Treatment and Research. 2016; 91(3):97-103

343. Kim YI, Jung YH, Hwang KT, Lee HY. Efficacy of 99mTc-sestamibi SPECT/CT for minimally invasive parathyroidectomy: comparative study with 99mTc-sestamibi scintigraphy, SPECT, US and CT. Annals of Nuclear Medicine. 2012; 26(10):804-10

344. Klieger P, O'Mara R. The diagnostic utility of dual phase Tc-99m sestamibi parathyroid imaging. Clinical Nuclear Medicine. 1998; 23(4):208-11

345. Kluijfhout WP, Pasternak JD, Beninato T, Drake FT, Gosnell JE, Shen WT et al. Diagnostic performance of computed tomography for parathyroid adenoma localization; a systematic review and meta-analysis. European Journal of Radiology. 2017; 88:117-128

346. Kluijfhout WP, Venkatesh S, Beninato T, Vriens MR, Duh QY, Wilson DM et al. Performance of magnetic resonance imaging in the evaluation of first-time and reoperative primary hyperparathyroidism. Surgery. 2016; 160(3):747-54

347. Kobayashi T, Asakawa H, Komoike Y, Nakano Y, Tamaki Y, Monden M. Identification of pathologic parathyroid glands in patients with primary hyperparathyroidism. Surgery Today. 1998; 28(6):604-7

348. Kobayashi T, Sugimoto T, Chihara K. Clinical and biochemical presentation of primary hyperparathyroidism in Kansai district of Japan. Endocrine Journal. 1997; 44(4):595-601

349. Koberstein W, Fung C, Romaniuk K, Abele JT. Accuracy of dual phase single-photon emission computed tomography/computed tomography in primary hyperparathyroidism: Correlation with serum parathyroid hormone levels. Canadian Association of Radiologists Journal. 2016; 67(2):115-21

350. Koksal H, Kurukahvecioglu O, Yazicioglu MO, Taneri F. Primary hyperparathyroidism due to parathyroid adenoma. Saudi Medical Journal. 2006; 27(7):1034-7

351. Koong HN, Choong LH, Soo KC. The role for preoperative localisation techniques in surgery for hyperparathyroidism. Annals of the Academy of Medicine, Singapore. 1998; 27(2):192-5

352. Koren I, Shpitzer T, Morgenshtern S, Shvero J. Lateral minimal parathyroidectomy: Safety and cosmetic benefits. American Journal of Otolaryngology. 2005; 26(2):83-6

353. Kovatcheva R, Vlahov J, Stoinov J, Lacoste F, Ortuno C, Zaletel K. US-guided high-intensity focused ultrasound as a promising non-invasive method for treatment of primary hyperparathyroidism. European Radiology. 2014; 24(9):2052-8

354. Koyuncu A, Dokmetas HS, Aydin C, Turan M, Erselcan T, Sozeri S et al. Surgical management strategies in patients with primary hyperparathyroidism: Which technique in which patients? Medical Principles and Practice. 2005; 14(3):194-8

355. Krakauer M, Wieslander B, Myschetzky PS, Lundstrom A, Bacher T, Sorensen CH et al. A prospective comparative study of parathyroid dual-phase scintigraphy, dual-isotope inftraction scintigraphy, 4d-ct, and ultrasonography in primary hyperparathyroidism. Clinical Nuclear Medicine. 2016; 41(2):93-100

356. Krausz Y, Bettman L, Guralnik L, Yosilevsky G, Keidar Z, Bar-Shalom R et al. Technetium-99m-MIBI SPECT/CT in primary hyperparathyroidism. World Journal of Surgery. 2006; 30(1):76-83

357. Kreidieh OI, Ahmadieh H, Akl EA, El-Hajj FG. Minimally invasive parathyroidectomy guided by intraoperative parathyroid hormone monitoring (IOPTH) and preoperative imaging versus bilateral neck exploration for primary hyperparathyroidism in adults. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD010787. DOI: 10.1002/14651858.CD010787.

358. Krubsack AJ, Wilson SD, Lawson TL, Kneeland JB, Thorsen MK, Collier BD et al. Prospective comparison of radionuclide, computed tomographic, sonographic, and magnetic resonance localization of parathyroid tumors. Surgery. 1989; 106(4):639-46

359. Kucuk NO, Arican P, Kocak S, Aras G. Radioguided surgery in primary hyperparathyroidism. Annals of Nuclear Medicine. 2002; 16(5):359-62

360. Kukar M, Platz TA, Schaffner TJ, Elmarzouky R, Groman A, Kumar S et al. The use of modified four-dimensional computed tomography in patients with primary hyperparathyroidism: An argument for the abandonment of routine sestamibi single-positron emission computed tomography (SPECT). Annals of Surgical Oncology. 2014; 22(1):139-45

361. Kumar A, Cozens NJA, Nash JR. Sestamibi scan-directed unilateral neck exploration for primary hyperparathyroidism due to a solitary adenoma. European Journal of Surgical Oncology. 2000; 26(8):785-8

362. Kuriloff DB, Sanborn KV. Rapid intraoperative localization of parathyroid glands utilizing methylene blue infusion. Otolaryngology - Head and Neck Surgery. 2004; 131(5):616-22

363. Kutler DI, Moquete R, Kazam E, Kuhel WI. Parathyroid localization with modified 4D-computed tomography and ultrasonography for patients with primary hyperparathyroidism. Laryngoscope. 2011; 121(6):1219-24

364. Kuzu F, Arpaci D, Cakmak GK, Emre AU, Elri T, Ilikhan SU et al. Focused parathyroidectomy without intra-operative parathormone monitoring: The value of PTH assay in preoperative ultrasound guided fine needle aspiration washout. Annals of Medicine and Surgery. 2016; 6:64-7

365. Kwon JH, Kim EK, Lee HS, Moon HJ, Kwak JY. Neck ultrasonography as preoperative localization of primary hyperparathyroidism with an additional role of detecting thyroid malignancy. European Journal of Radiology. 2013; 82(1):e17-e21

366. Lafferty FW, Hubay CA. Primary hyperparathyroidism. A review of the long-term surgical and nonsurgical morbidities as a basis for a rational approach to treatment. Archives of Internal Medicine. 1989; 149(4):789-96

367. Laird AM, Libutti SK. Minimally invasive parathyroidectomy versus bilateral neck exploration for primary hyperparathyroidism. Surgical Oncology Clinics of North America. 2016; 25(1):103-18

368. Larsson K, Lindh E, Lind L, Persson I, Ljunghall S. Increased fracture risk in hypercalcemia. Bone mineral content measured in hyperparathyroidism. Acta Orthopaedica Scandinavica. 1989; 60(3):268-70

369. Larsson K, Ljunghall S, Krusemo UB, Naessen T, Lindh E, Persson I. The risk of hip fractures in patients with primary hyperparathyroidism: A population-based cohort study with a follow-up of 19 years. Journal of Internal Medicine. 1993; 234(6):585-93

370. Lavely WC, Goetze S, Friedman KP, Leal JP, Zhang Z, Garret-Mayer E et al. Comparison of SPECT/CT, SPECT, and planar imaging with single- and dual-phase (99m)Tc-sestamibi parathyroid scintigraphy. Journal of Nuclear Medicine. 2007; 48(7):1084-9

371. Lebastchi AH, Aruny JE, Donovan PI, Quinn CE, Callender GG, Carling T et al. Real-time super selective venous sampling in remedial parathyroid surgery. Journal of the American College of Surgeons. 2015; 220(6):994-1000

372. Lee GS, McKenzie TJ, Mullan BP, Farley DR, Thompson GB, Richards ML. A multimodal imaging protocol, (123)I/(99)Tc-Sestamibi, SPECT, and SPECT/CT, in primary hyperparathyroidism adds limited benefit for preoperative localization. World Journal of Surgery. 2016; 40(3):589-94

373. Lee S, Ryu H, Morris LF, Grubbs EG, Lee JE, Harun N et al. Operative failure in minimally invasive parathyroidectomy utilizing an intraoperative parathyroid hormone assay. Annals of Surgical Oncology. 2014; 21(6):1878-83

374. Lee VS, Spritzer CE, Coleman RE, Wilkinson RH, Jr., Coogan AC, Leight GS, Jr. The complementary roles of fast spin-echo MR imaging and double-phase 99m Tc-sestamibi scintigraphy for localization of hyperfunctioning parathyroid glands. American Journal of Roentgenology. 1996; 167(6):1555-62

375. Lenschow C, Gassmann P, Wenning C, Senninger N, Colombo-Benkmann M. Preoperative 11C-methionine PET/CT enables focused parathyroidectomy in MIBI-SPECT negative parathyroid adenoma. World Journal of Surgery. 2015; 39(7):1750-7

376. Leong KJ, Sam RC, Garnham AW. Health-related quality of life improvement following surgical treatment of primary hyperparathyroidism in a United Kingdom population. Surgeon. 2010; 8(1):5-8

377. Leupe PK, Delaere PR, Vander Poorten VL, Debruyne F. Pre-operative imaging in primary hyperparathyroidism with ultrasonography and sestamibi scintigraphy. B-ENT. 2011; 7(3):173-80

378. Levin KE, Gooding GAW, Okerlund M, Higgins CB, Norman D, Newton TH et al. Localizing studies in patients with persistent or recurrent hyperparathyroidism. Surgery. 1987; 102(6):917-25

379. Lew JI, Irvin GL, III. Focused parathyroidectomy guided by intra-operative parathormone monitoring does not miss multiglandular disease in patients with sporadic primary hyperparathyroidism: A 10-year outcome. Surgery. 2009; 146(6):1021-7

380. Lew JI, Rivera M, Irvin GL, III, Solorzano CC. Operative failure in the era of focused parathyroidectomy: A contemporary series of 845 patients. Archives of Surgery. 2010; 145(7):628-33

381. Lezaic L, Rep S, Sever MJ, Kocjan T, Hocevar M, Fettich J. 18F-Fluorocholine PET/CT for localization of hyperfunctioning parathyroid tissue in primary hyperparathyroidism: a pilot study. European Journal of Nuclear Medicine and Molecular Imaging. 2014; 41(11):2083-9

382. Lim MS, Jinih M, Ngai CH, Foley NM, Redmond HP. The utility of the radionuclide probe in parathyroidectomy for primary hyperparathyroidism. Annals of the Royal College of Surgeons of England. 2017; 99(5):369-72

383. Lin JD, Huang BY, Huang HS, Wang PW, Jeng LB. Pre-operative localization of parathyroid tumor by ultrasonography. Chang Gung Medical Journal / Chang Gung Memorial Hospital. 1991; 14(1):1-7

384. Linda DD, Ng B, Rebello R, Harish S, Ioannidis G, Young JEM. The utility of multidetector computed tomography for detection of parathyroid disease in the setting of primary hyperparathyroidism Canadian Association of Radiologists Journal. 2012; 63(2):100-8

385. Lindqvist V, Jacobsson H, Chandanos E, Backdahl M, Kjellman M, Wallin G. Preoperative 99Tc(m)-sestamibi scintigraphy with SPECT localizes most pathologic parathyroid glands. Langenbeck's Archives of Surgery. 2009; 394(5):811-5

386. Livingston CD. Radioguided parathyroidectomy is successful in 98.7% of selected patients. Endocrine Practice. 2014; 20(4):305-9

387. Lloyd MNH, Lees WR, Milroy EJG. Pre-operative localisation in primary hyperparathyroidism. Clinical Radiology. 1990; 41(4):239-43

388. Lo CY, Chan WF, Luk JM. Minimally invasive endoscopic-assisted parathyroidectomy for primary hyperparathyroidism. Surgical Endoscopy and Other Interventional Techniques. 2003; 17(12):1932-6

389. Lo CY, Lang BH, Chan WF, Kung AWC, Lam KSL. A prospective evaluation of preoperative localization by technetium-99m sestamibi scintigraphy and ultrasonography in primary hyperparathyroidism. American Journal of Surgery. 2007; 193(2):155-9

390. Lombardi CP, Raffaelli M, Traini E, De Crea C, Corsello SM, Bellantone R. Video-assisted minimally invasive parathyroidectomy: Benefits and long-term results. World Journal of Surgery. 2009; 33(11):2266-81

391. Lombardi CP, Raffaelli M, Traini E, Di Stasio E, Carrozza C, De Crea C et al. Intraoperative PTH monitoring during parathyroidectomy: The need for stricter criteria to detect multiglandular disease. Langenbeck's Archives of Surgery. 2008; 393(5):639-45

392. Lowe H, McMahon DJ, Rubin MR, Bilezikian JP, Silverberg SJ. Normocalcemic primary hyperparathyroidism: further characterization of a new clinical phenotype. Journal of Clinical Endocrinology and Metabolism. 2007; 92(8):3001-5

393. Lubitz CC, Hunter GJ, Hamberg LM, Parangi S, Ruan D, Gawande A et al. Accuracy of 4-dimensional computed tomography in poorly localized patients with primary hyperparathyroidism. Surgery. 2010; 148(6):1129-37

394. Lueg MC. Hypertension and primary hyperparathyroidism: a five-year case review. Southern Medical Journal. 1982; 75(11):1371-4

395. Lumachi F, Tregnaghi A, Zucchetta P, Marzola MC, Cecchin D, Marchesi P et al. Technetium-99m sestamibi scintigraphy and helical CT together in patients with

primary hyperparathyroidism: A prospective clinical study. British Journal of Radiology. 2004; 77(914):100-3

396. Lundstam K, Heck A, Mollerup C, Godang K, Baranowski M, Pernow Y et al. Effects of parathyroidectomy versus observation on the development of vertebral fractures in mild primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2015; 100(4):1359-67

397. Lundstroem AK, Trolle W, Soerensen CH, Myschetzky PS. Preoperative localization of hyperfunctioning parathyroid glands with 4D-CT. European Archives of Oto-Rhino-Laryngology. 2016; 273(5):1253-9

398. Majors JD, Burke GJ, Mansberger AR, Jr, Wei JP. Technetium Tc 99m sestamibi scan for localizing abnormal parathyroid glands after previous neck operations: Preliminary experience in reoperative cases. Southern Medical Journal. 1995; 88(3):327-30

399. Malhotra A, Silver CE, Deshpande V, Freeman LM. Preoperative parathyroid localization with sestamibi. American Journal of Surgery. 1996; 172(6):637-40

400. Mandal R, Muthukrishnan A, Ferris RL, de Almeida JR, Duvvuri U. Accuracy of early-phase versus dual-phase single-photon emission computed tomography/computed tomography in the localization of parathyroid disease. Laryngoscope. 2015; 125(6):1496-501

401. Mandell DL, Genden EM, Mechanick JI, Bergman DA, Diamond EJ, Urken ML. The influence of intraoperative parathyroid hormone monitoring on the surgical management of hyperparathyroidism. Archives of Otolaryngology - Head and Neck Surgery. 2001; 127(7):821-7

402. Manhire AR, Anderson PN, Milroy E. Parathyroid venous sampling and ultrasonography in primary hyperparathyroidism due to multigland disease. British Journal of Radiology. 1984; 57(677):375-80

403. Marques TF, Vasconcelos R, Diniz E, Rego D, Griz L, Bandeira F. Normocalcemic primary hyperparathyroidism in clinical practice: an indolent condition or a silent threat? Arquivos Brasileiros de Endocrinologia e Metabologia. 2011; 55(5):314-7

404. Martin D, Rosen IB, Ichise M. Evaluation of single isotope technetium 99M-Sestamibi in localization efficiency for hyperparathyroidism. American Journal of Surgery. 1996; 172(6):633-6

405. Martin M, Robbins S, Lu ZJ. Use of cinacalcet in patients with intractable primary hyperparathyroidism (PHPT): A UK budget impact analysis. Endocrine Abstracts. 2010; 20:P228

406. Martin RC, 2nd, Greenwell D, Flynn MB. Initial neck exploration for untreated hyperparathyroidism. American Surgeon. 2000; 66(3):269-72

407. Martinez-Rodriguez I, Banzo I, Quirce R, Jimenez-Bonilla J, Portilla-Quattrociocchi H, Medina-Quiroz P et al. Early planar and early SPECT Tc-99m Sestamibi imaging: Can it replace the dual-phase technique for the localization of parathyroid adenomas by omitting the delayed phase? Clinical Nuclear Medicine. 2011; 36(9):749-53

408. Martinez-Rodriguez I, Martinez-Amador N, de Arcocha-Torres M, Quirce R, Ortega-Nava F, Ibanez-Bravo S et al. Comparison of ^{99m}Tc-sestamibi and ^{11}C-methionine PET/CT in the localization of parathyroid adenomas in primary hyperparathyroidism. Revista Espanola de Medicina Nuclear e Imagen Molecular. 2014; 33(2):93-8

409. Maweja S, Sebag F, Hubbard J, Giorgi R, Henry JF. Immediate and medium-term results of intraoperative parathyroid hormone monitoring during video-assisted parathyroidectomy. Archives of Surgery. 2004; 139(12):1301-3

410. Mazzeo S, Caramella D, Marcocci C, Lonzi S, Cambi L, Miccoli P et al. Contrast-enhanced color Doppler ultrasonography in suspected parathyroid lesions. Acta Radiologica. 2000; 41(5):412-6

411. McDermott VG, Mendez Fernandez RJ, Meakem ITJ, Stolpen AH, Spritzer CE, Gefter WB. Preoperative MR imaging in hyperparathyroidism: Results and factors affecting parathyroid detection. American Journal of Roentgenology. 1996; 166(3):705-10

412. McIntyre RC, Jr, Kumpe DA, Liechty RD, Thompson NW, Prinz RA, Clark OH et al. Reexploration and angiographic ablation for hyperparathyroidism. Archives of Surgery. 1994; 129(5):499-505

413. McMillan NC, Smith L, McKellar NJ, Beastall GH, Fogelman I, Duncan JG et al. The localisation of parathyroid tumours: A comparison of computed tomography with cervical vein hormone assay. Scottish Medical Journal. 1983; 28(2):153-6

414. Medas F, Erdas E, Longheu A, Gordini L, Pisano G, Nicolosi A et al. Retrospective evaluation of the pre- and postoperative factors influencing the sensitivity of localization studies in primary hyperparathyroidism. International Journal of Surgery. 2016; 25:82-7

415. Melton LJ, 3rd, Atkinson EJ, O'Fallon WM, Heath H, III Risk of age-related fractures in patients with primary hyperparathyroidism. Archives of Internal Medicine. 1992; 152(11):2269-73

416. Meyer SK, Zorn M, Frank-Raue K, Buchler MW, Nawroth P, Weber T. Clinical impact of two different intraoperative parathyroid hormone assays in primary and renal hyperparathyroidism. European Journal of Endocrinology. 2009; 160(2):275-81

417. Miccoli P, Bendinelli C, Berti P, Vignali E, Pinchera A, Marcocci C. Video-assisted versus conventional parathyroidectomy in primary hyperparathyroidism: a prospective randomized study. Surgery. 1999; 126(6):1117-21; discussion 1121-2

418. Miccoli P, Berti P, Materazzi G, Ambrosini CE, Fregoli L, Donatini G. Endoscopic bilateral neck exploration versus quick intraoperative parathormone assay (qPTHa) during endoscopic parathyroidectomy: A prospective randomized trial. Surgical Endoscopy. 2008; 22(2):398-400

419. Michel L, Dupont M, Rosiere A, Merlan V, Lacrosse M, Donckier JE. The rationale for performing MR imaging before surgery for primary hyperparathyroidism. Acta Chirurgica Belgica. 2013; 113(2):112-22

420. Mihai R, Palazzo FF, Gleeson FV, Sadler GP. Minimally invasive parathyroidectomy without intraoperative parathyroid hormone monitoring in patients with primary hyperparathyroidism. British Journal of Surgery. 2007; 94(1):42-7

421. Miller P, Kindred A, Kosoy D, Davidson D, Lang H, Waxman K et al. Preoperative sestamibi localization combined with intraoperative parathyroid hormone assay predicts successful focused unilateral neck exploration during surgery for primary hyperparathyroidism. American Surgeon. 2003; 69(1):82-5

422. Misiorowski W, Zgliczyski W. Prevalence of primary hyperparathyroidism among patients with low bone mass. Advances in Medical Sciences. 2012; 57(2):308-13

423. Miura D, Wada N, Arici C, Morita E, Duh QY, Clark OH. Does intraoperative quick parathyroid hormone assay improve the results of parathyroidectomy? World Journal of Surgery. 2002; 26(8):926-30

424. Mohammadi A, Moloudi F, Ghasemi-rad M. The role of colour Doppler ultrasonography in the preoperative localization of parathyroid adenomas. Endocrine Journal. 2012; 59(5):375-82

425. Moka D, Eschner W, Voth E, Dietlein M, Larena-Avellaneda A, Schicha H. Iterative reconstruction: An improvement of technetium-99m MIBI SPET for the detection of parathyroid adenomas? European Journal of Nuclear Medicine. 2000; 27(5):485-9

426. Moka D, Voth E, Dietlein M, Larena-Avellaneda A, Schicha H. Technetium 99m-MIBI-SPECT: A highly sensitive diagnostic tool for localization of parathyroid adenomas. Surgery. 2000; 128(1):29-35

427. Mole PA, Walkinshaw MH, Gunn A, Paterson CR. Bone mineral content in patients with primary hyperparathyroidism: A comparison of conservative management with surgical treatment. British Journal of Surgery. 1992; 79(3):263-5

428. Mollerup CL, Lindewald H. Renal stones and primary hyperparathyroidism: natural history of renal stone disease after successful parathyroidectomy. World Journal of Surgery. 1999; 23(2):173-5; discussion 176

429. Morks AN, Van Ginhoven TM, Pekelharing JM, Duschek EJJ, Smit PC, De Graaf PW. Intra-operative parathyroid hormone measurements - Experience of a non-academic hospital. South African Journal of Surgery. 2011; 49(3):123-6

430. Morris GS, Grubbs EG, Hearon CM, Gantela S, Lee JE, Evans DB et al. Parathyroidectomy improves functional capacity in "asymptomatic" older patients with primary hyperparathyroidism: a randomized control trial. Annals of Surgery. 2010; 251(5):832-7

431. Morris LF, Loh C, Ro K, Wiseman JE, Gomes AS, Asandra A et al. Nonsuper-selective venous sampling for persistent hyperparathyroidism using a systemic hypocalcemic challenge. Journal of Vascular and Interventional Radiology. 2012; 23(9):1191-9

432. Mortenson MM, Evans DB, Lee JE, Hunter GJ, Shellingerhout D, Vu T et al. Parathyroid exploration in the reoperative neck: Improved preoperative localization with 4D-computed tomography. Journal of the American College of Surgeons. 2008; 206(5):888-95

433. Moure D, Larranaga E, Dominguez-Gadea L, Luque-Ramirez M, Nattero L, Gomez-Pan A et al. ^{99M}Tc-sestamibi as sole technique in selection of primary hyperparathyroidism patients for unilateral neck exploration. Surgery. 2008; 144(3):454-9

434. Mozzon M, Mortier PE, Jacob PM, Soudan B, Boersma AA, Proye CAG et al. Surgical management of primary hyperparathyroidism: The case for giving up quick intraoperative PTH assay in favor of routine PTH measurement the morning after. Annals of Surgery. 2004; 240(6):949-54

435. Mshelia DS, Hatutale AN, Mokgoro NP, Nchabaleng ME, Buscombe JR, Sathekge MM. Correlation between serum calcium levels and dual-phase ^{99m}Tc-sestamibi parathyroid scintigraphy in primary hyperparathyroidism. Clinical Physiology and Functional Imaging. 2012; 32(1):19-24

436. Munk RS, Payne RJ, Luria BJ, Hier MP, Black MJ. Preoperative localization in primary hyperparathyroidism. Journal of Otolaryngology - Head and Neck Surgery. 2008; 37(3):347-54

437. Murchison J, McIntosh C, Aitken AGF, Logie J, Munro A. Ultrasonic detection of parathyroid adenomas. British Journal of Radiology. 1991; 64(764):679-82

438. Nael K, Hur J, Bauer A, Khan R, Sepahdari A, Inampudi R et al. Dynamic 4D MRI for characterization of parathyroid adenomas: Multiparametric analysis. American Journal of Neuroradiology. 2015; 36(11):2147-52

439. Nair CG, Babu MJ, Jacob P, Menon R, Mathew J. Is intraoperative parathyroid hormone monitoring necessary in symptomatic primary hyperparathyroidism with concordant imaging? Indian Journal of Endocrinology and Metabolism. 2016; 20(4):512-6

440. Najafian A, Kahan S, Olson MT, Tufano RP, Zeiger MA. Intraoperative PTH may not be necessary in the management of primary hyperparathyroidism even with only one positive or only indeterminate preoperative localization studies. World Journal of Surgery. 2017; 41(6):1500-5

441. Narayan R, Perkins RM, Berbano EP, Yuan CM, Neff RT, Sawyers ES et al. Parathyroidectomy versus cinacalcet hydrochloride-based medical therapy in the management of hyperparathyroidism in ESRD: a cost utility analysis. American Journal of Kidney Diseases. 2007; 49(6):801-13

442. Nasiri S, Soroush A, Hashemi AP, Hedayat A, Donboli K, Mehrkhani F. Parathyroid adenoma localization. Medical Journal of the Islamic Republic of Iran. 2012; 26(3):103-9

443. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

444. Nehs MA, Ruan DT, Gawande AA, Moore FD, Jr, Cho NL. Bilateral neck exploration decreases operative time compared to minimally invasive parathyroidectomy in patients with discordant imaging. World Journal of Surgery. 2013; 37(7):1614-7

445. Nelson CM, Victor NS. Rapid intraoperative parathyroid hormone assay in the surgical management of hyperparathyroidism. Permanente Journal. 2007; 11(1):3-6

446. Neumann DR, Esselstyn CB, Jr, Go RT, Wong CO, Rice TW, Obuchowski NA. Comparison of double-phase 99mTc-sestamibi with 123I-99mTc-sestamibi subtraction SPECT in hyperparathyroidism. American Journal of Roentgenology. 1997; 169(6):1671-4

447. Neumann DR, Esselstyn CB, Jr, Kim EY, Go RT, Obuchowski NA, Rice TW. Preliminary experience with double-phase SPECT using Tc-99m sestamibi in patients with hyperparathyroidism. Clinical Nuclear Medicine. 1997; 22(4):217-21

448. Neumann DR, Esselstyn CB, MacIntyre WJ, Go RT, Obuchowski NA, Chen EQ et al. Comparison of FDG-PET and sestamibi-SPECT in primary hyperparathyroidism. Journal of Nuclear Medicine. 1996; 37(11):1809-15

449. Neumann DR, Obuchowski NA, Difilippo FP. Preoperative 123I/99mTc-sestamibi subtraction SPECT and SPECT/CT in primary hyperparathyroidism. Journal of Nuclear Medicine. 2008; 49(12):2012-7

450. Neves MC, Ohe MN, Rosano M, Abrahao M, Cervantes O, Lazaretti-Castro M et al. A 10-year experience in intraoperative parathyroid hormone measurements for primary hyperparathyroidism: A prospective study of 91 previous unexplored patients. Journal of Osteoporosis. 2012; 2012:914214

451. NHS Business Services Authority. NHS electronic drug tariff September 2017. Available from: https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff Last accessed: 18/09/18.

452. Nilsen FS, Haug E, Heidemann M, Karlsen SJ. Does rapid intraoperative parathyroid hormone analysis predict cure in patients undergoing surgery for primary hyperparathyroidism? A prospective study. Scandinavian Journal of Surgery. 2006; 95(1):28-32

453. Nilsson IL, Aberg J, Rastad J, Lind L. Maintained normalization of cardiovascular dysfunction 5 years after parathyroidectomy in primary hyperparathyroidism. Surgery. 2005; 137(6):632-8

454. Noguchi Y. Hyperparathyroidism; Comparison of MR imaging with CT. Japanese Journal of Clinical Radiology. 1994; 39(3):367-72

455. Noltes ME, Coester AM, van der Horst-Schrivers ANA, Dorgelo B, Jansen L, Noordzij W et al. Localization of parathyroid adenomas using ^{11}C-methionine pet after prior inconclusive imaging. Langenbeck's Archives of Surgery. 2017; 402(7):1109-17

456. Nomura R, Sugimoto T, Tsukamoto T, Yamauchi M, Sowa H, Chen Q et al. Marked and sustained increase in bone mineral density after parathyroidectomy in patients with primary hyperparathyroidism; a six-year longitudinal study with or without parathyroidectomy in a Japanese population. Clinical Endocrinology. 2004; 60(3):335-42

457. Nordenstrom E, Westerdahl J, Bergenfelz A. Recovery of bone mineral density in 126 patients after surgery for primary hyperparathyroidism. World Journal of Surgery. 2004; 28(5):502-7

458. Nordin AJ, Larcos G, Ung O. Dual phase 99m-technetium Sestamibi imaging with single photon emission computed tomography in primary hyperparathyroidism: Influence on surgery. Australasian Radiology. 2001; 45(1):31-4

459. Norlen O, Wang KC, Tay YK, Johnson WR, Grodski S, Yeung M et al. No need to abandon focused parathyroidectomy: A multicenter study of long-term outcome after surgery for primary hyperparathyroidism. Annals of Surgery. 2015; 261(5):991-6

460. Numerow LM, Morita ET, Clark OH, Higgins CB. Persistent/recurrent hyperparathyroidism: a comparison of sestamibi scintigraphy, MRI, and ultrasonography. Journal of Magnetic Resonance Imaging. 1995; 5(6):702-8

461. O'Connell RL, Afors K, Thomas MH. Re-explorative parathyroid surgery for persistent and recurrent primary hyperparathyroidism. World Journal of Endocrine Surgery. 2011; 3(3):107-11

462. O'Doherty MJ, Kettle AG, Wells P, Collins REC, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: Preoperative localization and tissue uptake studies. Journal of Nuclear Medicine. 1992; 33(3):313-8

463. Ohe MN, Santos RO, Kunii IS, Carvalho AB, Abrahao M, Cervantes O et al. Usefulness of a rapid immunometric assay for intraoperative parathyroid hormone measurements. Brazilian Journal of Medical and Biological Research. 2003; 36(6):715-21

464. Opoku-Boateng A, Bolton JS, Corsetti R, Brown RE, Oxner C, Fuhrman GM. Use of a sestamibi-only approach to routine minimally invasive parathyroidectomy. American Surgeon. 2013; 79(8):797-801

465. Orevi M, Freedman N, Mishani E, Bocher M, Jacobson O, Krausz Y. Localization of parathyroid adenoma by 11C-Choline PET/CT: preliminary results. Clinical Nuclear Medicine. 2014; 39(12):1033-8

466. Orloff LA. Methylene blue and sestamibi: Complementary tools for localizing parathyroids. Laryngoscope. 2001; 111(11 I):1901-4

467. Oucharek JJ, O'Neill CJ, Suliburk JW, Sywak MS, Delbridge LW, Sidhu SB. Durability of focused minimally invasive parathyroidectomy in young patients with sporadic primary hyperparathyroidism. Annals of Surgical Oncology. 2011; 18(5):1290-2

468. Ozimek A, Gallwas J, Stocker U, Mussack T, Hallfeldt KKJ, Ladurner R. Validity and limits of intraoperative parathyroid hormone monitoring during minimally invasive parathyroidectomy: A 10-year experience. Surgical Endoscopy and Other Interventional Techniques. 2010; 24(12):3156-60

469. Ozkaya M, Elboga U, Sahin E, Kalender E, Korkmaz H, Demir HD et al. Evaluation of conventional imaging techniques on preoperative localization in primary hyperparathyroidism. Bosnian Journal of Basic Medical Sciences. 2015; 15(1):61-6

470. Ozkul MH, Uyar M, Bayram O, Dikmen B. Parathyroid scintigraphy and minimal invasive surgery in parathyroid adenomas. Journal of Ear, Nose, and Throat. 2015; 25(4):205-13

471. Paloyan E, Lawrence AM, Oslapas R, Shah KH, Ernst K, Hofmann C. Subtotal parathyroidectomy for primary hyperparathyroidism. Long-term results in 292 patients. Archives of Surgery. 1983; 118(4):425-31

472. Panzironi G, Falvo L, De Vargas Macciucca M, Catania A, Sorrenti S, Biancafarina A et al. Preoperative evaluation of primary hyperparathyroidism: role of diagnostic imaging. Chirurgia Italiana. 2002; 54(5):629-34

473. Parikh PP, Farra JC, Allan BJ, Lew JI. Long-term effectiveness of localization studies and intraoperative parathormone monitoring in patients undergoing reoperative parathyroidectomy for persistent or recurrent hyperparathyroidism. American Journal of Surgery. 2015; 210(1):117-22

474. Parker CR, Blackwell PJ, Fairbairn KJ, Hosking DJ. Alendronate in the treatment of primary hyperparathyroid-related osteoporosis: A 2-year study. Journal of Clinical Endocrinology and Metabolism. 2002; 87(10):4482-9

475. Pata G, Casella C, Besuzio S, Mittempergher F, Salerni B. Clinical appraisal of 99m technetium-sestamibi SPECT/CT compared to conventional SPECT in patients with primary hyperparathyroidism and concomitant nodular goiter. Thyroid. 2010; 20(10):1121-7

476. Pata G, Casella C, Magri GC, Lucchini S, Panarotto MB, Crea N et al. Financial and clinical implications of low-energy CT combined with 99m Technetium-sestamibi SPECT for primary hyperparathyroidism. Annals of Surgical Oncology. 2011; 18(9):2555-63

477. Patacsil ML, Dwarakanathan AA, Prinz RA. Sestamibi scanning and outcomes in minimally invasive parathyroidectomy. Endocrine Practice. 2006; 12(6):615-21

478. Patel PC, Pellitteri PK, Patel NM, Fleetwood MK. Use of a rapid intraoperative parathyroid hormone assay in the surgical management of parathyroid disease. Archives of Otolaryngology - Head and Neck Surgery. 1998; 124(5):559-62

479. Pattou F, Oudar C, Huglo D, Racadot A, Carnaille B, Proye C. Localization of abnormal parathyroid glands with jugular sampling for parathyroid hormone, and subtraction scanning with sestamibi or tetrofosmine. Australian and New Zealand Journal of Surgery. 1998; 68(2):108-11

480. Pattou F, Torres G, Mondragon-Sanchez A, Huglo D, N'Guyen H, Carnaille B et al. Correlation of parathyroid scanning and anatomy in 261 unselected patients with sporadic primary hyperparathyroidism. Surgery. 1999; 126(6):1123-31

481. Peacock M, Bilezikian JP, Bolognese MA, Borofsky M, Scumpia S, Sterling LR et al. Cinacalcet HCl reduces hypercalcemia in primary hyperparathyroidism across a wide spectrum of disease severity. Journal of Clinical Endocrinology and Metabolism. 2011; 96(1):E9-18

482. Peacock M, Bilezikian JP, Klassen PS, Guo MD, Turner SA, Shoback D. Cinacalcet hydrochloride maintains long-term normocalcemia in patients with primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2005; 90(1):135-41

483. Peacock M, Bolognese MA, Borofsky M, Scumpia S, Sterling LR, Cheng S et al. Cinacalcet treatment of primary hyperparathyroidism: biochemical and bone densitometric outcomes in a five-year study. Journal of Clinical Endocrinology and Metabolism. 2009; 94(12):4860-7

484. Pearl AJ, Chapnik JS, Freeman JL, Bain J, Salem S, Kirsh J et al. Pre-operative localization of 25 consecutive parathyroid adenomas: A prospective imaging/surgical correlative study. Journal of Otolaryngology. 1993; 22(4):301-6

485. Peck WW, Higgins CB, Fisher MR. Hyperparathyroidism: Comparison of MR imaging with radionuclide scanning. Radiology. 1987; 163(2):415-20

486. Pellitteri PK. Directed parathyroid exploration: evolution and evaluation of this approach in a single-institution review of 346 patients. Laryngoscope. 2003; 113(11):1857-69

487. Perez-Monte JE, Brown ML, Shah AN, Ranger NT, Watson CG, Carty SE et al. Parathyroid adenomas: Accurate detection and localization with Tc-99m sestamibi SPECT. Radiology. 1996; 201(1):85-91

488. Perrier ND, Balachandran D, Wefel JS, Jimenez C, Busaidy N, Morris GS et al. Prospective, randomized, controlled trial of parathyroidectomy versus observation in patients with "asymptomatic" primary hyperparathyroidism. Surgery. 2009; 146(6):1116-22

489. Perrier ND, Ituarte P, Kikuchi S, Siperstein AE, Duh QY, Clark OH et al. Intraoperative parathyroid aspiration and parathyroid hormone assay as an alternative to frozen section for tissue identification. World Journal of Surgery. 2000; 24(11):1319-22

490. Persson A, Bollerslev J, Rosen T, Mollerup CL, Franco C, Isaksen GA et al. Effect of surgery on cardiac structure and function in mild primary hyperparathyroidism. Clinical Endocrinology. 2011; 74(2):174-80

491. Philippon M, Guerin C, Taieb D, Vaillant J, Morange I, Brue T et al. Bilateral neck exploration in patients with primary hyperparathyroidism and discordant imaging

results: A single-centre study. European Journal of Endocrinology. 2014; 170(5):719-25

492. Politz D, Livingston CD, Victor B, Askew R, Jones L. Minimally invasive radio-guided parathyroidectomy in 152 consecutive patients with primary hyperparathyroidism. Endocrine Practice. 2006; 12(6):630-4

493. Posen S, Clifton-Bligh P, Reeve TS. Is parathyroidectomy of benefit in primary hyperparathyroidism? Quarterly Journal of Medicine. 1985; 54(215):241-51

494. Powell DK, Nwoke F, Goldfarb RC, Ongseng F. Tc-99m sestamibi parathyroid gland scintigraphy: Added value of Tc-99m pertechnetate thyroid imaging for increasing interpretation confidence and avoiding additional testing. Clinical Imaging. 2013; 37(3):475-9

495. Pradeep PV, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Long-term outcome after parathyroidectomy in patients with advanced primary hyperparathyroidism and associated vitamin D deficiency. World Journal of Surgery. 2008; 32(5):829-35

496. Prager G, Riss P, Bieglmayer C, Niederle B. The role of intraoperative quick PTH measurements in primary hyperparathyroidism. Annali Italiani di Chirurgia. 2003; 74(4):395-9

497. Prasannan S, Davies G, Bochner M, Kollias J, Malycha P. Minimally invasive parathyroidectomy using surgeon-performed ultrasound and sestamibi. ANZ Journal of Surgery. 2007; 77(9):774-7

498. Pratley SK, Posen S, Reeve TS. Primary hyperparathyroidism. Experiences with 60 patients. Medical Journal of Australia. 1973; 1(9):421-6

499. Preventza OA, Yang S, Karo JJ, Lobocki A, Mittal V, Sims DW et al. Pre-operative ultrasonography guiding minimal, selective surgical approach in primary hyperparathyroidism. International Surgery. 2000; 85(2):99-104

500. Profanter C, Gabriel M, Wetscher GJ, Gadenstatter M, Mittermair R, Moncayo R et al. Accuracy of preoperative pinhole subtraction single photon emission computed tomography for patients with primary and recurrent hyperparathyroidism in an endemic goiter area. Surgery Today. 2004; 34(6):493-7

501. Profanter C, Prommegger R, Gabriel M, Moncayo R, Wetscher GJ, Lang T et al. Computed axial tomography-MIBI image fusion for preoperative localization in primary hyperparathyroidism. American Journal of Surgery. 2004; 187(3):383-7

502. Profanter C, Wetscher GJ, Gabriel M, Sauper T, Rieger M, Kovacs P et al. CT-MIBI image fusion: A new preoperative localization technique for primary, recurrent, and persistent hyperparathyroidism. Surgery. 2004; 135(2):157-62

503. Purcell GP, Dirbas FM, Brookejeffrey R, Lane M, Desser T, Ross McDougall I et al. Parathyroid localization with high-resolution ultrasound and technetium Tc 99m sestamibi. Archives of Surgery. 1999; 134(8):824-30

504. Purnell DC, Smith LH, Scholz DA, Elveback LR, Arnaud CD. Primary hyperparathyroidism: a prospective clinical study. American Journal of Medicine. 1971; 50(5):670-8

505. Quiros RM, Alioto J, Wilhelm SM, Ali A, Prinz RA, Talpos GB et al. An algorithm to maximize use of minimally invasive parathyroidectomy. Archives of Surgery. 2004; 139(5):501-7

506. Rajeevan T, Cunning C, Abdulla A. 26 management of primary hyperparathyroidism (PHPT) in older people: A series review. Age and Ageing. 2014; 43(Suppl_1):i6-i6

507. Rameau A, Eng S, Vu J, Saket R, Jun P, Friduss M. Four-dimensional computed tomography scan utility in parathyroidectomy for primary hyperparathyroidism with low baseline intact parathyroid hormone. Laryngoscope. 2016; 127(6):1476-82

508. Ramirez AG, Shada AL, Martin AN, Raghavan P, Durst CR, Mukherjee S et al. Clinical efficacy of 2-phase versus 4-phase computed tomography for localization in primary hyperparathyroidism. Surgery. 2016; 160(3):731-7

509. Rao DS, Phillips ER, Divine GW, Talpos GB. Randomized controlled clinical trial of surgery versus no surgery in patients with mild asymptomatic primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2004; 89(11):5415-22

510. Rao DS, Wallace EA, Antonelli RF, Talpos GB, Ansari MR, Jacobsen G et al. Forearm bone density in primary hyperparathyroidism: Long-term follow-up with and without parathyroidectomy. Clinical Endocrinology. 2003; 58(3):348-54

511. Rauth JD, Sessions RB, Shupe SC, Ziessman HA. Comparison of Tc-99m MIBI and Tl-201/Tc-99m pertechnetate for diagnosis of primary hyperparathyroidism. Clinical Nuclear Medicine. 1996; 21(8):602-8

512. Reading CC, Charboneau JW, James EM. High-resolution parathyroid sonography. American Journal of Roentgenology. 1982; 139(3):539-46

513. Reading CC, Charboneau JW, James EM. Postoperative parathyroid high-frequency sonography: Evaluation of persistent or recurrent hyperparathyroidism. American Journal of Roentgenology. 1985; 144(2):399-402

514. Reasner CA, Stone MD, Hosking DJ, Ballah A, Mundy GR. Acute changes in calcium homeostasis during treatment of primary hyperparathyroidism with risedronate. Journal of Clinical Endocrinology and Metabolism. 1993; 77(4):1067-71

515. Reeve TS, Babidge WJ, Parkyn RF, Edis AJ, Delbridge LW, Devitt PG et al. Minimally invasive surgery for primary hyperparathyroidism: A systematic review. Australian and New Zealand Journal of Surgery. 2000; 70(4):244-50

516. Richards ML, Thompson GB, Farley DR, Grant CS. Reoperative parathyroidectomy in 228 patients during the era of minimal-access surgery and intraoperative parathyroid hormone monitoring. American Journal of Surgery. 2008; 196(6):937-43

517. Richards ML, Thompson GB, Farley DR, Grant CS. An optimal algorithm for intraoperative parathyroid hormone monitoring. Archives of Surgery. 2011; 146(3):280-5

518. Richmond BK, Eads K, Flaherty S, Belcher M, Runyon D. Complications of thyroidectomy and parathyroidectomy in the rural community hospital setting. American Surgeon. 2007; 73(4):332-6

519. Rickes S, Sitzy J, Neye H, Ocran KW, Wermke W. High-resolution ultrasound in combination with colour-Doppler sonography for preoperative localization of parathyroid adenomas in patients with primary hyperparathyroidism. Ultraschall in der Medizin. 2003; 24(2):85-9

520. Riss P, Scheuba C, Asari R, Bieglmayer C, Niederle B. Is minimally invasive parathyroidectomy without QPTH monitoring justified? Langenbeck's Archives of Surgery. 2009; 394(5):875-80

521. Rodgers SE, Hunter GJ, Hamberg LM, Schellingerhout D, Doherty DB, Ayers GD et al. Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography. Surgery. 2006; 140(6):932-41

522. Rolighed L, Heickendorff L, Hessov I, Garne JP, Rodt SA, Christiansen P. Primary hyperparathyroidism: Intraoperative PTH-measurements. Scandinavian Journal of Surgery. 2004; 93(1):43-7

523. Rolighed L, Vestergaard P, Heickendorff L, Sikjaer T, Rejnmark L, Mosekilde L et al. Bone mineral density improvements after operation for primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2012; 397 (5):845

524. Ronni-Sivula H. Causes of death in patients previously operated on for primary hyperparathyroidism. Annales Chirurgiae et Gynaecologiae. 1985; 74(1):13-8

525. Roskies M, Liu X, Hier MP, Payne RJ, Mlynarek A, Forest V et al. 3-phase dual-energy CT scan as a feasible salvage imaging modality for the identification of non-localizing parathyroid adenomas: A prospective study. Journal of Otolaryngology - Head and Neck Surgery. 2015; 44:44

526. Rossi HL, Ali A, Prinz RA. Intraoperative sestamibi scanning in reoperative parathyroidectomy. Surgery. 2000; 128(4):744-50

527. Rossini M, Gatti D, Isaia G, Sartori L, Braga V, Adami S. Effects of oral alendronate in elderly patients with osteoporosis and mild primary hyperparathyroidism. Journal of Bone and Mineral Research. 2001; 16(1):113-9

528. Rotstein L, Irish J, Gullane P, Keller MA, Sniderman K. Reoperative parathyroidectomy in the era of localization technology. Head and Neck. 1998; 20(6):535-9

529. Roza AM, Wexler MJ, Stein L, Goltzman D. Value of high-resolution computerized tomography in localizing diseased parathyroid glands. Canadian Journal of Surgery. 1984; 27(4):334-6

530. Rubello D, Mariani G, Al-Nahhas A, Pelizzo MR, Italian Study Group on Radioguided S, Immunoscintigraphy. Minimally invasive radio-guided parathyroidectomy: long-term results with the 'low 99mTc-sestamibi protocol'. Nuclear Medicine Communications. 2006; 27(9):709-13

531. Rubello D, Massaro A, Cittadin S, Rampin L, Al-Nahhas A, Boni G et al. Role of 99mTc-sestamibi SPECT in accurate selection of primary hyperparathyroid patients for minimally invasive radio-guided surgery. European Journal of Nuclear Medicine and Molecular Imaging. 2006; 33(9):1091-4

532. Rubello D, Pelizzo MR, Boni G, Schiavo R, Vaggelli L, Villa G et al. Radioguided surgery of primary hyperparathyroidism using the low-dose 99mTc-sestamibi protocol: multiinstitutional experience from the Italian Study Group on Radioguided Surgery and Immunoscintigraphy (GISCRIS). Journal of Nuclear Medicine. 2005; 46(2):220-6

533. Rubello D, Piotto A, Casara D, Muzzio PC, Shapiro B, Pelizzo MR. Role of gamma probes in performing minimally invasive parathyroidectomy in patients with primary hyperparathyroidism: Optimization of preoperative and intraoperative procedures. European Journal of Endocrinology. 2003; 149(1):7-15

534. Rubin MR, Bilezikian JP, McMahon DJ, Jacobs T, Shane E, Siris E et al. The natural history of primary hyperparathyroidism with or without parathyroid surgery after 15 years. Journal of Clinical Endocrinology and Metabolism. 2008; 93(9):3462-70

535. Ruckert Y, Gerl H, Ruckert RI, Wermke W. Value of colour Doppler in the pre-operative localization of parathyroid tumours. European Journal of Ultrasound. 1996; 4(2):107-14

536. Ruf J, Lopez Hanninen E, Steinmuller T, Rohlfing T, Bertram H, Gutberlet M et al. Preoperative localization of parathyroid glands: Use of MRI, scintigraphy, and image fusion. Nuklearmedizin. 2004; 43(3):85-90

537. Ruf J, Seehofer D, Denecke T, Stelter L, Rayes N, Felix R et al. Impact of image fusion and attenuation correction by SPECT-CT on the scintigraphic detection of parathyroid adenomas. Nuklearmedizin. 2007; 46(1):15-21

538. Russell CF, Dolan SJ, Laird JD. Randomized clinical trial comparing scan-directed unilateral versus bilateral cervical exploration for primary hyperparathyroidism due to solitary adenoma. British Journal of Surgery. 2006; 93(4):418-21

539. Ryan JA, Jr, Eisenberg B, Pado KM, Lee F. Efficacy of selective unilateral exploration in hyperparathyroidism based on localization tests. Archives of Surgery. 1997; 132(8):886-91

540. Ryhanen EM, Schildt J, Heiskanen I, Vaisanen M, Ahonen A, Loyttyniemi E et al. ^{99m}Technetium sestamibi-^{123}iodine scintigraphy is more accurate than ^{99m}technetium sestamibi alone before surgery for primary hyperparathyroidism. International Journal of Molecular Imaging. 2015; 2015:391625

541. Saaristo RA, Salmi JJO, Koobi T, Turjanmaa V, Sand JA, Nordback IH. Intraoperative localization of parathyroid glands with gamma counter probe in primary hyperparathyroidism: A prospective study. Journal of the American College of Surgeons. 2002; 195(1):19-22

542. Sadeghi N, Akin E, Lee JY, Roland J, Knoll S. Targeted parathyroidectomy: Effectiveness and intraoperative rapid-parathormone dynamics. Laryngoscope. 2008; 118(11):1997-2002

543. Sadeghi N, Li NW, Shokri T, Akin E, Joshi AS, Knoll S. Minimally elevated preoperative parathyroid hormone level influences the management of primary hyperparathyroidism Laryngoscope. 2018; 128(4):1016-21

544. Sadik KW, Kell M, Gorey T. Minimally invasive parathyroidectomy using surgical sonography. International Journal of Medical Sciences. 2011; 8(4):283-6

545. Sagan D, Gozdziuk K. Surgical treatment of mediastinal parathyroid adenoma: Rationale for intraoperative parathyroid hormone monitoring. Annals of Thoracic Surgery. 2010; 89(6):1750-5

546. Sager S, Shafipour H, Asa S, Yilmaz S, Teksoz S, Onsel C. Comparison of Tc-99m pertechnetate images with dual-phase Tc 99m MIBI and SPECT images in primary hyperparathyroidism. Indian Journal of Endocrinology and Metabolism. 2014; 18(4):531-6

547. Saguan N, Recabaren J. A unique use of intraoperative digital specimen radiography in the treatment of primary hyperparathyroidism. American Surgeon. 2013; 79(10):1098-101

548. Saint Marc O, Cogliandolo A, Pidoto RR, Pozzo A. Prospective evaluation of ultrasonography plus MIBI scintigraphy in selecting patients with primary hyperparathyroidism for unilateral neck exploration under local anaesthesia. American Journal of Surgery. 2004; 187(3):388-93

549. Sakimura C, Minami S, Hayashida N, Uga T, Inokuchi N, Eguchi S. Can the use of intraoperative intact parathyroid hormone monitoring be abandoned in patients with hyperparathyroidism? American Journal of Surgery. 2013; 206(4):574-7

550. Sand J, Salmi J, Saaristo J. Primary hyperparathyroidism: Surgical results of 147 consecutive patients. Annales Chirurgiae et Gynaecologiae. 1994; 83(1):35-9

551. Sandqvist P, Nilsson IL, Gryback P, Sanchez-Crespo A, Sundin A. SPECT/CT's advantage for preoperative localization of small parathyroid adenomas in primary hyperparathyroidism. Clinical Nuclear Medicine. 2017; 42(2):e109-e114

552. Sandrock D, Merino MJ, Norton JA, Neumann RD. Parathyroid imaging by Tc/Tl scintigraphy. European Journal of Nuclear Medicine. 1990; 16(8-10):607-13

553. Sankaran S, Gamble G, Bolland M, Reid IR, Grey A. Skeletal effects of interventions in mild primary hyperparathyroidism: A meta-analysis. Journal of Clinical Endocrinology and Metabolism. 2010; 95(4):1653-62

554. Sanzenbacher LJ, Pak CY, Bartter FC. Preoperative and postoperative evaluation of patients with normocalcemic primary hyperparathyroidism. Surgical Forum. 1970; 21(4):96-8

555. Saponaro F, Faggiano A, Grimaldi F, Borretta G, Brandi ML, Minisola S et al. Cinacalcet in the management of primary hyperparathyroidism: Post marketing experience of an Italian multicentre group. Clinical Endocrinology. 2013; 79(1):20-6

556. Schalin-Jantti C, Ryhanen E, Heiskanen I, Seppanen M, Arola J, Schildt J et al. Planar scintigraphy with 123I/99mTc-sestamibi, 99mTc-sestamibi SPECT/CT, 11C-methionine PET/CT, or selective venous sampling before reoperation of primary hyperparathyroidism? Journal of Nuclear Medicine. 2013; 54(5):739-47

557. Scheible W, Deutsch AL, Leopold GR. Parathyroid adenoma: accuracy of preoperative localization by high-resolution real-time sonography. Journal of Clinical Ultrasound. 1981; 9(6):325-30

558. Scheiner JD, Dupuy DE, Monchik JM, Noto RB, Cronan JJ. Pre-operative localization of parathyroid adenomas: A comparison of power and colour Doppler ultrasonography with nuclear medicine scintigraphy. Clinical Radiology. 2001; 56(12):984-8

559. Schenk WG, Hanks JB, Smith PW. Surgeon-performed ultrasound for primary hyperparathyroidism. American Surgeon. 2013; 79(7):681-5

560. Schneider DF, Mazeh H, Chen H, Sippel RS. Predictors of recurrence in primary hyperparathyroidism: An analysis of 1386 cases. Annals of Surgery. 2014; 259(3):563-8

561. Scholz DA, Purnell DC. Asymptomatic primary hyperparathyroidism. 10-year prospective study. Mayo Clinic Proceedings. 1981; 56(8):473-8

562. Schwarz P, Body JJ, Cap J, Hofbauer LC, Farouk M, Gessl A et al. The PRIMARA study: a prospective, descriptive, observational study to review cinacalcet use in patients with primary hyperparathyroidism in clinical practice. European Journal of Endocrinology. 2014; 171(6):727-35

563. Scott-Coombes DM, Rees J, Jones G, Stechman MJ. Is unilateral neck surgery feasible in patients with sporadic primary hyperparathyroidism and double negative localisation? World Journal of Surgery. 2017; 41(6):1494-9

564. Scott HW, Jr, Richie RE, Crane JM, Rosenfeld L, Jacobs JK, Ginn E et al. Surgical experience with hyperparathyroidism. American Surgeon. 1981; 47(2):54-62

565. Sebag F, Shen W, Brunaud L, Kebebew E, Duh QY, Clark OH et al. Intraoperative parathyroid hormone assay and parathyroid reoperations. Surgery. 2003; 134(6):1049-56

566. Seeliger B, Alesina PF, Koch JA, Hinrichs J, Meier B, Walz MK. Diagnostic value and clinical impact of complementary CT scan prior to surgery for non-localized primary hyperparathyroidism. Langenbeck's Archives of Surgery. 2015; 400(3):307-12

567. Sejean K, Calmus S, Durand-Zaleski I, Bonnichon P, Thomopoulos P, Cormier C et al. Surgery versus medical follow-up in patients with asymptomatic primary hyperparathyroidism: a decision analysis European Journal of Endocrinology. 2005; 153(6):915-27

568. Seniaray N, Sharma H, Arbind A, Jaimini A, D'Souza M, Saw S et al. (11)C-Methionine positron emission tomography-computed tomography in localization of methoxyisobutyl isonitrile negative ectopic parathyroid adenoma. Indian Journal of Nuclear Medicine. 2016; 31(1):49-51

569. Sepahdari AR, Bahl M, Harari A, Kim HJ, Yeh MW, Hoang JK. Predictors of multigland disease in primary hyperparathyroidism: A scoring system with 4D-CT imaging and biochemical markers. American Journal of Neuroradiology. 2015; 36(5):987-92

570. Serra A, Bolasco P, Satta L, Nicolosi A, Uccheddu A, Piga M. Role of SPECT/CT in the preoperative assessment of hyperparathyroid patients. Radiologia Medica. 2006; 111(7):999-1008

571. Seyednejad N, Healy C, Tiwari P, Vos P, Sexsmith G, Melck A et al. Dual-energy computed tomography: A promising novel preoperative localization study for treatment of primary hyperparathyroidism. American Journal of Surgery. 2016; 211(5):839-45

572. Shabtai M, Ben-Haim M, Muntz Y, Vered I, Rosin D, Kuriansky J et al. 140 Consecutive cases of minimally invasive, radio-guided parathyroidectomy: Lessons learned and long-term results. Surgical Endoscopy and Other Interventional Techniques. 2003; 17(5):688-91

573. Shafiei B, Hoseinzadeh S, Fotouhi F, Malek H, Azizi F, Jahed A et al. Preoperative 99m Tc-sestamibi scintigraphy in patients with primary hyperparathyroidism and concomitant nodular goiter: Comparison of SPECT-CT, SPECT, and planar imaging. Nuclear Medicine Communications. 2012; 33(10):1070-6

574. Shaha AR, Sarkar S, Strashun A, Yeh S. Sestamibi scan for preoperative localization in primary hyperparathyroidism. Head and Neck. 1997; 19(2):87-91

575. Shaheen F, Chowdry N, Gojwari T, Wani A, Khan S. Role of cervical ultrasonography in primary hyperparathyroidism. Indian Journal of Radiology and Imaging. 2008; 18(4):302-5

576. Sharma J, Mazzaglia P, Milas M, Berber E, Schuster DM, Halkar R et al. Radionuclide imaging for hyperparathyroidism (HPT): Which is the best technetium-99m sestamibi modality? Surgery. 2006; 140(6):856-65

577. Sharma J, Milas M, Berber E, Mazzaglia P, Siperstein A, Weber CJ. Value of intraoperative parathyroid hormone monitoring. Annals of Surgical Oncology. 2008; 15(2):493-8

578. Sheng SW, Zhu RS, Fan YB, Gao YC, Lu HK. Value of 99m Tc-MIBI SPECT/CT in diagnosis of primary hyperparathyroidism. Journal of Shanghai Jiaotong University. 2011; 31(10):1423-7

579. Shin JJ, Milas M, Mitchell J, Berber E, Ross L, Siperstein A. Impact of localization studies and clinical scenario in patients with hyperparathyroidism being evaluated for reoperative neck surgery. Archives of Surgery. 2011; 146(12):1397-403

580. Sho S, Yilma M, Yeh MW, Livhits M, Wu JX, Hoang JK et al. Prospective validation of two 4D-CT-based scoring systems for prediction of multigland disease in primary hyperparathyroidism. American Journal of Neuroradiology. 2016; 37(12):2323-7

581. Shoback DM, Bilezikian JP, Turner SA, McCary LC, Guo MD, Peacock M. The calcimimetic cinacalcet normalizes serum calcium in subjects with primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2003; 88(12):5644-9

582. Siilin H, Lundgren E, Mallmin H, Mellstrom D, Ohlsson C, Karlsson M et al. Prevalence of primary hyperparathyroidism and impact on bone mineral density in elderly men: MrOs Sweden. World Journal of Surgery. 2011; 35(6):1266-72

583. Silov G, Ozdal A, Erdogan Z, Turhal O, Karaman H. The relationship between technetium-99m-methoxyisobutyl isonitrile parathyroid scintigraphy and hormonal and biochemical markers in suspicion of primary hyperparathyroidism. Molecular Imaging and Radionuclide Therapy. 2013; 22(1):8-13

584. Silverberg SJ, Gartenberg F, Jacobs TP, Shane E, Siris E, Staron RB et al. Longitudinal measurements of bone density and biochemical indices in untreated primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 1995; 80(3):723-8

585. Silverberg SJ, Gartenberg F, Jacobs TP, Shane E, Siris E, Staron RB et al. Increased bone mineral density after parathyroidectomy in primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 1995; 80(3):729-34

586. Silverberg SJ, Shane E, Jacobs TP, Siris E, Bilezikian JP. A 10-year prospective study of primary hyperparathyroidism with or without parathyroid surgery. New England Journal of Medicine. 1999; 341(17):1249-55

587. Silverberg SJ, Shane E, Jacobs TP, Siris ES, Gartenberg F, Seldin D et al. Nephrolithiasis and bone involvement in primary hyperparathyroidism. American Journal of Medicine. 1990; 89(3):327-34

588. Siminovitch JM, James RE, Esselstyn CB, Jr., Straffon RA, Banowsky LH. The effect of parathyroidectomy in patients with normocalcemic calcium stones. Journal of Urology. 1980; 123(3):335-7

589. Simonella G, Massaccesi E, Marzi C, Staffolani P, Falco A, Morosini P. [Minimally invasive surgery versus bilateral neck exploration for primary hyperparathyroidism: controlled prospective study. Role of intraoperative rapid parathyroid hormone assay and radiological preoperative detection of adenomas]. Recenti Progressi in Medicina. 2005; 96(10):483-7

590. Singh N, Krishna BA. Role of radionuclide scintigraphy in the detection of parathyroid adenoma. Indian Journal of Cancer. 2007; 44(1):12-6

591. Singh Ospina N, Maraka S, Rodriguez-Gutierrez R, Espinosa de Ycaza AE, Jasim S, Gionfriddo M et al. Comparative efficacy of parathyroidectomy and active surveillance in patients with mild primary hyperparathyroidism: a systematic review and meta-analysis. Osteoporosis International. 2016; 27(12):3395-407

592. Singh Ospina NM, Rodriguez-Gutierrez R, Maraka S, Espinosa de Ycaza AE, Jasim S, Castaneda-Guarderas A et al. Outcomes of parathyroidectomy in patients with primary hyperparathyroidism: A systematic review and meta-analysis. World Journal of Surgery. 2016; 40(10):2359-77

593. Siperstein A, Berber E, Barbosa GF, Tsinberg M, Greene AB, Mitchell J et al. Predicting the success of limited exploration for primary hyperparathyroidism using ultrasound, sestamibi, and intraoperative parathyroid hormone: Analysis of 1158 cases. Annals of Surgery. 2008; 248(3):420-6

594. Siperstein A, Berber E, Mackey R, Alghoul M, Wagner K, Milas M. Prospective evaluation of sestamibi scan, ultrasonography, and rapid PTH to predict the success of limited exploration for sporadic primary hyperparathyroidism. Surgery. 2004; 136(4):872-80

595. Siperstein AE, Shen W, Chan AK, Duh QY, Clark OH, Giuliano AE et al. Normocalcemic hyperparathyroidism: Biochemical and symptom profiles before and after surgery. Archives of Surgery. 1992; 127(10):1157-63

596. Slater A, Gleeson FV. Increased sensitivity and confidence of SPECT over planar imaging in dual-phase sestamibi for parathyroid adenoma detection. Clinical Nuclear Medicine. 2005; 30(1):1-3

597. Slepavicius A, Beisa V, Janusonis V, Strupas K. Focused versus conventional parathyroidectomy for primary hyperparathyroidism: a prospective, randomized, blinded trial. Langenbeck's Archives of Surgery. 2008; 393(5):659-66

598. Smith N, Magnuson JS, Vidrine DM, Kulbersh B, Peters GE. Minimally invasive parathyroidectomy: Use of intraoperative parathyroid hormone assays after 2 preoperative localization studies. Archives of Otolaryngology - Head and Neck Surgery. 2009; 135(11):1108-11

599. Sofferman RA, Nathan MH, Fairbank JT, Foster RS, Jr, Krag DN. Preoperative technetium Tc 99m sestamibi imaging: Paving the way to minimal-access parathyroid surgery. Archives of Otolaryngology - Head and Neck Surgery. 1996; 122(4):369-74

600. Sofferman RA, Standage J, Tang ME. Minimal-access parathyroid surgery using intraoperative parathyroid hormone assay. Laryngoscope. 1998; 108(10):1497-503

601. Sofianides T, Chang YS, Leary JS, Nichols FX. Localization of parathyroid adenomas by cervical esophagram. Journal of Clinical Endocrinology and Metabolism. 1978; 46(4):587-92

602. Sohn JA, Oltmann SC, Schneider DF, Sippel RS, Chen H, Elfenbein DM. Is intraoperative parathyroid hormone testing in patients with renal insufficiency undergoing parathyroidectomy for primary hyperparathyroidism accurate? American Journal of Surgery. 2015; 209(3):483-7

603. Sokoll LJ, Drew H, Udelsman R. Intraoperative parathyroid hormone analysis: A study of 200 consecutive cases. Clinical Chemistry. 2000; 46(10):1662-8

604. Solorzano CC, Carneiro-Pla DM, Irvin IGL. Surgeon-performed ultrasonography as the initial and only localizing study in sporadic primary hyperparathyroidism. Journal of the American College of Surgeons. 2006; 202(1):18-24

605. Solorzano CC, Lee TM, Ramirez MC, Carneiro DM, Irvin GL. Surgeon-performed ultrasound improves localization of abnormal parathyroid glands. American Surgeon. 2005; 71(7):557-62; discussion 562-3

606. Solorzano CC, Mendez W, Lew JI, Rodgers SE, Montano R, Carneiro-Pla DM et al. Long-term outcome of patients with elevated parathyroid hormone levels after successful parathyroidectomy for sporadic primary hyperparathyroidism. Archives of Surgery. 2008; 143(7):659-63

607. Sommer B, Welter HF, Spelsberg F. Computed tomography for localizing enlarged parathyroid glands in primary hyperparathyroidism. Journal of Computer Assisted Tomography. 1982; 6(3):521-6

608. Song AU, Phillips TE, Edmond CV, Moore DW, Clark SK. Success of preoperative imaging and unilateral neck exploration for primary hyperparathyroidism. Otolaryngology - Head and Neck Surgery. 1999; 121(4):393-7

609. Soon PS, Delbridge LW, Sywak MS, Barraclough BM, Edhouse P, Sidhu SB. Surgeon performed ultrasound facilitates minimally invasive parathyroidectomy by the focused lateral mini-incision approach. World Journal of Surgery. 2008; 32(5):766-71

610. Soreide JA, Van Heerden JA, Grant CS, Lo CY, Schleck C, Ilstrup DM. Survival after surgical treatment for primary hyperparathyroidism. Surgery. 1997; 122(6):1117-23

611. Soyder A, Unubol M, Omurlu IK, Guney E, Ozbas S. Minimally invasive parathyroidectomy without using intraoperative parathyroid hormone monitoring or gamma probe. Turkish Journal of Surgery. 2015; 31(1):9-14

612. Sozio A, Schietroma M, Franchi L, Mazzotta C, Cappelli S, Amicucci G. [Parathyroidectomy: bilateral exploration of the neck vs minimally invasive radioguided treatment]. Minerva Chirurgica. 2005; 60(2):83-9

613. Sprouse LR, Roe SM, Kaufman HJ, Williams N. Minimally invasive parathyroidectomy without intraoperative localization. American Surgeon. 2001; 67(11):1022-9

614. Sreevathsa MR, Melanta K. Unilateral exploration for parathyroid adenoma. Indian Journal of Surgical Oncology. 2017; 8(2):142-5

615. Stalberg P, Sidhu S, Sywak M, Robinson B, Wilkinson M, Delbridge L. Intraoperative parathyroid hormone measurement during minimally invasive parathyroidectomy: Does it "value-add" to decision-making? Journal of the American College of Surgeons. 2006; 203(1):1-6

616. Starker LF, Mahajan A, Bjorklund P, Sze G, Udelsman R, Carling T. 4D parathyroid CT as the initial localization study for patients with de novo primary hyperparathyroidism. Annals of Surgical Oncology. 2011; 18(6):1723-8

617. Starr FL, DeCresce R, Prinz RA. Use of intraoperative parathyroid hormone measurement does not improve success of bilateral neck exploration for hyperparathyroidism. Archives of Surgery. 2001; 136(5):536-42

618. Staudenherz A, Abela C, Niederle B, Steiner E, Helbich T, Puig S et al. Comparison and histopathological correlation of three parathyroid imaging methods in a population with a high prevalence of concomitant thyroid diseases. European Journal of Nuclear Medicine. 1997; 24(2):143-9

619. Stein BL, Wexler MJ. Preoperative parathyroid localization: A prospective evaluation of ultrasonography and thallium-technetium scintigraphy in hyperparathyroidism. Canadian Journal of Surgery. 1990; 33(3):175-80

620. Stenner E, Dobrinja C, Micheli W, Trevisan G, Liguori G, Biasioli B. Intraoperative parathyroid hormone monitoring in minimally invasive video-assisted parathyroidectomy. Rivista Italiana della Medicina di Laboratorio. 2009; 5(1):24-8

621. Stevens SK, Chang JM, Clark OH, Chang PJ, Higgins CB. Detection of abnormal parathyroid glands in postoperative patients with recurrent hyperparathyroidism: Sensitivity of MR imaging. American Journal of Roentgenology. 1993; 160(3):607-12

622. Steward DL, Danielson GP, Afman CE, Welge JA. Parathyroid adenoma localization: Surgeon-performed ultrasound versus sestamibi. Laryngoscope. 2006; 116(8):1380-4

623. Stratmann SL, Kuhn JA, Bell MS, Preskitt JT, O'Brien JC, Gable DR et al. Comparison of quick parathyroid assay for uniglandular and multiglandular parathyroid disease. American Journal of Surgery. 2002; 184(6):578-81

624. Strewler GJ. Indications for surgery in patients with minimally symptomatic primary hyperparathyroidism. Surgical Clinics of North America. 1995; 75(3):439-47

625. Suarez JP, Dominguez ML, de Santos FJ, Gonzalez JM, Fernandez N, Enciso FJ. Radioguided surgery in primary hyperparathyroidism: Results and correlation with intraoperative histopathologic diagnosis. Acta Otorrinolaringologica Espanola. 2017; 69(2):86-94

626. Sugg SL, Fraker DL, Alexander HR, Doppman JL, Miller DL, Chang R et al. Prospective evaluation of selective venous sampling for parathyroid hormone concentration in patients undergoing reoperations for primary hyperparathyroidism. Surgery. 1993; 114(6):1004-10

627. Sugg SL, Krzywda EA, Demeure MJ, Wilson SD. Detection of multiple gland primary hyperparathyroidism in the era of minimally invasive parathyroidectomy. Surgery. 2004; 136(6):1303-9

628. Suh JM, Cronan JJ, Monchik JM. Primary hyperparathyroidism: is there an increased prevalence of renal stone disease? American Journal of Roentgenology. 2008; 191(3):908-11

629. Suh YJ, Choi JY, Kim S, Chun IK, Yun TJ, Lee KE et al. Comparison of 4D CT, ultrasonography, and 99mTc sestamibi SPECT/CT in localizing single-gland primary hyperparathyroidism. Otolaryngology - Head and Neck Surgery. 2015; 152(3):438-43

630. Sullivan DP, Scharf SC, Komisar A. Intraoperative gamma probe localization of parathyroid adenomas. Laryngoscope. 2001; 111(5):912-7

631. Sun PY, Thompson SM, Andrews JC, Wermers RA, McKenzie TJ, Richards ML et al. Selective parathyroid hormone venous sampling in patients with persistent or recurrent primary hyperparathyroidism and negative, equivocal or discordant noninvasive imaging. World Journal of Surgery. 2016; 40(12):2956-63

632. Szczech LA. The impact of calcimimetic agents on the use of different classes of phosphate binders: Results of recent clinical trials. Kidney International, Supplement. 2004; 66(90):S46-S48

633. Taieb A, Seman M, Menegaux F, Tresallet C. Surgical technique parathyroidectomy through a minimally invasive gland-centered localized approach for primary hyperparathyroidism. Journal of Visceral Surgery. 2013; 150(6):403-6

634. Taira N, Doihara H, Hara F, Shien T, Takabatake D, Takahashi H et al. Less invasive surgery for primary hyperparathyroidism based on preoperative ^{99m} Tc-hexakis-2-methoxyisobutylisonitrile imaging findings. Surgery Today. 2004; 34(3):197-203

635. Takei H, Iino Y, Endo K, Horiguchi J, Maemura M, Koibuchi Y et al. The efficacy of technetium-99m-MIBI scan and intraoperative methylene blue staining for the localization of abnormal parathyroid glands. Surgery Today. 1999; 29(4):307-12

636. Talpos GB, Bone HG, Kleerekoper M, Phillips ER, Alam M, Honasoge M et al. Randomized trial of parathyroidectomy in mild asymptomatic primary hyperparathyroidism: patient description and effects on the SF-36 health survey. Surgery. 2000; 128(6):1013-20;discussion 1020-1

637. Tampi C, Chavan N, Parikh D. Intraoperative parathyroid hormone assay-cutting the Gordian knot. Indian Journal of Endocrinology and Metabolism. 2014; 18(2):210-2

638. Tay YK, Khoo J, Chandran M. Surgery or no surgery: What works best for the kidneys in primary hyperparathyroidism? A study in a multi-ethnic Asian population. Indian Journal of Endocrinology and Metabolism. 2016; 20(1):55-61

639. Taylor J, Fraser W, Banaszkiewicz P, Drury P, Atkins P. Lateralization of parathyroid adenomas by intra-operative parathormone estimation. Journal of the Royal College of Surgeons of Edinburgh. 1996; 41(3):174-7

640. Taywade SK, Damle NA, Behera A, Devasenathipathy K, Bal C, Tripathi M et al. Comparison of 18F-fluorocholine positron emission tomography/computed tomography and four-dimensional computed tomography in the preoperative localization of parathyroid adenomas-initial results. Indian Journal of Endocrinology and Metabolism. 2017; 21(3):399-403

641. Tee MC, Chan SK, Nguyen V, Strugnell SS, Yang J, Jones S et al. Incremental value and clinical impact of neck sonography for primary hyperparathyroidism: A risk-adjusted analysis. Canadian Journal of Surgery. 2013; 56(5):325-31

642. Thakur A, Sebag F, Slotema E, Ippolito G, Taieb D, Henry JF. Significance of biochemical parameters in differentiating uniglandular from multiglandular disease and limiting use of intraoperative parathormone assay. World Journal of Surgery. 2009; 33(6):1219-1223

643. Thanseer N, Bhadada SK, Sood A, Mittal BR, Behera A, Gorla AKR et al. Comparative effectiveness of ultrasonography, 99mTc-Sestamibi, and 18F-Fluorocholine PET/CT in detecting parathyroid adenomas in patients with primary hyperparathyroidism. Clinical Nuclear Medicine. 2017; 42(12):e491-e497

644. Thielmann A, Kerr P. Validation of selective use of intraoperative PTH monitoring in parathyroidectomy. Journal of Otolaryngology: Head and Neck Surgery. 2017; 46(1):10

645. Thomas DL, Bartel T, Menda Y, Howe J, Graham MM, Juweid ME. Single photon emission computed tomography (SPECT) should be routinely performed for the detection of parathyroid abnormalities utilizing technetium-99m sestamibi parathyroid scintigraphy. Clinical Nuclear Medicine. 2009; 34(10):651-5

646. Thompson GB, Grant CS, Perrier ND, Harman R, Hodgson SF, Ilstrup D et al. Reoperative parathyroid surgery in the era of sestamibi scanning and intraoperative parathyroid hormone monitoring. Archives of Surgery. 1999; 134(7):699-705

647. Thule P, Thakore K, Vansant J, McGarity W, Weber C, Phillips LS. Preoperative localization of parathyroid tissue with technetium-99m sestamibi ^{123}I subtraction scanning. Journal of Clinical Endocrinology and Metabolism. 1994; 78(1):77-82

648. Timm S, Hamelmann W, Luster M, Blind E, Reiners C, Allolio B et al. Surgical approach to primary hyperparathyroidism - Impact of preoperative findings on surgical strategy: Minimally invasive vs. conventional parathyroidectomy. European Surgery - Acta Chirurgica Austriaca. 2004; 36(4):246-52

649. Tisell LE. Results of surgical and medical treatment in primary hyperparathyroidism. Annales Chirurgiae et Gynaecologiae. 1983; 72(3):129-34

650. Tokmak H, Demirkol MO, Alagol F, Tezelman S, Terzioglu T. Clinical impact of SPECT-CT in the diagnosis and surgical management of hyper-parathyroidism. International Journal of Clinical and Experimental Medicine. 2014; 7(4):1028-34

651. Toriie S, Sugimoto T, Hokimoto N, Funakoshi T, Ogawa M, Oki T et al. Evaluation of the minimally invasive parathyroidectomy in patients with primary hyperparathyroidism: A retrospective cohort study. Annals of Medicine and Surgery. 2016; 7:42-7

652. Treglia G, Sadeghi R, Schalin-Jantti C, Caldarella C, Ceriani L, Giovanella L. Detection rate of 99mTc-MIBI single photon emission computed tomography (SPECT)/CT in preoperative planning for patients with primary hyperparathyroidism: A meta-analysis. Head and Neck. 2016; 38(Suppl 1):E2159-E2172

653. Treglia G, Trimboli P, Huellner M, Giovanella L. Imaging in primary hyperparathyroidism: focus on the evidence-based diagnostic performance of different methods. Minerva Endocrinologica. 2018; 43(2):133-43

654. Trinh G, Noureldine SI, Russell JO, Agrawal N, Lopez M, Prescott JD et al. Characterizing the operative findings and utility of intraoperative parathyroid hormone (IOPTH) monitoring in patients with normal baseline IOPTH and normohormonal primary hyperparathyroidism. Surgery. 2017; 161(1):78-86

655. Trombetti A, Christ ER, Henzen C, Gold G, Brandle M, Herrmann FR et al. Clinical presentation and management of patients with primary hyperparathyroidism of the Swiss Primary Hyperparathyroidism Cohort: A focus on neuro-behavioral and cognitive symptoms. Journal of Endocrinological Investigation. 2016; 39(5):567-76

656. Tublin ME, Pryma DA, Yim JH, Ogilvie JB, Mountz JM, Bencherif B et al. Localization of parathyroid adenomas by sonography and technetium Tc 99m sestamibi single-photon emission computed tomography before minimally invasive parathyroidectomy are both studies really needed? Journal of Ultrasound in Medicine. 2009; 28(2):183-90

657. Tummers QRJG, Schepers A, Hamming JF, Kievit J, Frangioni JV, Van De Velde CJH et al. Intraoperative guidance in parathyroid surgery using near-infrared fluorescence imaging and low-dose Methylene Blue. Surgery. 2015; 158(5):1323-30

658. Tunca F, Akici M, Iscan Y, Sormaz IC, Giles Senyurek Y, Terzioglu T. The impact of combined interpretation of localization studies on image-guided surgical approaches for primary hyperparathyroidism Minerva Endocrinologica. 2017; 42(3):213-22

659. Turchi JJ, Flandreau RH, Forte AL, French GN, Ludwig GD. Hyperparathyroidism and pancreatitis. JAMA. 1962; 180(10):799-804

660. Tziakouri C, Eracleous E, Skannavis S, Pierides A, Symeonides P, Gourtsoyiannis N. Value of ultrasonography, CT and MR imaging in the diagnosis of primary hyperparathyroidism. Acta Radiologica. 1996; 37(5):720-6

661. Udelsman R, Aruny JE, Donovan PI, Sokoll LJ, Santos F, Donabedian R et al. Rapid parathyroid hormone analysis during venous localization. Annals of Surgery. 2003; 237(5):714-21

662. Ulanovski D, Feinmesser R, Cohen M, Sulkes J, Dudkiewicz M, Shpitzer T. Preoperative evaluation of patients with parathyroid adenoma: Role of high-resolution ultrasonography. Head and Neck. 2002; 24(1):1-5

663. Untch BR, Adam MA, Scheri RP, Bennett KM, Dixit D, Webb C et al. Surgeon-performed ultrasound is superior to 99Tc-sestamibi scanning to localize parathyroid

adenomas in patients with primary hyperparathyroidism: Results in 516 patients over 10 years. Journal of the American College of Surgeons. 2011; 212(4):522-9

664. Valdemarsson S, Bergenfelz A, Tennvall J, Ahren B. Thallium-technetium parathyroid scintigraphy during Na2 EDTA-stimulated parathyroid hormone secretion for localization of enlarged parathyroid glands. Surgical Research Communications. 1998; 19(2-4):299-310

665. Van Dalen A, Smit CP, Van Vroonhoven TJMV, Burger H, De Lange EE. Minimally invasive surgery for solitary parathyroid adenomas in patients with primary hyperparathyroidism: Role of US with supplemental CT. Radiology. 2001; 220(3):631-9

666. Van Der Vorst JR, Schaafsma BE, Verbeek FPR, Swijnenburg RJ, Tummers QRJG, Hutteman M et al. Intraoperative near-infrared fluorescence imaging of parathyroid adenomas with use of low-dose methylene blue. Head and Neck. 2014; 36(6):853-8

667. Van Ginhoven TM, Morks AN, Schepers T, De Graaf PW, Smit PC. Surgeon-performed ultrasound as preoperative localization study in patients with primary hyperparathyroidism. European Surgical Research. 2011; 47(2):70-4

668. VanderWalde LH, Liu IL, O'Connell TX, Haigh PI. The effect of parathyroidectomy on bone fracture risk in patients with primary hyperparathyroidism. Archives of Surgery. 2006; 141(9):885-9

669. VanderWalde LH, Liu ILA, Haigh PI. Effect of bone mineral density and parathyroidectomy on fracture risk in primary hyperparathyroidism. World Journal of Surgery. 2009; 33(3):406-11

670. Vaz A, Griffiths M. Parathyroid imaging and localization using SPECT/CT: Initial results. Journal of Nuclear Medicine Technology. 2011; 39(3):195-200

671. Vera L, Accornero M, Dolcino M, Oddo S, Giusti M. Five-year longitudinal evaluation of mild primary hyperparathyroidism - Medical treatment versus clinical observation. Endokrynologia Polska. 2014; 65(6):456-63

672. Vestergaard P, Mollerup CL, Frokjaer VG, Christiansen P, Blichert-Toft M, Mosekilde L. Cohort study of risk of fracture before and after surgery for primary hyperparathyroidism. BMJ. 2000; 321(7261):598-602

673. Vestergaard P, Mollerup CL, Frokjaer VG, Christiansen P, Blichert-Toft M, Mosekilde L. Cardiovascular events before and after surgery for primary hyperparathyroidism. World Journal of Surgery. 2003; 27(2):216-22

674. Vestergaard P, Mosekilde L. Cohort study on effects of parathyroid surgery on multiple outcomes in primary hyperparathyroidism. BMJ. 2003; 327(7414):530-3

675. Vestergaard P, Mosekilde L. Fractures in patients with primary hyperparathyroidism: Nationwide follow-up study of 1201 patients. World Journal of Surgery. 2003; 27(3):343-9

676. Vestergaard P, Mosekilde L. Parathyroid surgery is associated with a decreased risk of hip and upper arm fractures in primary hyperparathyroidism: a controlled cohort study. Journal of Internal Medicine. 2004; 255(1):108-14

677. Vignali E, Picone A, Materazzi G, Steffe S, Berti P, Cianferotti L et al. A quick intraoperative parathyroid hormone assay in the surgical management of patients with primary hyperparathyroidism: A study of 206 consecutive cases. European Journal of Endocrinology. 2002; 146(6):783-8

678. Vitetta GM, Neri P, Chiecchio A, Carriero A, Cirillo S, Mussetto AB et al. Role of ultrasonography in the management of patients with primary hyperparathyroidism: Retrospective comparison with technetium-99m sestamibi scintigraphy. Journal of Ultrasound. 2014; 17(1):1-12

679. Von Schulthess GK, Weder W, Goebel N, Buchmann P, Gadze A, Augustiny N et al. 1.5 T MRI, CT, ultrasonography and scintigraphy in hyperparathyroidism. European Journal of Radiology. 1988; 8(3):157-64

680. Wachtel H, Cerullo I, Bartlett EK, Kelz RR, Karakousis GC, Fraker DL. What can we learn from intraoperative parathyroid hormone levels that do not drop appropriately? Annals of Surgical Oncology. 2015; 22(6):1781-8

681. Wade TJ, Yen TW, Amin AL, Wang TS. Surgical management of normocalcemic primary hyperparathyroidism. World Journal of Surgery. 2012; 36(4):761-6

682. Wagner K, Miskulin J. Effect of parathyroidectomy on osteoporosis and bone metabolism. Clinical Reviews in Bone and Mineral Metabolism. 2007; 5(2):115-21

683. Weber CJ, Ritchie JC. Retrospective analysis of sequential changes in serum intact parathyroid hormone levels during conventional parathyroid exploration. Surgery. 1999; 126(6):1139-44

684. Weber CJ, Vansant J, Alazraki N, Christy J, Watts N, Phillips LS et al. Value of technetium 99m sestamibi iodine 123 imaging in reoperative parathyroid surgery. Surgery. 1993; 114(6):1011-8

685. Weber KJ, Misra S, Lee JK, Wilhelm SW, DeCresce R, Prinz RA. Intraoperative PTH monitoring in parathyroid hyperplasia requires stricter criteria for success. Surgery. 2004; 136(6):1154-9

686. Weber T, Cammerer G, Schick C, Solbach C, Hillenbrand A, Barth TF et al. C-11 methionine positron emission tomography/computed tomography localizes parathyroid adenomas in primary hyperparathyroidism. Hormone and Metabolic Research. 2010; 42(3):209-14

687. Weber T, Gottstein M, Schwenzer S, Beer A, Luster M. Is C-11 Methionine PET/CT able to localise sestamibi-negative parathyroid adenomas? World Journal of Surgery. 2017; 41(4):980-5

688. Weber T, Maier-Funk C, Ohlhauser D, Hillenbrand A, Cammerer G, Barth TF et al. Accurate preoperative localization of parathyroid adenomas with C-11 methionine PET/CT. Annals of Surgery. 2013; 257(6):1124-8

689. Wei JP, Burke GJ. Cost utility of routine imaging with Tc-99m-sestamibi in primary hyperparathyroidism before initial surgery. American Surgeon. 1997; 63(12):1097-101

690. Wei JP, Burke GJ, Mansberger AR, Jr. Prospective evaluation of the efficacy of technetium 99m sestamibi and iodine 123 radionuclide imaging of abnormal parathyroid glands. Surgery. 1992; 112(6):1111-7

691. Wei JP, Burke GJ, Mansberger AR, Jr, McGarity WC. Preoperative imaging of abnormal parathyroid glands in patients with hyperparathyroid disease using combination Tc-99m-pertechnetate and Tc-99m- sestamibi radionuclide scans. Annals of Surgery. 1994; 219(5):568-73

692. Wei WJ, Shen CT, Song HJ, Qiu ZL, Luo QY. Comparison of SPET/CT, SPET and planar imaging using 99mTc-MIBI as independent techniques to support minimally invasive parathyroidectomy in primary hyperparathyroidism: A meta-analysis. Hellenic Journal of Nuclear Medicine. 2015; 18(2):127-35

693. Wermers RA, Khosla S, Atkinson EJ, Grant CS, Hodgson SF, O'Fallon WM et al. Survival after the diagnosis of hyperparathyroidism: A population-based study. American Journal of Medicine. 1998; 104(2):115-22

694. Westerdahl J, Bergenfelz A. Sestamibi scan-directed parathyroid surgery: Potentially high failure rate without measurement of intraoperative parathyroid hormone. World Journal of Surgery. 2004; 28(11):1132-8

695. Westerdahl J, Bergenfelz A. Unilateral versus bilateral neck exploration for primary hyperparathyroidism: five-year follow-up of a randomized controlled trial. Annals of Surgery. 2007; 246(6):976-80; discussion 980-1

696. Westra WH, Pritchett DD, Udelsman R. Intraoperative confirmation of parathyroid tissue during parathyroid exploration: A retrospective evaluation of the frozen section. American Journal of Surgical Pathology. 1998; 22(5):538-44

697. Wheeler MH, Wade JSH. Intraoperative identification of parathyroid glands: Appraisal of methylene blue staining. American Journal of Surgery. 1982; 143(6):713-6

698. Whelan PJ, Rotstein LE, Rosen IB, Kucharczyk W. Do we really need another localizing technique for parathyroid glands? American Journal of Surgery. 1989; 158(4):382-4

699. Whitley NO, Bohlman M, Connor TB. Computed tomography for localization of parathyroid adenomas. Journal of Computer Assisted Tomography. 1981; 5(6):812-7

700. Wilson RJ, Rao S, Ellis B, Kleerekoper M, Parfitt AM. Mild asymptomatic primary hyperparathyroidism is not a risk factor for vertebral fractures. Annals of Internal Medicine. 1988; 109(12):959-62

701. Witteveen JE, Kievit J, Morreau H, Romijn JA, Hamdy NAT. No recurrence of sporadic primary hyperparathyroidism when cure is established 6 months after parathyroidectomy. European Journal of Endocrinology. 2010; 162(2):399-406

702. Witteveen JE, Kievit J, Stokkel MP, Morreau H, Romijn JA, Hamdy NA. Limitations of Tc99m-MIBI-SPECT imaging scans in persistent primary hyperparathyroidism. World Journal of Surgery. 2011; 35(1):128-39

703. Witteveen JE, Kievit J, Van Erkel AR, Morreau H, Romijn JA, Hamdy NAT. The role of selective venous sampling in the management of persistent hyperparathyroidism revisited. European Journal of Endocrinology. 2010; 163(6):945-52

704. Wong KK, Fig LM, Gross MD, Dwamena BA. Parathyroid adenoma localization with 99mTc-sestamibi SPECT/CT: a meta-analysis. Nuclear Medicine Communications. 2015; 36(4):363-75

705. Wong SW, Chan KW, Paulose NM, Leong HT. Scan-directed unilateral neck exploration for primary hyperparathyroidism: Eight-year results from a regional hospital. Hong Kong Medical Journal. 2009; 15(2):118-21

706. Wong W, Foo FJ, Lau MI, Sarin A, Kiruparan P. Simplified minimally invasive parathyroidectomy: A series of 100 cases and review of the literature. Annals of the Royal College of Surgeons of England. 2011; 93(4):290-3

707. Wu B, Haigh PI, Hwang R, Ituarte PHG, Liu ILA, Hahn TJ et al. Underutilization of parathyroidectomy in elderly patients with primary hyperparathyroidism. Journal of Clinical Endocrinology and Metabolism. 2010; 95(9):4324-30

708. Wu DD, Shaw JH. The use of pre-operative scan prior to neck exploration for primary hyperparathyroidism. Australian and New Zealand Journal of Surgery. 1988; 58(1):35-8

709. Yao M, Jamieson C, Blend R. Magnetic resonance imaging in preoperative localization of diseased parathyroid glands: a comparison with isotope scanning and ultrasonography. Canadian Journal of Surgery. 1993; 36(3):241-4

710. Yeh MW, Zhou H, Adams AL, Ituarte PHG, Li N, Liu ILA et al. The relationship of parathyroidectomy and bisphosphonates with fracture risk in primary hyperparathyroidism: An observational study. Annals of Internal Medicine. 2016; 164(11):715-23

711. Yen TWF, Wang TS, Doffek KM, Krzywda EA, Wilson SD. Reoperative parathyroidectomy: An algorithm for imaging and monitoring of intraoperative parathyroid hormone levels that results in a successful focused approach. Surgery. 2008; 144(4):611-21

712. Yen TWF, Wilson SD, Krzywda EA, Sugg SL. The role of parathyroid hormone measurements after surgery for primary hyperparathyroidism. Surgery. 2006; 140(4):665-74

713. Yip L, Pryma DA, Yim JH, Virji MA, Carty SE, Ogilvie JB. Can a lightbulb sestamibi SPECT accurately predict single-gland disease in sporadic primary hyperparathyroidism? World Journal of Surgery. 2008; 32(5):784-92

714. Younes NA, Hadidi AM, Mahafzah WS, Tarawneh ES, Al-Khatib YF, Sroujieh AS. Accuracy of single versus combined use of ultrasonography or computed tomography in the localization of parathyroid adenoma. Saudi Medical Journal. 2008; 29(2):213-7

715. Ypsilantis E, Charfare H, Wassif WS. Intraoperative PTH assay during minimally invasive parathyroidectomy may be helpful in the detection of double adenomas and may minimise the risk of recurrent surgery International Journal of Endocrinology. 2010; 2010:178671

716. Yu N, Donnan PT, Flynn RWV, Murphy MJ, Smith D, Rudman A et al. Increased mortality and morbidity in mild primary hyperparathyroid patients. the Parathyroid Epidemiology and Audit Research Study (PEARS). Clinical Endocrinology. 2010; 73(1):30-4

717. Yu N, Donnan PT, Leese GP. A record linkage study of outcomes in patients with mild primary hyperparathyroidism: the Parathyroid Epidemiology and Audit Research Study (PEARS). Clinical Endocrinology. 2011; 75(2):169-76

718. Yu N, Donnan PT, Murphy MJ, Leese GP. Epidemiology of primary hyperparathyroidism in Tayside, Scotland, UK. Clinical Endocrinology. 2009; 71(4):485-93

719. Yu N, Leese GP, Donnan PT. What predicts adverse outcomes in untreated primary hyperparathyroidism? the Parathyroid Epidemiology and Audit Research Study (PEARS). Clinical Endocrinology. 2013; 79(1):27-34

720. Yu N, Leese GP, Smith D, Donnan PT. The natural history of treated and untreated primary hyperparathyroidism: The parathyroid epidemiology and audit research study. QJM: An International Journal of Medicine. 2011; 104(6):513-21

721. Zawawi F, Mlynarek AM, Cantor A, Varshney R, Black MJ, Hier MP et al. Intraoperative parathyroid hormone level in parathyroidectomy: Which patients benefit from it? Journal of Otolaryngology Head and Neck Surgery. 2013; 42:56

722. Zeina AR, Nakar H, Reindorp DN, Nachtigal A, Krausz MM, Itamar I et al. Four-dimensional computed tomography (4DCT) for preoperative localization of parathyroid adenomas. Israel Medical Association Journal. 2017; 19(4):216-20

723. Zerizer I, Parsai A, Win Z, Al-Nahhas A. Anatomical and functional localization of ectopic parathyroid adenomas: 6-year institutional experience. Nuclear Medicine Communications. 2011; 32(6):496-502

724. Zhao DW, Yen TW, Doffek K, Evans DB, Wang TS. Changes in bone mineral density after parathyroidectomy in elderly patients with primary hyperparathyroidism. Journal of Surgical Research. 2014; 186 (2):557

725. Zmora O, Schachter PP, Heyman Z, Shabtay M, Avigad I, Ayalon A et al. Correct preoperative localization: Does it permit a change in operative strategy for primary hyperparathyroidism? Surgery. 1995; 118(6):932-5

726. Zotti D, Borsato N, Varotto S, Miotto D, Feltrin GP, Tasca A et al. Parathyroid localization in primary hyperparathyroidism: Double-tracer scintigraphy and venous sampling techniques combined. A first evaluation. Journal of Endocrinological Investigation. 1984; 7(4):363-6

Appendices

Appendix A: Review protocols

Table 10: Review protocol: Management options in failed primary surgery

Field	Content
Review question	What are the management options for people in whom primary parathyroid surgery has failed?
Type of review question	Intervention
Objective of the review	To determine management options for people in whom primary parathyroid surgery has failed.
Eligibility criteria – population	Adults (18 years or over) with primary hyperparathyroidism in whom primary surgery has failed. Strata: • Type of adenoma / hyperplasia (single adenoma, 4 gland hyperplasia or ectopic adenoma) • Pregnant women Exclude people: • with secondary and tertiary HPT • with multiple endocrine neoplasia • with familial hyperparathyroidism • with parathyroid carcinoma • people on medications interfering with calcium metabolism (for example, lithium).
Eligibility criteria – intervention(s)	• Re-operation • Surgical localisation • Calcimimetics • Bisphosphonates • Monitoring
Eligibility criteria – comparator(s)	All interventions compared to each other
Outcomes and prioritisation	**Critical outcomes:** • HRQOL (continuous outcome) • Mortality (dichotomous outcome) • Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) (dichotomous) **Important outcomes:** • Deterioration in renal function (dichotomous) • Persistent hypercalcaemia (dichotomous outcome) • Cardiovascular events (dichotomous outcome) • Adverse events (dichotomous outcome) • Cancer incidence (dichotomous outcome)
Eligibility criteria – study design	RCTs and systematic reviews of RCTs

Other inclusion exclusion criteria	• Non-English language articles • Conference abstracts
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups will follow those in the primary reviews for surgical indications, surgical interventions, surgical localisation, calcimimetics, bisphosphonates and monitoring.
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	• Pairwise meta-analyses were performed using Cochrane Review Manager (RevMan5). • GRADEpro was used to assess the quality of evidence for each outcome. • Endnote for bibliography, citations, sifting and reference management Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library, CINAHL, PsycINFO Date: all years Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2002 NHSEED, HTA – all years Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	N/A
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10051
Highlight if amendment to previous protocol	N/A
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international

	GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Jonathan Mant in line with section 3 of Developing NICE guidelines: the manual. Staff from the NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds the NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 11: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations (recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered). • Unpublished reports will not be considered unless submitted as part of a call

Review question	All questions – health economic evidence
	for evidence. Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[443] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Review question	All questions – health economic evidence
	Year of analysis: • The more recent the study, the more applicable it will be. • Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'. • Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 06 August 2018	Exclusions
Embase (OVID)	1974 – 06 August 2018	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to 2018 Issue 8 of 12 CENTRAL to 2018 Issue 7 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 06 August 2018	Exclusions
PsycINFO (ProQuest)	Inception – 06 August 2018	Exclusions

Medline (Ovid) search terms

1.	hyperparathyroidism/ or hyperparathyroidism, primary/
2.	((primary or asymptomatic or symptomatic or mild or familial or maternal) adj6 (HPT or hyperparathyroidis*)).ti,ab.

3.	PHPT.ti,ab.
4.	Parathyroid Neoplasms/
5.	(parathyroid* adj3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language

Embase (Ovid) search terms

1.	hyperparathyroidism/ or primary hyperparathyroidism/
2.	((primary or asymptomatic or symptomatic or mild or familial or maternal) adj6 (HPT or hyperparathyroidis*)).ti,ab.
3.	PHPT.ti,ab.
4.	parathyroid tumor/ or parathyroid adenoma/ or parathyroid carcinoma/
5.	(parathyroid* adj3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/

18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Hyperparathyroidism] explode all trees
#2.	MeSH descriptor: [Hyperparathyroidism, Primary] explode all trees
#3.	((primary or asymptomatic or symptomatic or mild or familial or maternal) near/6 (HPT or hyperparathyroidis*)):ti,ab
#4.	PHPT:ti,ab
#5.	MeSH descriptor: [Parathyroid Neoplasms] explode all trees
#6.	(parathyroid* near/3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)):ti,ab
#7.	(or #1-#6)

CINAHL (EBSCO) search terms

S1.	(MH "Hyperparathyroidism")
S2.	((primary or asymptomatic or symptomatic or mild or familial or maternal) n6 HPT) OR ((primary or asymptomatic or symptomatic or mild or familial or maternal) n6 hyperparathyroidis*)
S3.	PHPT
S4.	(MH "Parathyroid Neoplasms")
S5.	(parathyroid* n3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumor* or tumour* or cancer* or metasta* or hypercalcemi* or hypercalcaemi*))
S6.	S1 OR S2 OR S3 OR S4 OR S5
S7.	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT “questions and answers” or PT response or PT software or PT teaching materials or PT website
S8.	S6 NOT S7

PsycINFO (ProQuest) search terms

1.	su.Exact("parathyroid neoplasms" OR "hyperparathyroidism" OR "hyperparathyroidism, primary")
2.	PHPT
3.	((primary or asymptomatic or symptomatic or mild or familial or maternal) Near/6 (HPT or hyperparathyroidis*))
4.	(parathyroid* near/3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumor* or tumour* or cancer* or metasta* or hypercalcaemi* or hypercalcemi*))
5.	1 or 2 or 3 or 4
6.	(su.exact.explode("rodents") or su.exact.explode("mice") or (su.exact("animals") not (su.exact("human males") or su.exact("human females"))) or ti(rat or rats or mouse or mice))
7.	(s1 or s2 or s3 or s4) NOT (su.exact.explode("rodents") or su.exact.explode("mice") or (su.exact("animals") not (su.exact("human males") or su.exact("human females"))) or ti(rat or rats or mouse or mice))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to primary hyperparathyroidism population in the NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. The NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics papers published since 2002.

Table 13: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2002 – 06 August 2018	Exclusions Health economics studies
Embase	2002 – 06 August 2018	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 06 August 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	hyperparathyroidism/ or hyperparathyroidism, primary/
2.	((primary or asymptomatic or symptomatic or mild or familial or maternal) adj6 (HPT or hyperparathyroidis*)).ti,ab.
3.	PHPT.ti,ab.
4.	Parathyroid Neoplasms/
5.	(parathyroid* adj3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24

26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

Embase (Ovid) search terms

1.	hyperparathyroidism/ or primary hyperparathyroidism/
2.	((primary or asymptomatic or symptomatic or mild or familial or maternal) adj6 (HPT or hyperparathyroidis*)).ti,ab.
3.	PHPT.ti,ab.
4.	parathyroid tumor/ or parathyroid adenoma/ or parathyroid carcinoma/
5.	(parathyroid* adj3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/

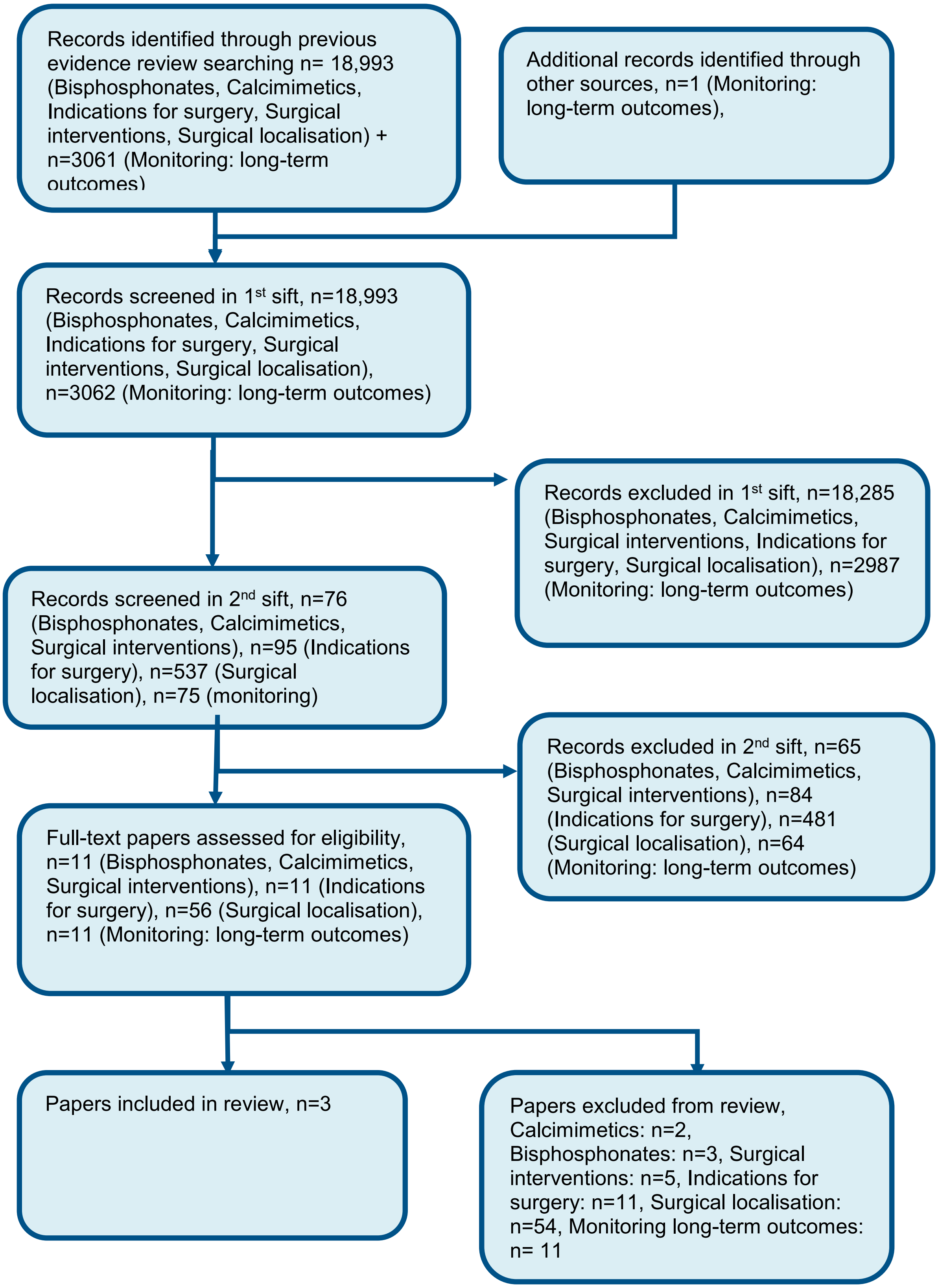
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Hyperparathyroidism EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Hyperparathyroidism, Primary EXPLODE ALL TREES
#3.	(((primary or asymptomatic or symptomatic or mild or familial or maternal) adj6 (HPT or hyperparathyroidis*)))
#4.	(PHPT)
#5.	MeSH DESCRIPTOR Parathyroid Neoplasms EXPLODE ALL TREES
#6.	((parathyroid* adj3 (adenoma* or carcinoma* or hyperplasia* or neoplas* or tumo?r* or cancer* or metasta* or hypercalc?emi*)))
#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8.	* IN NHSEED
#9.	* IN HTA
#10.	#7 AND #8
#11.	#7 AND #9

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of: Management options in failed primary surgery



•

Appendix D: Clinical evidence tables

Reference	**Bonjer 1997**[84]
Study type	Retrospective study
Countries and setting	The Netherlands, University Hospital
Study methodology	Data source: patient records Recruitment: all patients who had operations on the thyroid glands at the University hospital between May 1993 and April 1995.
Number of patients	n=27 (2/27 had secondary or tertiary HPT, but results reported separately so can exclude from calculations)
Patient characteristics	Age, mean (range): 59 (34–79) years Gender (male to female ratio): 6:21 Ethnicity: not reported Inclusion criteria: hyperparathyroidism confirmed by the findings of raised concentrations of serum parathyroid hormone by a two-site immunoassay; patients with pre-operative sestamibi scan. Exclusion criteria: patients about to undergo first operation of familial HPT, MEN, and secondary and tertiary HPT. Details of imaging tests and surgical intervention: patients had MIBI, SPECT and US of the neck and chest. All patients about to undergo their first parathyroidectomy had bilateral exploration (and an attempt made to identify all parathyroid glands). Patients being operated on for persistent or recurrent HPT or patients having local anaesthesia had unilateral exploration. Prior tests: no preselection based on prior imaging Patient details: 21 people had primary HPT, 6 people had persistent or recurrent HPT (3 persistent PHPT, 1 recurrent PHPT, and 2 excluded from this analysis due to secondary or tertiary HPT). 16% re-operation, results reported separately for 1st operation (n=21) and re-operation (n=4). n=27 solitary adenoma (n=25 PHPT).
Index test(s)	Index test (unable to calculate 2x2 table values for US)

<table>
<tr><td>Reference</td><td>Bonjer 1997[84]</td></tr>
<tr><td>and reference standard</td><td><u>MIBI:</u> ^{99m}Tc-sestamibi scans done 10, 90 and 150 minutes after 370MBq of ^{99m}Tc-sestamibi had been given IV. Anterior and posterior planar images of the neck and chest recorded using a gamma camera with a large field of view and a high resolution parallel-hole collimator.

Positive = not reported

<u>Reference standard</u>
The operative and histopathological findings of those explorations that resulted in normocalcaemia post-operatively (and states in results that all people became normocalcaemic).</td></tr>
<tr><td>2×2 table</td><td>
<table>
<tr><td>MIBI</td><td></td><td></td><td>Total</td><td rowspan="4">Correct localisation of single n=17 (TPs)
Correct localisation of single in persistent/recurrent PHPT n=4 (TPs)
Incorrect localisation of single n=1 (FNs)
Imaging negative, missed single n=3 (FNs)

Analyse separately for 1st operation (17TPs, 4FNs, n=21) and reoperation (4TPs, n=4).</td></tr>
<tr><td></td><td>‘True positives’
21</td><td>‘False positives’
0</td><td></td></tr>
<tr><td></td><td>‘False negatives’
4</td><td>‘True negatives’
0</td><td></td></tr>
<tr><td>Total</td><td>25</td><td>0</td><td>25</td></tr>
</table>
</td></tr>
<tr><td>Statistical measures</td><td><u>Index text: MIBI</u>
‘Sensitivity’: 84%
‘Specificity’: -</td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
<tr><td>Limitations</td><td>Risk of bias: none
Indirectness: none</td></tr>
</table>

Study	**Peacock 2005 [482]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	N/A (n=18 patients who had re-operation) [n=78 all participants]
Countries and setting	Conducted in USA
Line of therapy	Mixed line
Duration of study	Intervention time: 52 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: See inclusion criteria

Study	Peacock 2005 [482]
Stratum	Patients with failed primary surgery for primary hyperparathyroidism
Subgroup analysis within study	Not applicable
Inclusion criteria	Serum calcium concentration between 10.3 mg/dL (2.57 mmol/L) and 12.5 mg/dL (3.12 mmol/L), and plasma PTH concentration >45 pg/mL. Parathyroid hormone was measured on ≥2 occasions ≥7 days apart during the 12-month before baseline.
Exclusion criteria	Pregnancy; creatinine clearance < 50 ml/min; treatment with bisphosphonates/fluoride within 90 days before baseline; familial hypocalciuric hypercalcaemia; fasting urine calcium/creatinine in mg (molar) ratio less than 0.05 (0.14); requirement for drugs which are metabolised by P450 2D6 (CYP2D6) and have a narrow therapeutic index (e.g. flecainide, thioridazine, tricyclic antidepressants).
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age (overall sample) - Mean (range): 62 (27 - 83). Gender (M:F): 21:57. Ethnicity: Not reported
Further population details	1. Adjusted serum calcium: Not stated / Unclear (See inclusion criteria). 2. Presence of end-organ effects (end organ effects defined as kidney stones, history of fragility fractures or osteoporosis [BMD T-score <-2.5 at any site]): Not stated / Unclear
Extra comments	Adults with PHPT. Women on stable doses of selective oestrogen receptor modulators or oestrogen replacement therapy were eligible. Usually, similar studies exclude people who are on hormone replacement therapy.
Indirectness of population	No indirectness
Interventions	(n=9) Intervention 1: Calcimimetics - Cinacalcet. 30 mg twice daily, but if patients were still hypercalcaemic (serum calcium > 10.3 mg/dL) then the dose was increased to 40 mg twice daily at Week 4 and increased to 50 mg twice daily at Week 8. Duration 52 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=9) Intervention 2:Placebo. 30 mg twice daily, but if the patients were still hypercalcaemic the dose was increased to 40 mg twice daily at Week 4 and 50 mg twice daily at Week 8. Duration 52 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Study funded by industry (Amgen Inc.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CINACALCET versus PLACEBO

Protocol outcome 1: Persistent hypercalcaemia
- Actual outcome: Proportion of participants who achieved a mean serum calcium of ≤10.3 mg/dL (2.57 mmol/L) and a reduction from baseline of

Study	Peacock 2005 [482]
≥0.5 mg/dL (0.12 mmol/L) at 24/52 weeks; Group 1: 7/9, Group 2: 1/9; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Some difference in baseline mean plasma parathyroid hormone (SD) was observed: Cinacalcet 105 (36) vs. Placebo 120 (54) pg/mL.	
Protocol outcomes not reported by the study	Health related quality of life; Mortality; Preservation of end organ functions (bone mineral density, fractures, renal stones and renal function); Deterioration in renal function; Cardiovascular events; Adverse events; Cancer incidence

Reference	Rossi 2000 [526]
Study type	Unclear
Countries and setting	USA, Medical Centre
Study methodology	Data source: N/A Recruitment: consecutive re-operations for HPT performed by 1 surgeon from February 1999 to February 2000.
Number of patients	n=11
Patient characteristics	Age, mean (range): 58.3 (35–78 years) Gender (male to female ratio): 5:6 Ethnicity: not reported Inclusion criteria: hypercalcaemia and elevated PTH caused by PHPT; reoperation Exclusion criteria: not reported Details of imaging tests and surgical intervention: pre-operative studies included sestamibi and US in all patients, MRI in 4 patients, CT in 3, parathyroid arteriogram in 1 and selective venous sampling in 1. All patients underwent intraoperative Tc-99m-sestamibi scanning and IOPTH. Prior tests: no preselection based on prior tests Patient details: n=11

Reference	Rossi 2000 [526]
	All reoperation (but only 8/11 reoperation for PHPT – 73%) – analyse separately for IOPTH (can subgroup for IOPTH as they were all TPs)
Index test(s) and reference standard	Index test IOPTH: intraoperative PTH immunochemiluminescent assay. Plasma from a neck or peripheral vein obtained prior to incision, after the thyroid gland was mobilised, and at 5 and 10 minutes post-excision. Positive = drop of >50% from baseline (unclear if pre-incision or pre-excision) at 5 or 10 minutes. Index test MIBI: pre-operatively all patients injected with 15mCi of technetium 99m sestamibi. Early images of the neck and chest were obtained at 3 hours post injection. The distribution of sestamibi in the early and delayed images was compared. Positive = not reported Index test US: high resolution US Positive = not reported Index test MRI: not reported Index test CT: not reported Reference standard Pathology. States all had low or normal post-operative calcium levels.

2×2 table	**IOPTH**	Reference standard +	Reference standard −	Total	Analyse separately for 1st operation (8TPs, n=8) and reoperation (3TPs, n=3).
	Index test +	11	0	11	
	Index test −	0	0	0	
	Total	11	0	11	

Statistical measures	Index text: IOPTH Sensitivity: 100% Specificity: -

2×2 table	**MIBI**			Total	Correctly localised single n=7 (TPs)
		'True positives'	'False positives'		Negative imaging, final outcome single n=4 (FNs)

Reference	Rossi 2000 [526]				
		7	0		
		'False negatives' 4	'True negatives' 0		
	Total	11	0	11	
Statistical measures	Index text: MIBI 'Sensitivity': 63.6% 'Specificity': -				
2×2 table	**US**			Total	Correctly localised single n=7 (TPs) Incorrectly localised single n=2 (FNs) Negative imaging, final outcome single n=2 (FNs)
		'True positives' 7	'False positives' 0		
		'False negatives' 4	'True negatives' 0		
	Total	11	0	11	
Statistical measures	Index text: US 'Sensitivity': 63.6% 'Specificity': -				
2×2 table	**MRI**			Total	Correctly localised single n=2 (TPs) Incorrectly localised single n=1 (FNs) Negative imaging, final outcome single n=1 (FNs)
		'True positives' 2	'False positives' 0		
		'False negatives' 2	'True negatives' 0		
	Total	4	0	4	
Statistical measures	Index text: MRI 'Sensitivity': 50.0% 'Specificity': -				
2×2 table	**CT**			Total	Correctly localised single n=1 (TPs) Negative imaging, final outcome single n=2 (FNs)
		'True positives' 1	'False positives' 0		
		'False negatives' 2	'True negatives' 0		
	Total	3	0	3	

Reference	Rossi 2000 [526]
Statistical measures	<u>Index text: CT</u> 'Sensitivity': 33.3% 'Specificity': -
Source of funding	Not reported
Limitations	Risk of bias: unclear if only people with sporadic PHPT were included and whether people with familial PHPT or MEN were excluded Indirectness: none

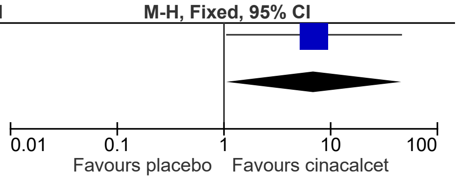
Appendix E: Forest plots

E.1 Cinacalcet versus placebo in failed surgery for primary hyperparathyroidism

Figure 2: Normocalcaemia (serum calcium ≤ 2.57 mmol/L)

Study or Subgroup	Cinacalcet Events	Cinacalcet Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Peacock 2005	7	9	1	9	100.0%	7.00 [1.07, 45.90]
Total (95% CI)		**9**		**9**	**100.0%**	**7.00 [1.07, 45.90]**
Total events	7		1			

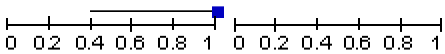
Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)



E.2 Diagnostic accuracy of imaging tests in re-operation for primary hyperthyroidism

Figure 3: Sestamibi

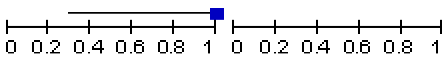
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bonjer 1997	4	0	0	0	1.00 [0.40, 1.00]	Not estimable



E.3 Diagnostic accuracy of intra-operative tests in re-operation for primary hyperthyroidism

Figure 4: IOPTH (>50% drop at ≤10 minutes)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rossi 2000	3	0	0	0	1.00 [0.29, 1.00]	Not estimable



Appendix F: GRADE tables

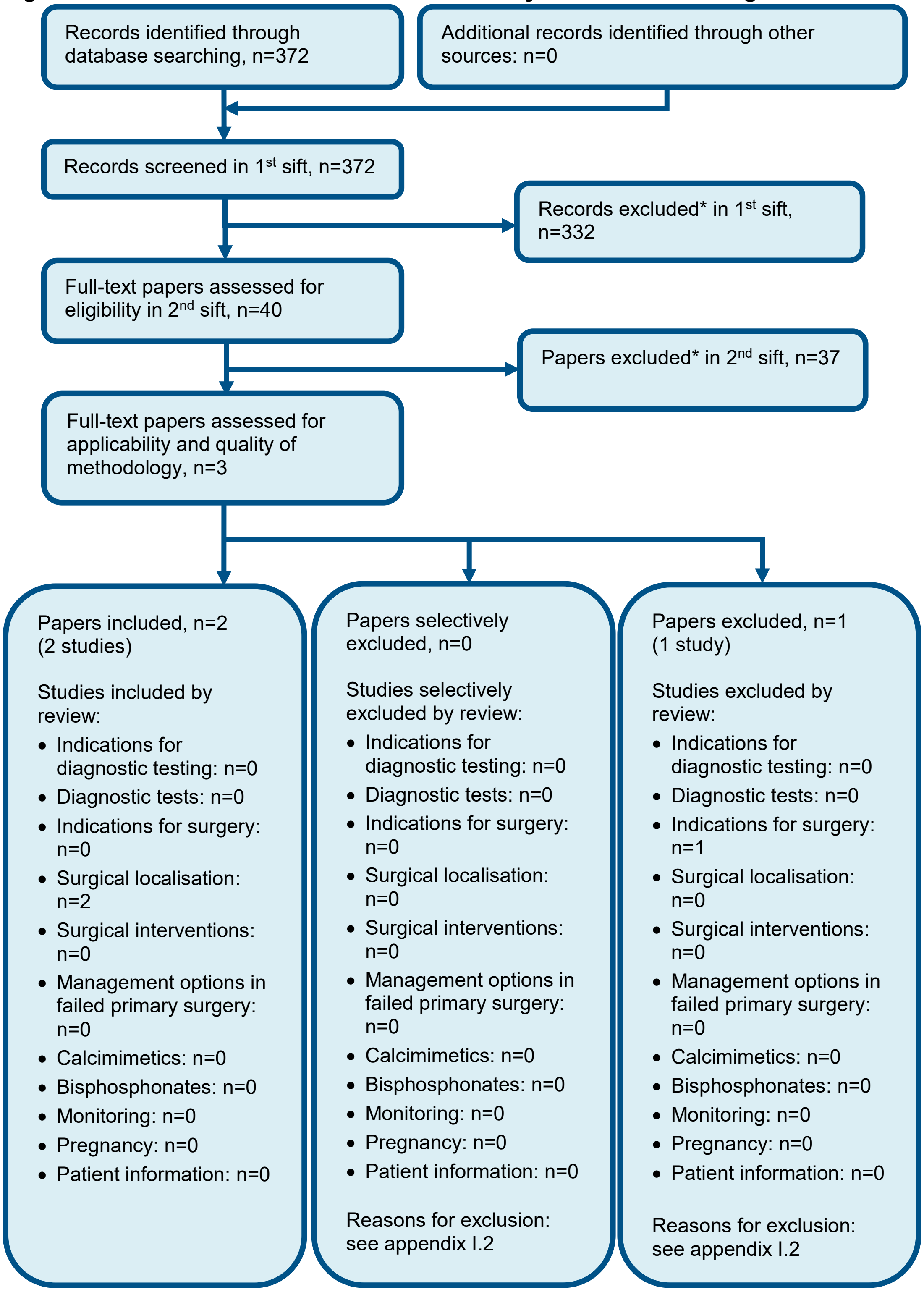
Table 14: Clinical evidence profile: Cinacalcet versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Cinacalcet**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Normocalcaemia (serum Ca ≤2.57 mmol/L) (follow-up 24 & 52 weeks; assessed with: cases)												
1	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	7/9 (77.8%)	11.1%	RR 7 (1.07 to 45.9)	666 more per 1000 (from 8 more to 1000 more)	⊕OOO VERY LOW	IMPORTANT

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G: Health economic evidence selection

Figure 5: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H: Health economic evidence tables

No economic studies were included in this review.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 15: Studies excluded from the bisphosphonates clinical review

Study	Exclusion reason
Akbaba 2013[15]	Incorrect comparator (raloxifene)
Brardi 2015[89]	Incorrect interventions
Casez 2003[121]	Incorrect interventions
Cesareo 2017[128]	Did not include re-operation patients
Chow 2003 [146]	Did not include re-operation patients
Hamdy 1987[255]	Non-comparative study
Hassani 2001[262]	Not a randomised controlled trial
Horiuchi 2002[287]	Inappropriate intervention – 2-week administration only of oral etidronate. This bisphosphonate is no longer used.
Khan 2004 [337]	Did not include re-operation patients
Khan 2009[336]	Post-hoc subgroup analysis of a previously published study
Khan 2014[335]	Conference abstract
Khan 2015[333]	Incorrect interventions (calcimimetics)
Martin 2010[405]	Conference abstract
Narayan 2007[441]	Incorrect population (end stage renal disease)
Parker 2002[474]	Not a randomised controlled trial
Peacock 2005[482]	Incorrect interventions (calcimimetics)
Peacock 2009[483]	Open label non-comparative extension study of an RCT
Peacock 2011[481]	Pooled analysis of 3 clinical trials (checked for references)
Reasner 1993[514]	Dose study
Rossini 2001[527]	Comparative outcomes not available
Sankaran 2010[553]	Non-systematic literature review
Schwarz 2014[562]	Incorrect interventions (calcimimetics)
Shoback 2003[581]	Incorrect interventions (calcimimetics)
Szczech 2004[632]	Non-systematic literature review

Table 16: Studies excluded from the calcimimetics clinical review

Study	Exclusion reason
Akbaba 2013[15]	Incorrect comparator
Brardi 2015[89]	Incorrect interventions
Casez 2003[121]	Incorrect interventions
Cesareo 2017 [128]	Incorrect interventions (bisphosphonates)
Chow 2003[146]	Incorrect interventions (bisphosphonates)
Hamdy 1987[255]	Incorrect interventions (bisphosphonates)
Hassani 2001[262]	Incorrect interventions (bisphosphonates)
Horiuchi 2002[287]	Incorrect interventions (bisphosphonates)
Khan 2004 [337]	Incorrect interventions (bisphosphonates)
Khan 2009[336]	Incorrect interventions (bisphosphonates)
Khan 2014[335]	Conference abstract

Study	Exclusion reason
Khan 2015[333]	Did not include re-operation patients
Martin 2010[405]	Conference abstract
Narayan 2007[441]	Incorrect population (end stage renal disease)
Parker 2002[474]	Incorrect interventions (bisphosphonates)
Peacock 2009[483]	Open label non-comparative extension study of an RCT
Peacock 2011[481]	Pooled analysis of 3 clinical trials checked for references
Reasner 1993[514]	Dose study
Rossini 2001[527]	Incorrect interventions (bisphosphonates)
Sankaran 2010[553]	Non-systematic literature review
Schwarz 2014[562]	Non-comparative observational study (PRIMARA study)
Shoback 2003[581]	Did not report information from patients with re-operation separately
Szczech 2004[632]	Non-systematic literature review

Table 17: Studies excluded from the surgical indications clinical review

Study	Exclusion reason
Adler 2008[5]	Inappropriate comparison – study compares different types of surgery
Agus 1993[11]	An opinion piece
Alhava 1988[21]	Non-comparative before and after study
Almqvist 2002[25]	No relevant outcomes
Almqvist 2004[24]	Inappropriate comparison. Incorrect interventions. Comparison of different timings of surgery.
Alvarez-Allende 2014[26]	Conference abstract
Amborgini 2007 [28]	Did not include re-operation patients
Anonymous 2000[32]	Not a primary study – article
Anonymous 2000[31]	Not a primary study – article
Barkun 2006[56]	Commentary of an included RCT
Blanchard 2014[78]	Non-comparative before-and-after study
Bollerlslev 2007[82]	Did not include re-operation patients
Bollerslev 2009[83]	No relevant outcomes
Bonzelaar 2016[85]	Conference abstract
Britton 1971[91]	Non-comparative study
Brothers 1987[92]	Non-comparative study
Broulik 2011[93]	Non-comparative before-and-after study
Bruining 1981[95]	Non-comparative study
Burney 1996[100]	Non-comparative study
Burney 1998[101]	Non-comparative study
Calo 2016[105]	Inappropriate comparison
Carneiro-Pla 2007[115]	Non-comparative study (all patients underwent surgery)
Chen 1998[136]	Non-comparative study
Cheng 2015[139]	Systematic review. Screened for relevant references.
Chigot 1995[142]	Non-comparative study (all patients underwent surgery)
Clifton-Bligh 2015[152]	Did not report information from patients with re-operation separately
Cowie 1982[157]	Incorrect study design – case series
D'Andrea 1996[163]	Non-comparative study (all patients underwent surgery)

Study	Exclusion reason
Diaz-Guerra 2015[179]	Conference abstract
Dy 2012[190]	Non-comparative study (all patients underwent surgery)
Edwards 2006[193]	Non-comparative study (all patients underwent surgery)
Elvius 1995 [198]	Did not include re-operation patients
Espiritu 2011[202]	No relevant outcomes reported
Falkheden 1980[207]	Non-comparative study (all patients underwent surgery)
Fang 2008[209]	NRS – no multivariate analysis or adjustment for confounders
Farnebo 1984[210]	Non-comparative study (all patients underwent surgery)
Freaney 1978[216]	Non-comparative study (all patients underwent surgery)
Ghose 1981[231]	Non-comparative before and after study
Hagstrom 2006[252]	Non-comparative before and after study
Hedback 1990[270]	Non-comparative retrospective study
Hedback 1991[269]	Non-comparative retrospective study
Horiuchi 2002	Inappropriate intervention – 2 week administration only of oral etidronate. This bisphosphonate is no longer used.
Jansson 2006[302]	Conference abstract
Khosla 1999[340]	NRS – only reports the effect of surgery on fracture risk from a univariate model and not the adjusted HR for this factor from the MV model
Lafferty 1989[366]	Non-comparative study (all patients underwent surgery)
Larsson 1993[369]	NRS with no adjustment for confounders
Leong 2010[376]	NRS with no adjustment for confounders
Lundstam 2015 [396]	Did not include re-operation patients
Melton 1992[415]	Non-comparative study (all patients underwent surgery)
Mole 1992[427]	NRS – surgery effect on fracture risk only reported from a univariate model (risk adjusted for confounders not reported)
Morris 2010[430]	NRS with no adjustment for confounders. Study also provides an analysis of eight people who underwent surgery compared with eight age-matched conservatively managed people (but other key confounders not matched).
Nomura 2004[456]	No relevant outcomes reported – for some outcomes results are only reported for the intervention group. Paper includes a statement that there was no morbidity or mortality but it is unclear if this refers to both the intervention and control group or just the control group.
Nordenstrom 2004[457]	NRS with no adjustment for confounders
Oucharek 2011[467]	Non-comparative before and after study
Paloyan 1983[471]	Non-comparative study (all patients underwent surgery)
Perrier 2009[488]	Non-comparative study (all patients underwent surgery)
Persson 2011[490]	No relevant outcomes
Posen 1985[493]	Follow-up study of an included RCT but with no relevant outcomes
Rao 2003[510]	NRS with no adjustment for confounders
Rao 2004 [509]	NRS with no adjustment for confounders
Richmond 2007[518]	Did not include re-operation patients
Rolighed 2012[523]	Non-comparative study
Rubin 2008[534]	Conference abstract
Sankaran 2010[553]	NRS with no adjustment for confounders
Sanzenbacher 1970[554]	A literature review not specified as systematic review and without

Study	Exclusion reason
	quality assessment of the studies included
Saponaro 2013[555]	Inappropriate study design
Schneider 2014[560]	Incorrect interventions
Scott Jr 1981[564]	Inappropriate study design
Sejean 2005[567]	Inappropriate comparison. Incorrect interventions
Silverberg 1995[585]	Inappropriate study design
Silverberg 1999[586]	Incorrect study design – decision analysis
Singh Ospina 2016[591]	Non-comparative study (all patients underwent surgery)
Singh Ospina 2016[592]	NRS —study performed a multivariate analysis but factors included are unclear and no adjusted risk given for the effect of surgery on the outcome
Siperstein 1992[595]	Systematic review screened for references
Solorzano 2008[606]	Systematic review screened for relevant references
Soreide 1997[610]	Non-comparative study (all patients underwent surgery)
Strewler 1995[624]	Non-comparative retrospective case series
Talpos 2000[636]	Did not include re-operation patients
Tay 2016[638]	Non-comparative study (all patients underwent surgery)
Tisell 1983[649]	Literature review with commentary and opinion
Trombetti 2016[655]	NRS with multivariate analysis but no relevant outcomes
VanderWalde 2009 [669]	Did not include re-operation patients
Vera 2014[671]	Inappropriate comparison. Inappropriate study design.
Vestergaard 2003[675]	NRS with no adjustment for confounders
Wagner 2007[682]	NRS with no adjustment for confounders
Wermers 1998[693]	Overlap in recruitment of participants with an already included study (Vestergaard 2003) – larger study included in this review
Witteveen 2010[701]	Review. Screened for relevant references.
Wu 2010[707]	NRS with mulitvariate analysis but the effect of surgery on risk of death is not reported from the univariate or multivariate analysis
Yeh 2016[710]	Non-comparative study (all patients underwent surgery)
Yu 2010[716]	Inappropriate comparison
Zhao 2014[724]	NRS – adjusted relative risk for the effect of surgery on fracture risk not reported

Table 18: Studies excluded from the surgical interventions clinical review

Study	Exclusion reason
Aarum 2007[1]	Inappropriate comparison – patients randomised to pre-operative localisation (group 1) and no pre-operative localisation (group 2). In group 1, minimally invasive parathyroidectomy for positive localisation findings and conventional bilateral neck exploration for negative localisation findings. In group 2 all patients underwent conventional bilateral neck exploration.
Agus 1993[11]	An opinion piece
Barczynski 2006[51]	Inappropriate comparison – minimally invasive video assisted parathyroidectomy versus open minimally invasive parathyroidectomy.

Bergenfelz 2002[66]	Inappropriate comparison. Does not compare focused versus non-focused, compares unilateral versus bilateral
Bergenfelz 2005[65]	Did not include re-operation patients
Bruno 2010[96]	Conference abstract
Chen 1999[138]	Incorrect study design – non randomised study
Gracie 2012[242]	Systematic review. Screened for relevant references.
Hessman 2010[276]	Inappropriate comparison – open minimally invasive parathyroidectomy versus minimally invasive video-assisted parathyroidectomy
Jinih 2016[308]	Conference abstract
Jinih 2017[309]	Systematic review. Screened for relevant references.
Kreidieh 2013[357]	Protocol for a Cochrane review
Laird 2016[367]	Literature review. Screened for relevant references.
Lombardi 2009[390]	Systematic review. Screened for relevant references.
Miccoli 1999[417]	Did not include re-operation patients
Miccoli 2008[418]	Inappropriate comparison. Both arms compared minimally invasive-study compares focused parathyroidectomy plus quick intra-operative parathormone assay (qPTHa) during minimally invasive video-assisted parathyroidectomy (MIVAP) versus MIVAP with endoscopic bilateral neck exploration.
Nelson 2007[445]	Incorrect study design – cohort study
Norlen 2015[459]	Incorrect study design – retrospective cohort study. Study investigated long term outcomes after focussed parathyroidectomy.
Reeve 2000[515]	Systematic review. Screened for relevant references.
Russell 2006[538]	Did not include re-operation patients
Sadik 2011[544]	Did not include re-operation patients
Simonella 2005[589]	Paper not in English
Singh Ospina 2016[591]	Systematic review. Screened for relevant references.
Slepavicius 2008[597]	Did not include re-operation patients
Sozio 2005[612]	Paper not in English
Taieb 2013[633]	Article on minimally invasive parathyroidectomy
Westerdahl 2007[695]	Inappropriate comparison. Study compares unilateral versus bilateral; does not compare focused versus non-focused.

Table 19: Studies excluded from the monitoring clinical review

Study	Exclusion reason
Abdulkader 2012[3]	Conference abstract
Agarwal 2003[6]	Incorrect study design – case report
Ahsan 2017[13]	n=25. Excluding studies less than 50 participants.
Alvarez-Allende 2014[26]	Conference abstract
Amaral 2012[27]	Inappropriate comparison. Study compared the clinical and laboratory data between the normocalcaemic and mild hypercalcaemic patients.
Antonelli 2011[34]	Conference abstract
Babey 2010[40]	Conference abstract
Bai 2012[43]	Incorrect study design – literature review to explore association between primary hyperparathyroidism (PHPT) and acute or chronic pancreatitis
Bailey 1974[44]	Incorrect population – patients with urinary stones
Bandeira 2009[46]	Inappropriate comparison. Study aims to determine the prevalence of cortical osteoporosis in patients with symptomatic PHPT and compare it with the asymptomatic form.
Bandeira 2016[48]	Conference abstract
Bao 2013[49]	Conference abstract
Battersby 1969[58]	Incorrect study design – case report (of pancreatitis with PHPT)
Beard 1950[59]	Incorrect study design – case series.
Bhadada 2018 [71]	Non-comparative study
Bonzelaar 2016[85]	Conference abstract
Cannon 2010[110]	Inappropriate comparison. Study describes the surgical outcome and long term results of hypercalcaemic crisis patients after parathyroidectomy compared to non-crisis patients.
Carnaille 1998[112]	Incorrect comparison. Study looked at association of pancreatitis with PHPT.
Cassibba 2014[122]	Incorrect study design – retrospective analysis of a case series
Clifton-Bligh 2015[152]	Did not include re-operation patients
Corlew 1985[156]	n=47. Excluding studies less than 50 participants.
Csupor 2005[158]	Inappropriate comparison. Study aimed to assess the potential association between the surgically confirmed location of the disease and the presence of kidney stone.
Danzi 1974[164]	Incorrect study design – case report.
Deaconson 1987[169]	Inappropriate population group. Study reports the influence of parathyroidectomy on the natural history of nephrolithiasis and changes in the rates of new stone formation.
De Geronimo 2006[167]	Did not include re-operation patients
Diaz de la Guardia 2010[180]	Not in English
Dimkovic 2002[182]	Inappropriate population. Study aimed to examine patients with kidney stone disease, elevated iPTH, but normal serum calcium level and normal urinary excretion of calcium.
Dolgin 1979[183]	Study analysed the effect of routine screening of calcium and phosphate levels on the incidence and spectrum of PHPT. No useable outcomes.
Dumitrescu 2008[187]	Incorrect population. Study aimed to determine the prevalence of contributors to secondary osteoporosis in patients presenting with a clinical vertebral or non-vertebral fracture.
Eufrazino 2013[204]	Incorrect study design-cross-sectional study

Study	Exclusion reason
Falko 1984[208]	No comparison group. Study assessed clinical and biochemical spectrum of patients with PHPT who had surgery.
Hedback 1998 [268]	Did not include re-operation patients
Heath 1991[267]	Incorrect study design – case series.
Hedback 2002[271]	Incorrect study design – case series.
Jha 2016 [307]	Non-comparative study
Kenny 1995[331]	Did not include re-operation patients
Khosla 1999[340]	Did not include re-operation patients
Kobayashi 1997 [348]	Non-comparative study
Larsson 1989[368]	No useable outcomes
Larsson 1993[369]	Did not include re-operation patients
Lowe 2007[392]	No comparison group. Study described the clinical course of 37 patients with normocalcaemic PHPT who were followed for up to 8 years.
Lueg 1982[394]	Incorrect study design – case series
Marques 2011[403]	Incorrect study design. Retrospective review of medical records to describe the characteristics of normocalcaemic primary hyperparathyroidism (NPHPT) in patients seen for osteoporosis evaluation.
Melton 1992[415]	Did not include re-operation patients
Misiorowski 2012[422]	No useable outcomes. The aim of the study was to evaluate the diagnostic power of the bone densitometry in diagnosis of PHPT.
Mollerup 1999[428]	Inappropriate comparison – before and after surgery. The study aimed to evaluate the risk of renal stone recurrence after successful surgical treatment of PHPT.
Nilsson 2005[453]	Inappropriate population and outcomes. Study explored long term effects of parathyroidectomy on cardiovascular functions in PHPT.
Pradeep 2008[495]	Non-comparative study
Pratley 1973[498]	Incorrect study design – case series.
Purnell 1971 [504]	Non-comparative study
Rajeevan 2014[506]	Incorrect study design – series review
Ronni-Sivula 1985[524]	Did not include re-operation patients
Rubin 2008[534]	Inappropriate comparison. Study compared PHPT patients who had undergone surgery versus those without surgery.
Scholz 1981[561]	Non-comparative study
Siilin 2011[582]	Study assessed BMD between PHPT and men without PHPT. No clinical outcomes.
Silverberg 1990[587]	No comparison group
Silverberg 1995[584]	Non-comparative study
Siminovitch 1980[588]	Study assessed the effect of parathyroidectomy in patients with normocalcaemic calcium stones. No useable outcomes.
Soreide 1997[610]	Inappropriate comparison. The study evaluated survival after surgical treatment for primary hyperparathyroidism.
Strewler 1995[624]	Literature review. Screened for references.
Suh 2008[628]	Did not include re-operation patients
Turchi 1962[659]	Incorrect study design – case report
Vanderwalde 2006[668]	Study aimed to determine the effect of parathyroidectomy on fracture risk in patients with PHPT. Inappropriate comparison – comparison groups were parathyroidectomy versus observation.

Study	Exclusion reason
Vanderwalde 2009[669]	Inappropriate comparison – comparison groups were parathyroidectomy versus observation
Vestergaard 2000[672]	Inappropriate comparison
Vestergaard 2003[674]	Study included in surgery review
Vestergaard 2003[675]	Study included in surgery review
Vestergaard 2003[673]	Inappropriate comparison. The aim of this study was to evaluate cardiovascular morbidity before and after surgery for PHPT.
Vestergaard 2004[676]	Inappropriate comparison
Wermers 1998 [693])	Non-comparative study
Wilson 1988[700]	Did not include re-operation patients
Yu 2009[718]	Study did not meet protocol criteria. Study evaluated prevalence and incidence of PHPT.
Yu 2011[717]	Did not include re-operation patients
Yu 2011[720]	No protocol outcomes. Study provided information on the natural history of asymptomatic 'mild' PHPT patients with a long follow-up period, in terms of the biochemical progression of the disease.
Yu 2013[719]	No useable outcomes. Study aimed to identify the best biochemical risk factors for predicting adverse outcomes in untreated PHPT.

Table 20: Studies excluded from the surgical localisation review

Reference	Reason for exclusion
Aarum 2007[1]	Did not include re-operation patients
Abboud 2007[2]	Unable to calculate 2x2 table values for protocol method
Adler 2011[4]	Unable to calculate 2x2 table for either MIBI or US (for MIBI, number of correct scans only reported for 291/310 people who had either a negative scan or a single adenoma on scan; for US, only reported as the added benefit over MIBI)
Agarwal 2012[7]	Did not include re-operation patients
Agha 2007[10]	Did not include re-operation patients
Agha 2012[8]	Incorrect index test (contrast enhanced ultrasonography, and unable to calculate 2x2 table values for protocol method for other imaging tests). IOPTH incorrect criteria (only reports for >60% drop at 15 minutes, unclear if all people also had a >50% drop at 10 minutes).
Agha 2013[9]	Unable to calculate 2x2 table values for protocol method
Ahmed 2013[12]	Incorrect reference standard (for IOPTH, unclear if histology also used as part of the reference standard or if only intraoperative findings and normocalcaemia)
Akbaba 2012[14]	Unable to calculate 2x2 table values for protocol method
Akin 2009[16]	Unable to calculate 2x2 table values for protocol method
Al-Askari 2012[17]	Incorrect reference standard (unclear if normocalcaemia used as part of the reference standard and 6/204 had recurrent or persistent hypercalcaemia)
Alabdulkarim 2010[18]	Unable to calculate 2x2 table values for protocol method

Reference	Reason for exclusion
Albuja-Cruz 2013[19]	Unable to calculate 2x2 table values for protocol method. Sensitivity and specificity values provided for IOPTH but unclear how calculated from the numbers provided in the results.
Alexandrides 2006[20]	Incorrect index test (people either had thallium-201/technetium-99m pertechnetate subtraction scan, 99mTc-tetrofosmin scan or 99mTc-sestamibi scan). Unable to calculate 2x2 table values for protocol method for US.
Alhefdhi 2011[22]	Incorrect reference standard (for IOPTH, unclear if histology also used as part of the reference standard or if only intraoperative findings and normocalcaemia)
Aliyev 2014[23]	Incorrect reference standard (surgical findings)
Ammori 1998[29]	Unable to calculate 2x2 table for protocol method
Anderson 2008[30]	Unable to calculate 2x2 table values for protocol method (accuracy of MIBI for lateralisation not precise localisation)
Ansquer 2008[33]	Unable to calculate 2x2 table values for protocol method (accuracy calculated on a per-gland basis)
Apostolopoulos 1998[35]	Incorrect index test (99mTc-tetrofosmin)
Arciero 2004[36]	Incorrect reference standard (for IOPTH, no mention of histology used as part of the reference standard)
Arici 2001[37]	Unable to calculate 2x2 table values for protocol method.
Aspinall 2012[38]	Incorrect reference standard (normocalcaemia not part of the reference standard, assumption made that parathyroid glands left in situ were not pathologically enlarged or hyperfunctioning)
Attie 1988[39]	Unable to calculate 2x2 table values for protocol method
Bacher 2011[41]	Unable to calculate 2x2 table values for protocol method (accuracy for localisation to the correct side)
Badii 2016[42]	Unable to calculate 2x2 table values for protocol method (for pre-operative imaging or IOPTH)
Bambach 1978[45]	Incorrect population (recruited people with a diagnosis of primary or tertiary HPT and numbers included unclear)
Bandeira 2008[47]	No relevant outcomes (sensitivity, specificity or values for 2x2 table not provided). Incorrect reference standard (histology only).
Barber 2016[50]	Incorrect reference standard (IOPTH and pathology)
Barczynski 2006[52]	Unable to calculate 2x2 table values for protocol method
Barczynski 2007[53]	Did not include re-operation patients
Barczynski 2009[55]	Incorrect index test (venous sampling test in isolation (not in conjunction with previous surgery results), for lateralisation and not precise localisation)
Barczynski 2009[54]	Incorrect reference standard (accuracy of IOPTH for prediction of normocalcaemia, but no pathological confirmation [states ‘intraoperative frozen sections were performed only to confirm the parathyroid origin of the resected tissue’])
Barraclough 1981[57]	Incorrect index test (US imaging using a 5MHz frequency probe)
Berczi 2002[60]	Sensitivity and specificity provided of MIBI and US for correct lateralisation but unable to calculate 2x2 values for protocol method
Bergenfelz 1994[62]	Unable to calculate accuracy of IOPTH (study reports average decline in IOPTH at various time points, not the accuracy at a

Reference	Reason for exclusion
	particular threshold)
Bergenfelz 1996[61]	Incorrect index test (accuracy of venous sampling test in isolation, for lateralisation and not precise localisation)
Bergenfelz 1997[67]	Incorrect reference standard (findings at neck exploration – although all people were rendered normocalcaemic, there is no mention of histological confirmation)
Bergenfelz 1998 [63]	Unable to calculate 2x2 table values for IOPTH (sensitivity and specificity values are provided in the paper but it is unclear if these refer to the whole study population or only people with single adenoma)
Bergenfelz 2009[68]	Unable to calculate 2x2 table values for protocol method (as not reported whether the people with negative imaging had a final outcome of single or multigland disease)
Bergenfelz 2007[64]	Unable to calculate 2x2 table values for protocol method
Bergenfelz 2011[69]	Not assessing accuracy of imaging or IOPTH
Bewick 2014[70]	Incorrect reference standard (unclear if normocalcaemia used as part of the reference standard)
Bhansali 2006[72]	Unable to calculate 2x2 table values for protocol method
Bhatnagar 1998[73]	Incorrect reference standard (surgical resection and histopathology)
Biertho 2003[74]	Incorrect population (5% had carcinoma)
Billotey 1996[76]	Incorrect population (44% had secondary or tertiary HPT)
Bilezikian 1973[75]	Incorrect reference standard (not all people rendered normocalcaemic)
Bishop 2015[77]	Accuracy results only presented for different age subgroups and no overall accuracy reported
Blower 1992[79]	Incorrect reference standard (no mention of normocalcaemia)
Bobanga 2017[80]	Did not include re-operation patients
Boggs 1996[81]	Incorrect reference standard (for IOPTH, post-operative normocalcaemia reported but unclear if histology was used to confirm final outcome in all patients – only reported narratively in the results for some patients)
Borel Rinkes 2001[86]	Incorrect reference standard (post-operative normocalcaemia, but no histology)
Bradford Carter 1997[87]	Unable to calculate 2x2 table values for protocol method (classification of TPs from table 1 suggests accuracy for correct lateralisation of MIBI, not precise location)
Bradley 2016 [88]	Did not include re-operation patients
Brennan 1981[90]	Incorrect population (unclear if only people with primary HPT included and 9% had FHH, suspected FHH or non-parathyroid hypercalcaemia).
Brown 2015[94]	Unable to calculate 2x2 table values for protocol method

Reference	Reason for exclusion
Bugis 1995[97]	Unable to calculate 2x2 table values for protocol method
Bumpous 2009[98]	Unable to calculate 2x2 table values for protocol method
Burke 2013[99]	Unable to calculate sensitivity and specificity for correct gland localisation in the correct quadrant (scans were considered accurate if they localized an abnormal gland on the ipsilateral side of the gland removed at operation)
Butt 2015[102]	Incorrect reference standard (unclear if normocalcaemia used as part of the reference standard and 7% weren't rendered normocalcaemic)
Caixas 1997[103]	Incorrect population (around 17% of the population had either secondary HPT or MEN)
Cakal 2012[104]	Incorrect reference standard (surgical and histopathological examination)
Calo 2012[108]	Overlap in the included participants with the Calo 2013[106] study (Calo 2013 study larger and therefore included in this review)
Calo 2013[106]	Did not include re-operation patients
Calo 2013[107]	Unable to calculate 2x2 table values for IOPTH
Campbell 2015 [109]	Unable to calculate 2x2 table values for protocol method (per-gland method used in study)
Carlier 2008[111]	Unable to calculate sensitivity and specificity values or 2x2 table for protocol method (per-gland method used in study)
Carnaille 1998[113]	Incorrect index test (pre-operative PTH, not IOPTH monitoring)
Carneiro 2003[117]	Incorrect reference standard (intraoperative findings and post-operative normocalcaemia, but no histology)
Carneiro-Pla 2006[116]	Incorrect reference standard (intraoperative findings and post-operative normocalcaemia, but no histology)
Carneiro-Pla [114]	Incorrect reference standard (intraoperative findings and post-operative normocalcaemia, but no histology)
Casara 2001[118]	Incorrect population (6% with MEN, parathyroid carcinoma or familial HPT). Incorrect reference standard (unclear if all patients had normocalcaemia following operation).
Casas 1993[120]	Unable to calculate sensitivity and specificity values or 2x2 table for protocol method
Casas 1994[119]	Did not include re-operation patients
Catania 2002[123]	Unable to calculate 2x2 table values for IOPTH
Catargi 1999[124]	Incorrect reference standard (operative findings/surgical exploration)
Caveny 2012[126]	Incorrect reference standard (histology and drop in IOPTH)
Caudle 2006[125]	Unable to calculate sensitivity and specificity values. Incorrect reference standard (calcium levels at 6 months only available in around 50% of people)
Cayo 2009[127]	Did not include re-operation patients
Cham 2015[130]	Unable to calculate sensitivity and specificity values or 2x2 tables
Chan 2005[131]	Conference Paper. Incorrect reference standard (histology)
Chapuis 1996[132]	Incorrect index test (IOPTH assay results weren't available until 2 hours after completion of surgery). Incorrect reference standard (surgical findings used as the reference standard for MIBI and US imaging).
Chatterton 1987[133]	Incorrect index test (Thallium-201-Technetium-99m subtraction

Reference	Reason for exclusion
	scan)
Chen 1997[134]	Incorrect population (16% had secondary or tertiary HPT)
Chen 2005[135]	Incorrect reference standard (intraoperative findings and post-operative normocalcaemia, but no histology)
Chen 2005[137]	Did not include re-operation patients
Cheung 2012[140]	Incorrect reference standard (systematic review – normocalcaemia as part of the reference standard was not an inclusion criteria for studies)
Chick 2017[141]	Did not include re-operation patients
Chiu 2006[143]	Agreement and comparison of different IOPTH criteria.
Cho 2014[144]	Incorrect population (6% had MEN)
Chou 1997[145]	Unable to calculate 2x2 table values for protocol method.
Chun 2013[147]	Incorrect reference standard (histology and decrease in PTH, no mention of cure/normocalcaemia)
Ciappuccini 2012[148]	Incorrect reference standard (surgical findings and pathology)
Civelek 2002[149]	Incorrect reference standard (histology)
Clark 1984[150]	Incorrect population (11% had secondary HPT)
Clark 2003[151]	Unable to calculate 2x2 table values for protocol method (accuracy of MIBI for lateralisation, not precise localisation)
Cook 1998[154]	Incorrect population (38% had tertiary HPT). Incorrect reference standard (histology).
Cook 2010[155]	Incorrect population (subgroup of people who had an IOPTH rise at 5 minutes)
Czerniak 1991[160]	Incorrect index test (dual radionucleotide parathyroid-radioiodinated toluidine blue / technetium 99m-thyroid scintigraphy). Unable to calculate 2x2 table values for protocol method.
D'Agostino 2013[162]	Incorrect reference standard. Reference standard was exploratory surgery or IOPTH drop (not normocalcaemia) – so in some people the reference standard for a negative gland was only IOPTH. “Glands were considered negative if they were either explored and deemed normal by the surgeon or not explored with drop in IOPTH that met the Miami criteria”.
D'Agostino 2013[161]	Unable to calculate 2x2 values for protocol method (per-gland method used in the study)
Davis 2013[165]	Comparing different IOPTH criteria
Day 2015[166]	Incorrect study design for test and treat (comparing 4DCT to no 4DCT, but not randomised). Incorrect reference standard (pathology and IOPTH).
De Simone[168]	Incorrect reference standard (unclear if all people rendered normocalcaemic)
Del Rio 2008[170]	Incorrect reference standard (histology). Unable to calculate 2x2 table values for protocol method.
Demirkurek 2003[171]	Unable to calculate 2x2 table values for protocol method
Denham 1998[172]	Incorrect reference standard (systematic review – normocalcaemia as part of the reference standard was not an inclusion criteria for studies)
Derom 1993[177]	Incorrect population (includes people with secondary and tertiary HPT)
Derom 1994[176]	Article not in English

Reference	Reason for exclusion
Deutmeyer 2011[178]	Unable to calculate 2x2 table values for protocol method
Dillavou 2000[181]	Unable to calculate 2x2 values for protocol method (accuracy of MIBI for lateralisation)
Doppman 1998[184]	Incorrect reference standard (some participants had angiographic ablation rather than surgery)
Drews 2003[185]	Incorrect population (50% of people had secondary HPT)
Dudek 1994[186]	Incorrect population (>75% secondary HPT). Incorrect index test (thallium-technetium scan)
Dunlop 1980[188]	Incorrect reference standard (histology)
Dwarakanathan 1986[189]	Incorrect reference standard (operative and pathological findings).
Dy 2012[191]	Incorrect index test (for IOPTH, accuracy only reported for a drop of 50% or more and to a normal or near-normal level – unable to calculate for a 50% drop alone)
Ebisuno 1997[192]	Incorrect reference standard (histology)
Eichhorn-Wharry 2011[194]	Incorrect reference standard (post-operative normocalcaemia not reported)
Eisenberg 1974[195]	Incorrect population (included people with secondary HPT)
Elaraj 2010[196]	Unable to calculate 2x2 values for protocol method
Eloy 2006[197]	Incorrect index test (accuracy of venous sampling test in isolation, for lateralisation and not precise localisation)
Emmolo 2005[199]	Unable to calculate the accuracy of IOPTH
Erdman 1989[200]	Incorrect reference standard (surgical findings)
Ersoy 2014[201]	Incorrect reference standard (states that all participants included in the analysis had biochemical improvement, unclear if this refers to all patients having normocalcaemia).
Estella 2003[203]	Incorrect population (8% MEN). Incorrect reference standard (not all people were rendered normocalcaemic).
Ezzat 2011[206]	Incorrect population (people with indication for total thyroidectomy)
Ezzat 2012[205]	Unable to calculate 2x2 values for protocol method
Fayet 1997[211]	Incorrect reference standard (surgical and pathological findings)
Feingold 2000[212]	Unable to calculate 2x2 values for protocol method
Fogelman 1984[214]	Incorrect reference standard (surgical exploration)
Foster 1989[215]	Incorrect index test (thallium-technetium subtraction scintigraphy). Incorrect reference standard (normocalcaemia not reported).
Freudenberg 2006[217]	Unable to calculate 2x2 values for protocol method (study uses per-gland method)
Gallacher 1993[218]	Unclear how sensitivity and specificity were calculated ('per-gland' or 'per-patient', and not enough information provided to complete 2x2 table)
Gallowitsch 1997[219]	Incorrect reference standard (histology in people who had surgery, not all people underwent surgery)
Gallowitsch 2000[220]	Incorrect reference standard (histology)
Garcia-Santos 2014[221]	Unable to calculate 2x2 table values for IOPTH and sensitivity or specificity not reported
Garcia-Talavera 2010[224]	Incorrect reference standard (pathology and post-operative PTH, no mention of normocalcaemia)
Garcia-Talavera 2011 [223]	Incorrect index test (accuracy of intra-operative gamma probe)
Garcia-Talavera 2016[222]	Unable to calculate 2x2 table values for protocol method
Garner 1999[225]	Did not include re-operation patients

Reference	Reason for exclusion
Gauger 2001[226]	Only included people with double adenoma and assessed IOPTH after excision of the first gland (therefore not possible to obtain true positive or false negative results)
Gawande 2006[227]	Unable to calculate 2x2 table values for protocol method
Gedik 2017[228]	Unable to calculate 2x2 table values for protocol method
Ghemigian 2015[230]	Unable to calculate 2x2 table values for protocol method
Gergel 2014[229]	Unable to calculate 2x2 table for protocol method (study gives accuracy of US and MIBI for lateralisation and per-gland method)
Gil-Cardenas 2006[232]	Unable to calculate 2x2 table values for protocol method
Gilat 2005[233]	Incorrect population (unclear age range of participants, one 13 year old included)
Gill 2011[234]	Incorrect reference standard (operative findings and histopathology)
Gimm 2012[235]	Incorrect index test (super-selective venous sampling: involved an initial conventional venous sampling, followed by a second round of additional samples taken from small venous branches in the region with the highest PTH level)
Giraldez-Rodriguez 2008[236]	Unable to calculate 2x2 table values for protocol (unclear if MIBI accurately localised in all cases, only states that it was positive or negative)
Glynn 2011[237]	Unable to calculate 2x2 table values for protocol method
Gofrit 1997[238]	Unable to calculate 2x2 table values for protocol method
Gogas 2003[239]	Unable to calculate 2x2 table values for protocol method (unclear if the two people with inaccurate pre-operative localisation would be classified as an incorrectly localised single adenoma by protocol method).
Goldstein 2006[240]	Incorrect reference standard (no mention of histopathology)
Gooding 1986[241]	Incorrect reference standard (surgical findings)
Grant 2005[243]	Incorrect population (people with familial HPT or MEN included).
Grayev 2012[244]	Provides sensitivity and PPV of MRI for lateralisation but unable to calculate 2x2 values for protocol method
Griffith 2015[245]	Incorrect reference standard (surgical and pathological findings. Although all patients were cured, this could be based on normocalcaemia at 6 months or a 50% drop in IOPTH levels)
Gross 2004[246]	Incorrect population (14% had tertiary HPT)
Grosso 2007[247]	Unable to calculate 2x2 values for protocol method
Guerin 2015[248]	Unable to calculate 2x2 values for protocol method (study uses 'per-patient' method to calculate sensitivity, but differs to protocol method)
Haber 2002[249]	Incorrect reference standard (biochemical cure could be based on IOPTH or normocalcaemia at 6 months, so not all people had confirmation of normocalcaemia).
Habibollahi 2018[250]	Incorrect reference standard (cure based on post-operative normocalcaemia ***or*** positive IOPTH)
Haciyanli 2003[251]	Incorrect population (10% of people had familial disease).
Halvorson 1994[253]	Incorrect reference standard (surgical, anatomical and pathological findings)
Hamamci 2011[254]	Paper not in English
Hamilton 1988[256]	Did not include re-operation patients
Hammonds 1976[257]	Not assessing the accuracy of imaging techniques for localisation
Hanif 2006[258]	Did not report information from patients with re-operation separately

Reference	Reason for exclusion
Hanninen 2000[259]	Incorrect population (18% of people had secondary hyperparathyroidism)
Hara 2007[260]	Incorrect population (79% of people in the study were receiving regular haemodialysis)
Harris 2008[261]	Did not include re-operation patients
Hasselgren 1992[263]	Unable to calculate 2x2 table values for protocol method.
Hassler 2014[264]	Incorrect reference standard (surgery and histopathology, PTH measured after surgery to ensure cure). Unable to calculate 2x2 values for protocol method.
Hathaway 2013[265]	Did not include re-operation patients
Hayakawa 2014[266]	Incorrect population (3/15 (20%) of people had MEN). Incorrect reference standard (histological confirmation without mention of normocalcaemia)
Heiba 2015[272]	Incorrect reference standard (histopathology)
Heineman 2015[273]	Incorrect reference standard (PTH levels used to determine cure, so elevated PTH in the setting of normocalcaemia could be considered as no cure)
Heizmann 2009[274]	Unable to calculate 2x2 table values for protocol method
Heller 1993[275]	Incorrect reference standard (surgical findings without normocalcaemia)
Hewin 1997[277]	Unable to calculate 2x2 table values for protocol method (paper reports accuracy of US and MRI for lateralisation, not precise location)
Hindie 1995[280]	Incorrect reference standard (surgical findings and normocalcaemia without histology)
Hindie 1997[279]	Unable to calculate 2x2 table values for protocol method
Hindie 1998[278]	Did not include re-operation patients
Hinson 2015[281]	Incorrect reference standard (normocalcaemia not reported)
Hjern 1975[282]	Incorrect reference standard (pathology, not all people rendered normocalcaemic)
Ho Shon 2001[283]	Unable to calculate 2x2 table values for protocol method
Ho Shon 2008[284]	Incorrect reference standard (histopathology)
Hoda 2013[285]	Only included people with negative or inconclusive imaging (only 3 participants included)
Horanyi 2010[286]	Incorrect population (secondary hyperparathyroidism and MEN included). Incorrect index test (fine needle tissue aspirate).
Hornung 2011[288]	Incorrect index test (contrast enhanced ultrasonography). Unable to calculate 2x2 values for protocol method for conventional US.
Hughes 2011[289]	Did not include re-operation patients
Hunter 2012[290]	Incorrect reference standard (histology alone, no mention of cure/normocalcaemia). Histology alone used to confirm presence of adenoma in a region identified on the scan. Unclear how absence of adenomas in all other glands was confirmed (suggested that surgeries were focused or unilateral and no mention of cure/normocalcaemia).
Hwang 2010[291]	Did not include re-operation patients
Iacobone 2005[292]	Did not include re-operation patients
Inabnet 1999[294]	Unable to calculate sensitivity and specificity or 2x2 values. Incorrect index test (IOPTH assay taken at 30, 60, 90 and 120

Reference	Reason for exclusion
	minutes after excision (our protocol specifies 5, 10 or 20 minutes)
Ibrahim 2015[293]	Incorrect reference standard (brief statement in abstract 'surgical findings and results of clinical follow-up as a reference standard', but no details provided in methods, unclear if normocalcaemia was used).
Irvin 1993[295]	Incorrect reference standard (IOPTH prediction of post-operative normocalcaemia, but no histology)
Irvin 1994[296]	Incorrect reference standard (normocalcaemia not reported for all included participants)
Isidori 2017[297]	Incorrect reference standard (histology)
Ito 2007[298]	Incorrect index test (accuracy of venous sampling test in isolation, for lateralisation and not precise localisation)
Itoh 2003[299]	Incorrect population (secondary hyperparathyroidism)
Jabiev 2009[300]	Unable to calculate 2x2 table values for protocol method
James 2014[301]	Incorrect population (used tissue from patients undergoing surgery for thyroid or parathyroid disease)
Jarhult 1985[303]	Incorrect reference standard (histology)
Jaskowiak 1996[304]	Unclear if accuracy measures are calculated against a reference standard using normocalcaemia
Jaskowiak 2002[305]	Did not report information from patients with re-operation separately
Javaid 1999[306]	Incorrect reference standard (histology)
Johnson 2001[310]	Incorrect population (also included people with MEN, renal failure and carcinoma)
Johnson 2010[311]	Incorrect population (1 participant out of 15 had MEN). Unable to calculate 2x2 table values for protocol method
Johnston 1996[312]	Unable to calculate 2x2 table values for protocol method (unclear if those not cured had a final diagnosis of single or multi-gland disease).
Joliat 2015[314]	Incorrect reference standard (unclear if normocalcaemia measured as part of the reference standard)
Jones 2001[316]	Unable to calculate 2x2 table values for protocol method.
Jones 2002[315]	Incorrect population (23% of people had either secondary HPT, parathyroid cancer, parathyromatosis or MEN)
Jorna 2007[317]	Unable to calculate 2x2 table values for protocol method
Kairaluoma 1993[320]	Incorrect population (10% had familial hyperparathyroidism or MEN). Incorrect reference standard (intraoperative findings)
Kairaluoma 1994[319]	Did not include re-operation patients
Kairaluoma 1994[318]	Incorrect population (27% of people had MEN)
Kairys 2006[321]	Unable to calculate 2x2 table values for protocol method
Kandil 2012[322]	Incorrect reference standard (normocalcaemia not mentioned)
Kang 1993[323]	Incorrect reference standard (surgical reports)
Karakas 2012[324]	Incorrect reference standard (states surgical cure was achieved in all patients, but unclear if this was defined by normocalcaemia or a positive IOPTH decline)
Katayama 1990[325]	Paper not in English
Kaur 2016[326]	Incorrect reference standard (normocalcaemia not mentioned)
Keane 2013[327]	Incorrect reference standard (histological confirmation used to confirm the true location of the adenoma, post-operative PTH or calcium returning to normal used to confirm the true location if histology inconclusive). Unable to calculate 2x2 table.

Reference	Reason for exclusion
Kebapci 2004[328]	Unable to calculate 2x2 table for protocol method
Keidar 2017[329]	Incorrect reference standard (states intra-op and post-op biochemical workup as well as surgical findings and histopathological results, but unclear if post-op normocalcaemia used). Gives number of adenomas with same Perrier localisation on imaging and surgery, but unable to calculate 2x2 table.
Kelly 2014[330]	Incorrect reference standard (pathological findings used as the reference standard without normocalcaemia)
Khaliq 2003[332]	Unable to calculate 2x2 table values for protocol method.
Khan 1994[334]	Incorrect population (type of HPT not reported and unclear if any people had MEN or familial HPT)
Khan 2015[338]	No relevant outcomes (diagnostic accuracy not reported)
Khorasani 2014[339]	Incorrect reference standard (histopathology)
Kim 2012[343]	Incorrect reference standard (lesions confirmed pathologically only)
Kim 2015 [341]	Did not include re-operation patients
Kim 2016[342]	Unable to calculate 2x2 table values for protocol method
Klieger 1998[344]	Incorrect population (31% had a history of chronic renal failure)
Kluijfhout 2016[346]	Unable to calculate 2x2 table values for protocol method (per-gland accuracy reported).
Kluijfhout 2017[345]	Systematic review (unable to calculate 2x2 table values for protocol method)
Kobayashi 1998[347]	Accuracy of individual preoperative imaging tests not assessed
Koberstein 2016[349]	Incorrect reference standard (intraoperative findings)
Koksal 2006[350]	Unable to calculate 2x2 table values for protocol method (not enough detail provided to determine if imaging is accurately localising to the precise location, or to side of adenoma)
Koong 1998[351]	Incorrect reference standard (surgical findings and histology only). Unable to calculate 2x2 values for protocol method.
Koren 2005[352]	Unable to calculate 2x2 table values for protocol method
Kovatcheva 2014[353]	No diagnostic accuracy measures for localisation (assessing US-guided high-intensity focused ultrasound as a non-invasive treatment for PHPT)
Koyuncu 2005[354]	Incorrect reference standard (histology only). Histology used to confirm presence of abnormal gland and if no adenoma was found then other glands were explored. But if an abnormal gland was located first time, there was no use of cure/normocalcaemia to confirm no other abnormal glands.
Krakauer 2016[355]	Unable to calculate 2x2 values for protocol method
Krausz 2006[356]	Did not report information from patients with re-operation separately
Krubsack 1989[358]	Unable to calculate values for 2x2 table (gives sensitivity and specificity values for locating adenomas in the correct region – 3 regions: right and left lobe of thyroid and below the thyroid gland)
Kucuk 2002[359]	Incorrect reference standard (presence of adenoma in people with positive imaging was only confirmed using histology – no mention of normocalcaemia to ensure no abnormal glands were missed)
Kukar 2014[360]	Unable to calculate 2x2 values for protocol method (accuracy in

Reference	Reason for exclusion
	study based on laterality and not precise quadrant localisation). Incorrect reference standard (surgical cure was assessed but unclear if it was included as part of the reference standard).
Kumar 2000[361]	Did not include re-operation patients
Kuriloff 2004[362]	Unable to calculate sensitivity and specificity values
Kutler 2011[363]	Incorrect reference standard (radiology reports and the operative and histopathologic findings)
Kuzu 2016[364]	Incorrect reference standard (histology)
Kwon 2013[365]	Incorrect reference standard (surgical findings and histology)
Lavely 2007[370]	Incorrect reference standard (surgical findings/determined by the surgeon)
Lebastchi 2015[371]	Unable to calculate 2x2 table values for protocol method (number with correct localisation, localisation to wrong gland and negative on imaging given, but unclear if final outcome was single adenoma in all participants)
Lee 1996[374]	Incorrect population (16% had either secondary or tertiary HPT or MEN)
Lee 2014[373]	Did not include re-operation patients
Lee 2016[372]	Unable to calculate 2x2 table values for protocol method
Lenschow 2015[375]	Incorrect reference standard (intraoperative and pathologic finding. Incorrect index test (11C-Methionine PET/CT).
Leupe 2011[377]	Incorrect reference standard (surgical and pathological findings); also looked at pathology from one or more normal glands but unclear if all glands assessed in this way. Normocalcaemia following resection of a pathological gland was used to assume other glands normal, but suggested this was only done if unable to visualise all glands during the operation.
Levin 1987[378]	Incorrect population (27% had either MEN, secondary or tertiary HPT or familial HPT)
Lew 2009[379]	No accuracy data reported
Lew 2010[380]	Incorrect reference standard (no histological verification of adenomas, only IOPTH and post-operative normocalcaemia)
Lezaic 2014[381]	Unable to calculate 2x2 values for protocol method.
Lim 2017[382]	Gives sensitivity of IOPTH for predicting operative failure but not reported how operative failure was measured (unclear if normocalcaemia)
Lin 1991[383]	Incorrect population (people with hypercalcaemia and suspected parathyroid adenoma or carcinoma, and some included participants had chronic renal failure).
Linda 2012[384]	Incorrect reference standard (two reference standards used: surgical findings and histologic diagnosis)
Lindqvist 2009[385]	Unable to calculate sensitivity, specificity or 2x2 table values (methods state a 'per-gland' method and a 'per-patient' method, but results only given for the sensitivity and specificity of localising to the correct side)
Livingston 2014[386]	Not assessing accuracy of pre-operative imaging techniques
Lloyd 1990[387]	Incorrect reference standard (not all people had post-operative normocalcaemia)
Lo 2003[388]	Did not include re-operation patients
Lo 2007[389]	Did not include re-operation patients
Lombardi 2008[391]	Did not include re-operation patients
Lubitz 2010[393]	Unable to calculate 2x2 values for protocol method

Reference	Reason for exclusion
Lumachi 2004[395]	Incorrect reference standard (IOPTH and final histology)
Lundstroem 2016[397]	Incorrect reference standard (quadrant of adenoma determined by anatomical findings at surgery, histopathological results and IOPTH). Normocalcaemia/hypercalcaemia at 1 year or more is reported but not included within the determination of the reference standard result.
Majors 1995[398]	Incorrect population (33% had secondary or tertiary HPT)
Malhotra 1996[399]	Incorrect population (29% had secondary or tertiary HPT)
Mandal 2015[400]	Unable to calculate 2x2 values for protocol method
Mandell 2001[401]	Incorrect reference standard (accuracy of IOPTH for prediction of normocalcaemia, but no mention of pathological confirmation)
Manhire 1984[402]	Incorrect population (32% had MEN or family history of MEN)
Martin 1996[404]	Incorrect reference standard (compared with surgical and pathological findings, states the post-operative results were also reviewed but unclear if normocalcaemia/cure was assessed as part of reference standard)
Martin 2000[406]	Incorrect reference standard (sustained post-operative normocalcaemia given as an outcome (% of people) but unclear if used as part of the reference standard to calculate accuracy of localisation)
Martinez-Rodriguez 2011[407]	Incorrect reference standard (histopathologic diagnosis)
Martinez-Rodriguez 2014[408]	Incorrect reference standard (histopathological result, unclear if normocalcaemia used as part of the reference standard)
Maweja 2004[409]	Incorrect reference standard (unclear reference standard as states all participants were normocalcaemic post-operatively, but also that there was 1 FP and 8TNs)
Mazzeo 2000[410]	Incorrect reference standard (histopathology)
McDermott 1996[411]	Incorrect population (6% had parathyroid carcinoma). Unable to calculate 2x2 table values for protocol method.
McIntyre 1994[412]	Incorrect reference standard (unclear if histology and normocalcaemia used as part of the reference standard)
McMillan 1983[413]	Incorrect reference standard (normocalcaemia not mentioned)
Medas 2016[414]	Unable to calculate 2x2 values for protocol method
Meyer 2009[416]	Comparison of 2 different IOPTH assays
Miccoli 2008[418]	Did not include re-operation patients
Michel 2013[419]	Did not include re-operation patients
Mihai 2007[420]	Unable to calculate 2x2 values for protocol method (146/150 people had correctly localised adenoma but unclear if the imaging correctly located the adenoma in the other 4 people who were not cured after the first surgery)
Miller 2003[421]	Incorrect reference standard (normocalcaemia not reported in all people)
Miura 2002[423]	Did not report information from patients with re-operation separately.
Mohammadi 2012[424]	Incorrect reference standard (post-operative histopathology results and IOPTH monitoring)
Moka 2000[425]	Unable to calculate 2x2 values for protocol method
Moka 2000[426]	Unable to calculate 2x2 values for protocol method
Morks 2011[429]	Did not include re-operation patients
Morris 2012[431]	Incorrect reference standard (surgical results)
Mortenson 2008 [432]	Unable to calculate 2x2 values for protocol method

Reference	Reason for exclusion
Mozzon 2004[434]	Did not report information from patients with re-operation separately.
Moure 2008 [433]	Unable to calculate 2x2 values for protocol method
Mshelia 2012[435]	Not assessing the diagnostic accuracy of imaging to locate adenomas (correlation of imaging results with serum calcium levels)
Munk 2008[436]	Unable to calculate 2x2 table values for protocol method
Murchison 1991[437]	Incorrect index test (US imaging using a 7.5MHz frequency probe)
Nael 2015[438]	Incorrect reference standard (surgical pathology)
Nair 2016[439]	Incorrect population (7% had carcinoma)
Najafian 2017[440]	Unable to calculate 2x2 values for protocol method
Nasiri 2012[442]	Incorrect reference standard (histology only). Bilateral exploration performed and the decision to terminate the surgery was based on gross morphology in combination with frozen section – no use of cure/normocalcaemia to confirm absence of other abnormal glands.
Nehs 2013[444]	Accuracy of IOPTH to correctly lateralise and not for precise localisation
Nelson 2007[445]	Incorrect study design. No relevant outcomes.
Neves 2012[450]	Incorrect population (15.4% had MEN or carcinoma)
Neumann 1996[448]	Incorrect reference standard (surgical and histopathological findings)
Neumann 1997[447]	Incorrect reference standard (surgical and histopathological findings)
Neumann 1997[446]	Incorrect reference standard (surgical and histopathological findings)
Neumann 2008[449]	Incorrect reference standard (surgical findings and histology only)
Nilsen 2006[452]	Did not include re-operation patients
Noguchi 1994[454]	Paper not in English
Noltes 2017[455]	For US and MIBI, can only deduce accuracy for lateralisation, not precise localisation. Incorrect index test (for IOPTH, a decrease of 65% was required).
Nordin 2001[458]	Did not include re-operation patients
Numerow 1995[460]	Incorrect population (primary or secondary HPT).
O'Connell[461]2011	Unable to calculate values for 2x2 table (breakdown given of imaging resultsand surgical outcome, but imaging results only state left-sided or right-sided so unable to determine if imaging indicates 1 or more adenoma)
O'Doherty 1992[462]	No relevant outcomes (sensitivity, specificity or values for 2x2 table not provided)
Ohe 2003[463]	Incorrect index test (IOPTH results were not assessed while surgery was being performed). Average decline in PTH reported at each timepoint, and not number of people achieving >50% decline
Opoku-Boateng 2013[464]	Unable to calculate sensitivity and specificity values
Orevi 2014[465]	Incorrect population (only 50% of people had primary HPT)
Orloff 2001[466]	Did not include re-operation patients
Ozimek 2010[468]	Incorrect reference standard (gives diagnostic accuracy of IOPTH but unclear if normocalcaemia was used as the reference standard for all people, mentions subsequent cervical explorations and the accuracy for preditcting 'operative outcome')
Ozkaya 2015[469]	Incorrect reference standard (normocalcaemia not part of reference standard; diagnosis confirmed by surgical resection, IOPTH, frozen

Reference	Reason for exclusion
	section and histopathology)
Ozkul 2015[470]	Did not include re-operation patients
Panzironi 2002[472]	Unable to calculate 2x2 table values for protocol method
Parikh 2015[473]	Unable to calculate 2x2 table values for protocol method
Pata 2010[475]	Unable to calculate 2x2 table for protocol method (study gives accuracy of SPECT and SPECT/CT for lateralisation and per-gland method)
Pata 2011[476]	Unable to calculate 2x2 table for protocol method (study gives accuracy of SPECT and SPECT/CT for lateralisation)
Patacsil 2006[477]	Unable to calculate 2x2 table values for protocol method
Patel 1998[478]	Did not include re-operation patients
Pattou 1998[479]	Incorrect index test (accuracy of venous sampling test in isolation, for lateralisation and not precise localisation)
Pattou 1999[480]	Incorrect index test (participants had either 99mTc-labelled sestamibi or 99mTc-labelled tetrofosmin). Unable to calculate sensitivity and specificity or 2x2 values for new method.
Pearl 1993[484]	Incorrect index test (methods of ultrasound not reported).
Peck 1987[485]	Unable to calculate 2x2 table for protocol method (study gives information on lateralisation of MRI
Pellitteri 2003[486]	Incorrect reference standard (surgical findings)
Perez-Monte 1996[487]	Incorrect reference standard (surgical and histopathologic findings)
Perrier 2000[489]	Incorrect population (secondary HPT, tertiary HPT, MEN and parathyroid cancer included). Incorrect index test (fine needle tissue aspirate).
Philippon 2014[491]	Incorrect population (MEN not excluded and unclear how many people had MEN)
Politz 2006[492]	Incorrect reference standard (pathology)
Powell 2013[494]	Incorrect reference standard (details of reference standard not reported). Unable To calculate 2x2 table for protocol method.
Prager 2003[496]	No accuracy results for IOPTH reported
Prasannan 2007[497]	Unable to calculate 2x2 table for protocol method (accuracy of US and MIBI for correct lateralisation, not precise quadrant)
Preventza 2000[499]	Unable to calculate 2x2 table for protocol method (number classed as false negative by protocol method unclear).
Profanter 2004[501]	Incorrect index test (CAT-MIBI image fusion, unable to calculate 2x2 table values for protocol method for SPECT)
Profanter 2004[502]	Incorrect index test (CAT-MIBI image fusion, unable to calculate 2x2 table values for protocol method for SPECT)
Profanter 2004[500]	Incorrect index test ($^{99m}TcO_4$-$^{201}T1$ pinhole subtraction SPECT). Unable to calculate 2x2 table values for protocol method for US (unclear if a false positive in the study refers to an incorrect location or an additional normal gland localised)
Purcell 1999[503]	Unable to calculate 2x2 table values for protocol method (using 4-gland method)
Quiros 2004[505]	Incorrect reference standard (histopathology not reported)
Rameau 2016[507]	Incorrect reference standard (final pathology and IOPTH decline, not all patients were normocalcaemia after surgery)
Ramirez 2016[508]	Incorrect reference standard (pathology)
Rauth 1996[511]	Incorrect reference standard (surgical and pathologic reports)
Reading 1982[512]	Not a human clinical study (study in dogs)

Reference	Reason for exclusion
Reading 1985[513]	Incorrect population (15% had MEN, familiar disease or carcinoma)
Richards 2008[516]	Incorrect population (9% had MEN)
Richards 2011[517]	Did not include re-operation patients
Rickes 2003 [519]	Incorrect reference standard (surgery and histpathology)
Riss 2009[520]	Sensitivity, specificity and 2x2 table values not given for IOPTH
Rodgers 2006[521]	Unable to calculate 2x2 table values for protocol method
Roligheed 2004[522]	Incorrect index test (IOPTH drop of ≥80% at 5 minutes post-excision)
Roskies 2015[525]	Unable to calculate 2x2 table values for protocol method
Rotstein 1998[528]	Incorrect population (7% of participants had carcinoma). Unable to calculate 2x2 values for protocol method.
Roza 1984[529]	Incorrect population (7% of participants had carcinoma). Unable to calculate 2x2 values for protocol method.
Rubello 2003[533]	Incorrect population (6% tertiary HPT). Incorrect reference standard (surgical and pathological findings – all normal looking glands biopsied but normocalcaemia not measured).
Rubello 2005[532]	No relevant outcomes (sensitivity, specificity or values for 2x2 table not provided)
Rubello 2006[530]	No relevant outcomes (sensitivity, specificity or values for 2x2 table not provided)
Rubello 2006[531]	Did not include re-operation patients
Ruckert 1996[535]	Unable to calculate 2x2 table values for protocol method
Ruf 2004[536]	Incorrect reference standard (unclear if normocalcaemia used as part of reference standard). Unable to calculate 2x2 values.
Ruf 2007[537]	Incorrect reference standard (histopathology only)
Ryan 1997 [539]	Unable to calculate 2x2 table values for protocol method (unclear if scintigraphy results given in the table are the same for planar and SPECT)
Ryhanen 2015[540]	Unable to calculate 2x2 table values for protocol method
Saaristo 2002[541]	Did not include re-operation patients
Sadeghi 2008[542]	Unable to calculate 2x2 table values for protocol method (not all people cured, unable to confirm final diagnosis of single or multi-gland disease in all people)
Sadeghi 2018[543]	Unable to calculate 2x2 table values for IOPTH
Sagan 2010[545]	Did not include re-operation patients
Sager 2014[546]	Unable to calculate 2x2 table values for protocol method
Saguan 2013[547]	Incorrect reference standard (pathology only)
Saint Marc 2004[548]	Incorrect reference standard (histology only)
Sakimura 2013[549]	Incorrect reference standard (not all people had normocalcaemia)
Sand 1994[550]	Incorrect reference standard (reference standard of cure based on post-operative PTH level, not serum calcium level).
Sandqvist 2017[551]	Unable to calculate 2x2 table values for protocol method
Sandrock 1990[552]	Unable to calculate 2x2 table values for protocol method (paper uses a 'per-gland' method)

Reference	Reason for exclusion
Schalin-Jantti 2013[556]	Incorrect reference standard (histopathology)
Scheible 1981[557]	Incorrect reference standard (not all people had cure, therefore final pathology unclear). Unable to calculate 2x2 table values for protocol method.
Scheiner 2001[558]	Incorrect population (people with hypercalcaemia suspected of having PHPT, but parathormone assays not routinely obtained).
Schenk 2013[559]	Incorrect reference standard (histopathology and IOPTH)
Scott-Coombes 2017[563]	Unable to calculate 2x2 table values for protocol method
Sebag 2003[565]	Sensitivity and specificity of IOPTH reported separately for people with negative and positive pre-operative imaging (overall sensitivity and specificity or 2x2 table values not reported)
Seeliger 2015[566]	Unable to calculate 2x2 table values for protocol method (unclear numbers used to calculate sensitivity for IOPTH, so unable to determine 2x2 table values)
Seniaray 2016[568]	Unable to calculate 2x2 table values for protocol method
Sepahdari 2015[569]	Incorrect study design (case report). Incorrect index test (PET scan).
Serra 2006[570]	Unable to calculate 2x2 table values for protocol method
Seyednejad 2016[571]	Paper not in English
Shabtai 2003[572]	Unable to calculate 2x2 table values for protocol method
Shafiei 2012[573]	Unable to calculate 2x2 table values for protocol method
Shaha 1997[574]	Incorrect population (6% had MEN). Unable to calculate 2x2 table values for protocol method (per-gland method used).
Shaheen 2008[575]	Unable to calculate 2x2 table values for protocol method
Sharma 2006[576]	Unable to calculate 2x2 table values for protocol method
Sharma 2008[577]	Unable to calculate sensitivity, specificity or 2x2 values for protocol method
Sheng 2011[578]	Incorrect reference standard (a proportion of people had unclear pathology, therefore unable to assess the accuracy of IOPTH)
Shin 2011[579]	Paper not in English
Sho 2016[580]	Incorrect population (included people with secondary and tertiary hyperparathyroidism, MEN and parathyroid cancer)
Silov 2013[583]	Unable to calculate 2x2 table values for protocol method.
Singh 2007[590]	Incorrect reference standard (histology only). No relevant outcomes. Not looking at accuracy for correctly localising the adenoma, but for correctly predicting the presence of an adenoma (at any location).
Siperstein 2004[594]	Incorrect reference standard (histopathology)
Siperstein 2008[593]	Unable to calculate 2x2 table values for protocol method
Slater 2005[596]	Unable to calculate 2x2 table values for protocol method
Smith 2009[598]	Unable to calculate 2x2 table values for protocol method
Sofferman 1996[599]	Incorrect reference standard (normocalcaemia not reported)
Sofferman 1998[600]	Incorrect reference standard (surgical and pathological findings)
Sofianides 1978[601]	Accuracy measures or 2x2 table values for IOPTH not reported
Sohn 2015[602]	Incorrect index test (cervical oesophagram). Incorrect reference standard (histology only).
Sokoll 2000[603]	Assessing the difference between IOPTH decline in people with PHPT and renal insufficiency and people with PHPT without renal insufficiency (although the 2x2 table can be calculated for the group without renal insufficiency, the study only included people with

Reference	Reason for exclusion
	single adenoma who were cured – no reference standard negative)
Solorzano 2005[605]	Incorrect reference standard (for IOPTH, no mention of pathology, unclear if histology used to confirm final outcome)
Solorzano 2006[604]	Incorrect reference standard (IOPTH, macroscopic evaluation and post-operative normocalcaemia but without histopathology)
Sommer 1982[607]	Incorrect reference standard (post-operative normocalcaemia but without histopathology)
Song 1999[608]	Unable to calculate 2x2 values for protocol method
Soon 2008[609]	Incorrect reference standard (surgical and pathologic findings)
Soyder 2015[611]	Unable to calculate 2x2 table values for protocol method (study looked at accuracy for localisation of the correct side, not precise quadrant)
Spouse 2001[613]	Did not include re-operation patients
Sreevathsa 2017[614]	Unable to calculate 2x2 table values for protocol method.
Stalberg 2006[615]	Did not include re-operation patients
Starker 2011[616]	Incorrect population (secondary and tertiary hyperparathyroidism included)
Starr 2001[617]	Incorrect population (15% had familial hyperparathyroidism). Unable to calculate 2x2 table values for protocol method.
Staudenherz 1997[618]	Incorrect population (included people with secondary HPT, MEN and carcinoma)
Stein 1990[619]	Incorrect reference standard (histopathology – 'a biopsy of a normal gland was also taken for reference' but normocalcaemia not measured)
Stenner 2009[620]	Did not include re-operation patients
Stevens 1993[621]	Incorrect population (people with secondary and tertiary HPT included). Incorrect reference standard (operative and histologic findings).
Steward 2006[622]	Incorrect reference standard (surgical and pathological findings)
Stratmann 2002[623]	Unable to calculate 2x2 table values for protocol method
Suarez 2017[625]	Incorrect reference standard (accuracy of IOPTH in relation to post-operative serum calcium, but no mention of histology).
Sugg 1993[626]	Unable to access full text paper
Sugg 2004[627]	Incorrect reference standard (unclear if normocalcaemia used as part of the reference standard for all people, to confirm all adenomas removed)
Suh 2015[629]	Unable to calculate 2x2 table values for protocol method (accuracy for lateralisation not precise localisation)
Sullivan 2001[630]	Unable to calculate 2x2 table values for protocol method
Sun 2016[631]	Incorrect population (6% had secondary HPT or papillary thyroid carcinoma). Unable to calculate 2x2 table values for protocol method.
Taira 2004[634]	Incorrect population (people with MEN included in study population but unclear if included in the people with surgery who underwent final analysis). Incorrect reference standard (not all people rendered normocalcaemic by surgery and further investigation not reported).
Takei 1999[635]	Incorrect reference standard (histopathology)
Tampi 2014[637]	Did not include re-operation patients
Taylor 1996[639]	Incorrect reference standard (normocalcaemia not reported). Incorrect population (1 participant out of 15 had MEN).

Reference	Reason for exclusion
Taywade 2017[640]	Incorrect index test (accuracy of venous sampling test in isolation, for lateralisation and not precise localisation)
Tee 2013[641]	Incorrect reference standard (histopathology)
Thakur 2009[642]	Unable to calculate 2x2 table values for protocol method
Thanseer 2017[643]	Incorrect reference standard (accuracy of IOPTH reported but unclear reference standard, details not reported)
Thielmann 2017[644]	Incorrect reference standard (no confirmation that all people were normocalcaemic post-operatively)
Thomas 2009[645]	No accuracy data reported for IOPTH
Thompson 1999[646]	Incorrect reference standard (histology)
Thule 1994[647]	Incorrect population (19% had MEN or familial disease)
Timm 2004[648]	Did not include re-operation patients
Tokmak 2014[650]	Incorrect population (included people with primary or secondary HPT).
Toriie 2016[651]	Incorrect reference standard (surgical findings)
Treglia 2016[652]	Incorrect reference standard (unclear if all had normocalcaemia).
Treglia 2018[653]	Incorrect reference standard (systematic review – normocalcaemia as part of the reference standard was not an inclusion criteria for studies)
Trinh 2017[654]	Review article – unable to obtain full text
Tublin 2009[656]	Incorrect reference standard -data given for recurrence on follow-up [hypercalcaemia at ≥6 months], not for operative cure.
Tummers 2015[657]	Incorrect reference standard (surgery and pathology reports, surgical failure based on IOPTH, no details of post-operative normocalcaemia)
Tunca 2017[658]	Incorrect reference standard (presence of adenomas were confirmed using histology of resected specimen and IOPTH, but no use of normocalcaemia/cure, so unable to eliminate the possibility of further adenomas)
Tziakouri 1996[660]	Unable to calculate 2x2 table values for protocol method
Udelsman 2003[661]	Incorrect reference standard (histopathology)
Ulanovski 2002[662]	Incorrect reference standard (no details of reference standard given for positive confirmation of abnormal gland)
Untch 2011[663]	Incorrect reference standard (pathology)
Valdemarsson 1998 [664]	Unable to calculate 2x2 table values for protocol method (accuracy of US and MIBI for lateralisation not precise localisation)
Van Dalen 2001[665]	Unable to calculate 2x2 table values for protocol method (accuracy of scintigraphy for lateralisation not precise localisation)
Van der Vorst 2014[666]	Unable to calculate 2x2 table values for protocol method
Van Ginhoven 2011[667]	Did not report information from patients with re-operation separately.
Vaz 2011[670]	Incorrect reference standard (histopathology)
Vignali 2002[677]	Did not include re-operation patients
Vitetta 2014[678]	Incorrect reference standard (unclear what was used for the reference standard)
Von Schulthess 1988[679]	Unable to calculate 2x2 table values for protocol method
Wachtel 2015[680]	Incorrect reference standard (surgical and pathological findings)
Wade 2012[681]	Did not include re-operation patients
Weber 1993[684]	Incorrect index test (for IOPTH, accuracy only reported for a drop of 50% and into the normal range – unable to calculate for a 50% drop

Reference	Reason for exclusion
	alone)
Weber 1999[683]	Incorrect population (29% had either secondary hyperparathyroidism or MEN)
Weber 2004[685]	Incorrect index test (IOPTH samples taken but results not available until 48 hours – not available intraoperatively for decision making)
Weber 2010[686]	Incorrect population (around 50% had secondary HPT)
Weber 2013[688]	Incorrect reference standard (intraoperative and histological findings). Unable to calculate sensitivity and specificity for protocol method.
Weber 2017[687]	Incorrect index test (C-11 Methionine PET/CT). Unable to calculate 2x2 table values for protocol method for US.
Wei 1992[690]	Incorrect index test (assessing the accuracy of Methionine PET/CT, unable to calculate 2x2 table values for US and only selected patients with a negative MIBI)
Wei 1994[691]	Incorrect reference standard (histopathology). Incorrect population (20% had secondary or tertiary HPT and were analysed with the results of people with multigland primary HPT).
Wei 1997[689]	Did not include re-operation patients
Wei 2015[692]	Incorrect population (43% had either MEN, secondary hyperparathyroidism or tertiary hyperparathyroidism and results mixed)
Westerdahl 2004[694]	Incorrect reference standard (systematic review – normocalcaemia as part of the reference standard not required as an inclusion criteria of the studies)
Westra 1998[696]	Unable to calculate 2x2 table values for protocol method
Wheeler 1982[697]	Incorrect reference standard (histopathology)
Whelan 1989[698]	Unable to calculate 2x2 table values for protocol method
Whitley 1981[699]	Incorrect population (25% of people had MEN). Accuracy for lateralisation of MRI and US, not precise localisation.
Witteveen 2010[703]	Can calculate the accuracy for predicting the correct side of adenoma location, but not the precise quadrant.
Witteveen 2011[702]	Did not include re-operation patients
Wong 2009[705]	Incorrect population (50% had either tertiary HPT, MEN or parathyroid carcinoma)
Wong 2011[706]	Unable to calculate 2x2 table values for protocol method
Wong 2015[704]	Diagnostic accuracy of US and MIBI for correct lateralisation of the adenoma, not for localisation of the abnormal gland
Wu 1988[708]	Incorrect reference standard (systematic review – normocalcaemia as part of the reference standard was not an inclusion criteria for studies)
Yao 1993[709]	Incorrect reference standard (unclear if normocalcaemia used as part of the reference standard)
Yen 2006[712]	Unable to calculate 2x2 table values for protocol method
Yen 2008[711]	Incorrect reference standard (reference standard for IOPTH for ‘failed operations’ included people who were initially normocalcaemia but were then hypercalcaemic after 6 months [recurrent PHPT]).
Yip 2008[713]	Incorrect population (13% had MEN or parathyromatosis)
Ypsilantis 2010[715]	Did not include re-operation patients
Younes 2008[714]	Unable to calculate 2x2 table values for protocol method
Zawawi 2013[721]	Incorrect reference (intraoperative and histopathology)

Reference	Reason for exclusion
Zeina 2017[722]	Incorrect reference standard (pathology and drop in IOPTH but no use of cure/normocalcaemia). Presence of adenoma confirmed if frozen section showed hypercellular gland or adenoma and the IOPTH dropped. If IOPTH did not drop then other glands were explored.
Zerizer 2011[723]	Unable to calculate 2x2 table values for protocol method
Zmora 1995[725]	Incorrect reference standard (histopathology)
Zotti 1984[726]	Incorrect index test (US with a 7MHz scanner and scintigraphy with radioiodinated toluidine blue-technetium 99m or thallium 201-technetium 99m)

I.2 Excluded health economic studies

None.

Appendix J: Research recommendations

J.1 Failed primary surgery

Research question: What is the best and most cost-effective management strategy for people whose first surgery for primary hyperparathyroidism is not successful?

Why this is important:

Repeat parathyroid surgery is relatively uncommon; failure rates are higher than for primary surgery and it carries a higher risk. Currently there is limited evidence available on the management of people with failed surgery. The committee therefore felt that there is a need for a robust evidence base to guide an optimal management pathway for those who have had failed primary surgery.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults (18 years or over) with primary hyperparathyroidism in whom primary surgery has failed. Intervention(s): • Re-operation with or without surgical localisation -surgical localisation to include non-invasive techniques (for example parathyroid ultrasound, sestamibi scanning, CT and MRI scanning) or invasive techniques prior to surgery (for example parathyroid venous sampling); and intra-operative tests such as intraoperative parathyroid hormone assays (IOPTH), methylene blue and intra operative frozen sections. • Calcimimetics • Bisphosphonates • Monitoring Comparison: All interventions compared to each other Outcome(s) for intervention studies: • HRQOL • Mortality • Preservation of end organ function (bone mineral density, fractures, renal stones and renal function) • Deterioration in renal function • Persistent hypercalcaemia • Cardiovascular events • Adverse events • Cancer incidence Outcomes for diagnostic test-and-treat studies: • HRQOL • Mortality • Success (cure) / failure • Adverse events • BMD of the distal radius or the lumbar spine • Deterioration in renal function • Fractures (vertebral or long bone) • Length of hospital stay • Occurrence of kidney stones • Persistent hypercalcaemia

	• Reoperation • Unnecessary neck exploration Outcomes for diagnostic accuracy studies: • Specificity • Sensitivity Target condition (for localisation studies): correct localisation of adenoma. Target condition (for intra-operative tests): correct prediction of removal of all abnormal tissue.
Importance to patients or the population	The research will allow an evidence-based approach to the management of people with failed primary surgery and help improve the cure rate in such people.
Relevance to NICE guidance	This research will enable future guidelines to clearly recommend an evidence-based approach to the management of people with failed primary surgery.
Relevance to the NHS	This research would standardise the approach to the management of people with failed surgery. Appropriate management of such patients will reduce recurrence or persistent disease.
National priorities	No
Current evidence base	The systematic review on management options in failed surgery identified one study on calcimimetics and this was from a sub-group of patients who had previous failed parathyroidectomy. There was evidence available from two more studies assessing the diagnostic accuracy of sestamibi scanning (MIBI) and intra-operative parathyroid hormone monitoring (IOPTH) in patients undergoing repeat surgery. However the evidence was of low quality and based on a very small number of patients. There was no evidence available for indications for repeat surgery, surgical interventions (focused/4-gland exploration), bisphosphonates and monitoring. Due to the limited evidence the committee made a consensus recommendation on the management of this population. The committee considered that there is a need for a stronger evidence-based recommendation for management of people with failed surgery.
Equality	The recommendation is unlikely to impact on equality issues.
Study design	RCTs and systematic reviews of RCTs Diagnostic test and treat (surgical localisation and intra-operative tests) Diagnostic accuracy (surgical localisation and intra-operative tests)
Feasibility	The time scale will need to be at least 6 months to ensure adequate follow-up so that differences in interventions can be seen between the groups. As there is only a small proportion of patients who are not cured after first surgery (4–5%), there may be difficulty in conducting large RCTs.
Other comments	None
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.