Table1 Study characteristics.

First Author	Country	Study design	Patients (n)	Rate of Postoperative hypocalcemia (%)	NOS score	Risk factor
Liu 2020 (8)	USA	retrospective cross-sectional analysis	126,766	30-day follow-up after surgery:19.1%	★★★★★★★	Age, women, vitamin D deficiency, concurrent lateral neck dissection, concurrent central neck dissection, intraoperative parathyroid, recurrent laryngeal nerve injury, magnesium disorders
				1-year follow-up after surgery: 4.4%		
Lale 2019 (9)	Turkey	Retrospective case control	818	Permanent hypocalcaemia（>one year):26.7%	★★★★★★	Female, specimen weight, substernal localization, cervical lymph node dissection (CLND)
				Transient hypocalcaemia(calcium level is lower than 8 mg/dl at 24 and 72 h after thyroidectomy)： 1.7%		

Carvalho 2019 (10)	Brazil	Retrospective cohort study	1347	Hypocalcaemia: 21%	★★★★★★	Neck dissection, malignancy, gender, age, preoperative total Ca, preoperative PTH; preoperative vitamin D, central compartment dissection (CCD)
Wang W 2019(11)	China	Retrospective cohort study	242	Hypocalcaemia 60%	★★★★★★	Gender, extent of surgery, hypoparathyroidism, LND, hypomagnesemia, pre-Ca
Claudius 2018(12)	Germany	Retrospective case study	702	Postoperative biochemical hypocalcaemia (48 h)：22.8% Persistent biochemical hypocalcaemia (> 6 months)：6.8%	★★★★★	Symptomatic hypocalcaemia, female, parathyroid reimplantation, surgery time (≥189 min), thyreostatic drug therapy
Docimo 2017(13)	Italian	Retrospective case control	328	Symptomatic hypocalcaemia：7.9% Transient hypocalcaemia：14.6% Permanent hypocalcaemia: 0.6%	★★★★★★★	malignant pathology, CCND
Luo 2017(14)	China	Retrospective case control	304	Biochemical hypocalcemia：26.9%	★★★★★	Sex(male/female), Po hypomagnesemia：Po hypocalcemia, Po

				Symptomatic hypocalcemia：not reported		hypomagnesemia, Po iPTH<1.6 pmol/L, relative decline of iPTH>70%
Wang X2017(15)	China	Retrospective case control	237	Biochemical hypocalcemia：52.3% Symptomatic hypocalcemia：33.8%	★★★★★ ★	Bilateral CCND, MRND, PTG autotransplantation, hypoparathyroidism, hypomagnesaemia
Cho 2016(16)	Korea	Retrospective cohort study	1030	Transient hypocalcemia：28.2%； Permanent hypocalcemia：2.6%	★★★★★ ★	Age, gender (female), CND, MRND, extent of CND (bilateral), operation time, implant of parathyroid gland, parathyroid gland in pathology
Jason 2016(17)	USA	Retrospective cohort study	620,744	Hypocalcaemia 6%	★★★★★ ★★★	Magnesium disorder, phosphate disorder, female, age, medicaid payor status, thyroid cancer, total thyroidectomy, neck dissection, recurrent laryngeal nerveinjury, high-volume surgeon

Garrahy 2015(18)	Ireland	Retrospective cohort study	201	Biochemical hypocalcaemia (22.9%); Symptomatic hypocalcaemia: (12.4%)	★★★★★ ★★	Cancer diagnosis, central neck dissection, hypomagnesemia, inadvertent parathyroid resection
Bove(19) 2016	Italian	Retrospective cohort study	142	Temporary hypocalcemia：33% Permanent hypocalcemia：2.8%	★★★★★ ★	substernal goiter (SG)
LeeG2015(20)	Korea	Rerospective case study	134	Laboratory pocalcemia：(39 %) Symptomatic pocalcemia：(19 %)	★★★★★ ★	Age, sex (women), BMI, preoperative calcium, preoperative PTH, vitamin D (<20 ng/mL), vitamin D (<10 ng/mL), selective neck dissection, incidental parathyroidectomy
Talal 2014(21)	Arab	Retrospective cohort study.	213	Laboratorial Hypocalcemia：19.7% Clinical Hypocalcemia：17.8%	★★★★★ ★	Postoperative serum PTH, preoperative serum 25(OH)D<25 nmol/L

Pavol 2014(22)	Ireland	Prospective cohort study	788	Temporary hypocalcemia：23.9% Symptomatic hypocalcemia：14.0%	★★★★★ ★★★	Sex, age, preoperative diagnosis benign, biclamp hemostasis, thyroid gland weight, substernal extension, tracheal deviation, operation time, multinodular goiter, Graves disease, Hashimoto thyroiditis, thyroid cancer, incidental parathyroidectomy
Servicio 2013(23)	Spain	prospective cohort study	113	Hypocalcaemia 38.90%	★★★★★ ★	Vitamina D preoperatoria < 15 ng/mL, PTH postoperatoria < 13 pg/mL

Randall2012 (24)	USA	Retrospective case section	118,375	Hypocalcaemia 5.50%	★★★★★ ★★★	Age, female gender, ethnicity, Hispanic, Asian or Pacific islander, native American, total thyroidectomy, thyroidectomy with unilateral neck dissection, thyroidectomy with bilateral neck dissection, complete substernal thyroidectomy, partial substernal thyroidectomy, substernal thyroidectomy, isthmectomy, partial thyroidectomy, length of stay (per day), nonteaching hospital, malignant neoplasm of thyroid gland
Sevim 2009(25)	Turkey	Retrospective cohort study	417	Permanent hypocalcemia：7.7%	★★★★★ ★★	Incidental parathyroidectomy, extrathyroidal soft tissue invasion
Erbil 2009(26)	Turkey	Prospective cohort study	200	Symptomatic hypocalcemia：73% Asymptomatic hypocalcemia：27%	★★★★★ ★	Age (older than 50 years); preoperative serum 25-OHD level less than15 ng/mL

Bhandari 2017(27)	China	Retrospective case study	278	Hypocalcaemia 27.30%	★★★★★★★★	Age (years), lateral lymph node dissection, lobectomy plus isthmusectomy versus lobectomy, near-total thyroidectomy versus lobectomy, total thyroidectomy versus lobectomy, injected versus non-injected, gender (female), preoperative PTH levels
Aqtashi 2017(28)	Switzerland	Retrospective cohort study	34	Hypocalcaemia 33%	★★★★★★	Operation interval, PTH pre-OP2 , Calcium pre-OP2
Lin2016(29)	Taiwan	Retrospective case study	3186	Hypocalcaemia 30.90%	★★★★★★★	Age, gender(female), multituberous goiter, Graves disease, malignant tumors, total thyroidectomy, reoperation, central cervical lymph node (CCLN), thyroid malignancy

Tongol 2013 (30)	Philippines	Retrospective case study	242	Symptomatic hypocalcemia: 10.74%	★★★★★★★	Age, gender, thyroid disease (toxic, nontoxic or malignant), thyroid gland weight in grams, presence concomitant complication of thyroidectomy
				Asymptomatic hypocalcemia: 1.24%		Hoarseness and/or hematoma, type of surgery (total thyroidectomy), neck dissection, duration of surgery in hours, inadvertent, parathyroidectomy

Table 2 Results of quality assessment

Case control study evaluation results			
Include study	select	Comparability	Exposure

	1) Is the case definition adequate? a) yes, with independent validation ★ b) yes, eg record linkage or based on self reports c) no description	2) Representativeness of the cases a) consecutive or obviously representative series of cases ★ b) potential for selection biases or not stated	3) Selection of Controls a) community controls ★ b) hospital controls c) no description	4) Definition of Controls a) no history of disease (endpoint) ★ b) no description of source	1) Comparability of cases and controls on the basis of the design or analysis a) study controls for _____ (Select the most important factor.) ★ b) study controls for any additional factor ★ (This criteria could be modified to	1) Ascertainment of exposure a) secure record (eg surgical records) ★ b) structured interview where blind to case/control status ★ c) interview not blinded to case/control status d) written	2) Same method of ascertainment for cases and controls a) yes ★ b) no	3) Non-Response rate a) same rate for both groups ★ b) non respondents described c) rate different and no designation	Result

					indicate specific control for a second important factor.)	self report or medical record only e) no description			
Liu 2020	a	b	a	a	a	a	a	a	★★ ★★

									★★★
Lale 2019	a	b	a	a	b	a	a	b	★★★★★
Claudius 2018	a	a	c	a	a	e	a	b	★★★★★
Docimo 2017	c	b	a	a	a	a	a	a	★★★★★★
Luo 2017	c	a	a	a	a	e	b	a	★★★★★
Wang X 2017	a	a	c	a	b	a	b	b	★★★★★

Lee G 2015	a	a	c	a	a	a	a	b	★★ ★★ ★★
Randall2012	a	a	a	a	a	a	a	a	★★ ★★ ★★ ★★
Bhandari 2017	a	a	a	a	a	a	a	a	★★ ★★ ★★ ★★
Lin2016	a	a	c	a	a	a	a	a	★★ ★★ ★★ ★
Tongol 2013	a	a	a	a	a	a	a	b	★★ ★★ ★★ ★

Cohort study evaluation results

Include study	Selection	Comparability	Outcome

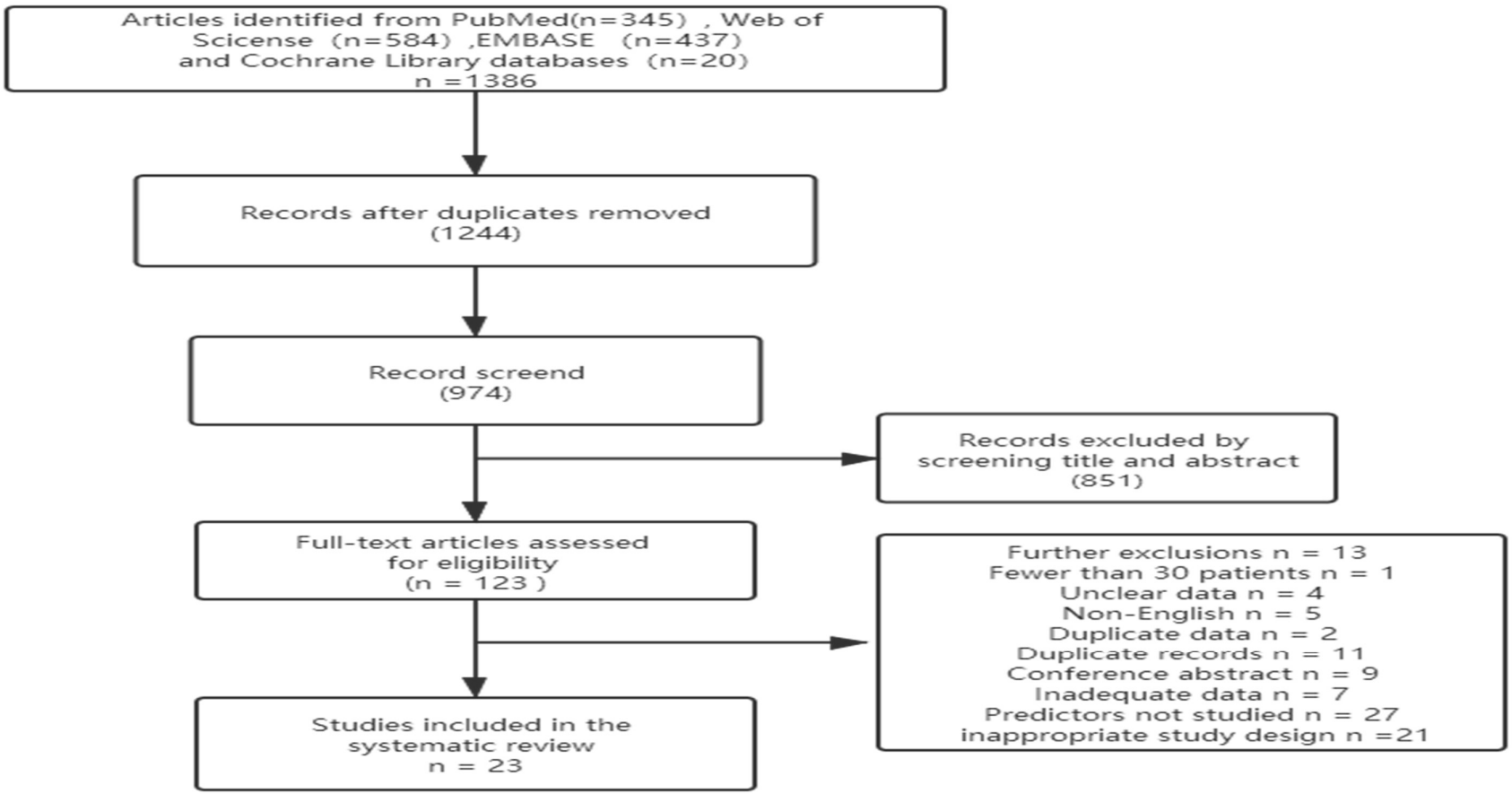
	1) Representativeness of the exposed cohort a) truly representative of the average _____ (describe) in the community ★ b) somewhat representative of the average _____ in the community ★ c) selected group of users eg nurses, volunteers d) no description of	2) Selection of the non exposed cohort a) drawn from the same community as the exposed cohort ★ b) drawn from a different source c) no description of the derivation of the non exposed cohort	3) Ascertainment of exposure a) secure record (eg surgical records) ★ b) structured interview ★ c) written self report d) no description	4) Demonstration that outcome of interest was not present at start of study a) yes ★ b) no	1) Comparability of cohorts on the basis of the design or analysis a) study controls for _____ (select the most important factor) ★ b) study controls for any additional factor ★ (This criteria could be modified to indicate	1) Assessment of outcome a) independent blind assessment ★ b) record linkage ★ c) self report d) no description	2) Was follow-up long enough for outcomes to occur a) yes (select an adequate follow up period for outcome of interest) ★ b) no	3) Adequacy of follow up of cohorts a) complete follow up - all subjects accounted for ★ b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ %	Result

	the derivation of the cohort				specific control for a second important factor.)			(select an adequate %) follow up, or description provided of those lost) ★ c) follow up rate < ____% (select an adequate %) and no description of those lost d) no statement	

Carvalho 2018	a	a	a	a	b	d	a	d	★★ ★★ ★★
Wang W 2019 等	a	a	a	a	a	a	b	d	★★ ★★ ★★
Jason 2016	b	a	b	a	a	b	a	a	★★ ★★ ★★ ★★
Garrahy 2015	a	a	b	a	a	d	a	a	★★ ★★ ★★ ★
Bove 2016	b	a	b	a	a	d	a	d	★★ ★★ ★★
Talal 2014	a	a	a	a	b	d	b	a	★★ ★★ ★★

Pavol 2014	a	a	b	a	a	d	b	a	★★ ★★ ★★
Servicio 2013	b	a	a	a	a	a	b	d	★★ ★★ ★★
Sevim 2009	a	a	a	a	a	b	a	d	★★ ★★ ★★ ★
Erbil 2009	a	a	b	a	a	d	a	d	★★ ★★ ★★
Aqtashi 2017	a	a	a	a	a	d	a	d	★★ ★★ ★★
Cho 2016	a	a	a	a	a	b	b	d	★★ ★★ ★★

Figure 1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Fewer than 30 patients n = 1
Unclear data n = 4
Non-English n = 5
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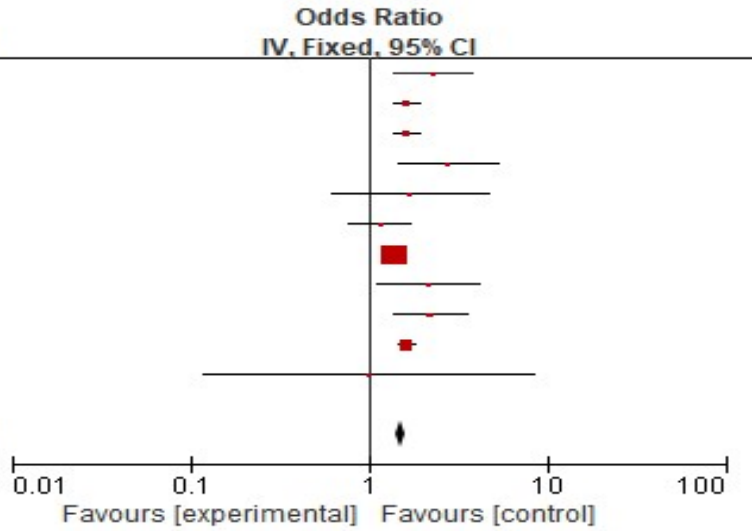
Conference abstract n = 9
Inadequate data n = 7
Predictors not studied n = 27
inappropriate study design n =21
Studies included in the systematic review n = 23

Female Figure 2

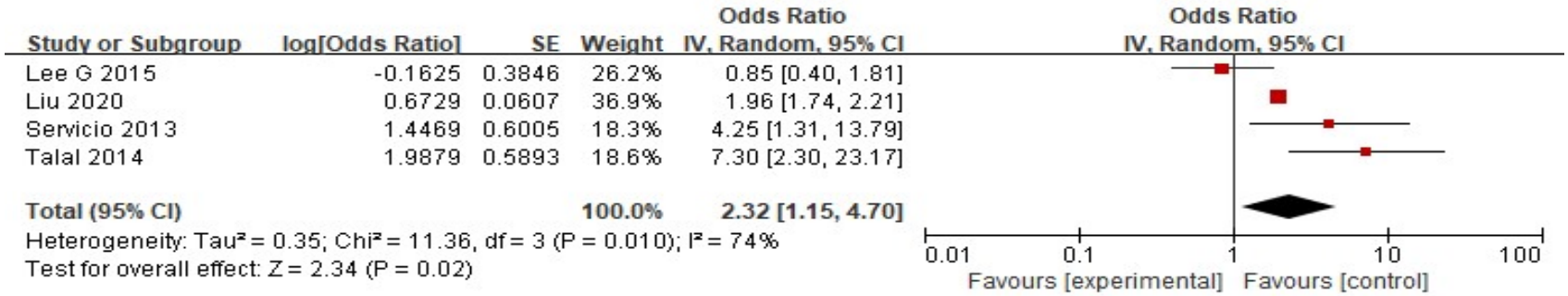
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Cho 2016	0.8264	0.2529	1.2%	2.29 [1.39, 3.75]
Claudius 2018	0.4886	0.0924	8.9%	1.63 [1.36, 1.95]
Jason 2016	0.4886	0.0924	8.9%	1.63 [1.36, 1.95]
Lale 2019	1.0225	0.3251	0.7%	2.78 [1.47, 5.26]
Lee G 2015	0.5423	0.5206	0.3%	1.72 [0.62, 4.77]
Lin2016	0.151	0.2025	1.9%	1.16 [0.78, 1.73]
Liu 2020	0.3293	0.0381	52.4%	1.39 [1.29, 1.50]
Luo 2017	0.7655	0.33	0.7%	2.15 [1.13, 4.11]
Pavol 2014	0.7925	0.2409	1.3%	2.21 [1.38, 3.54]
Randall 2012	0.4824	0.0566	23.7%	1.62 [1.45, 1.81]
Tongol 2013	0	1.0956	0.1%	1.00 [0.12, 8.56]
Total (95% CI)			**100.0%**	**1.51 [1.43, 1.59]**

Heterogeneity: $Chi^2 = 19.35$, $df = 10$ ($P = 0.04$); $I^2 = 48\%$

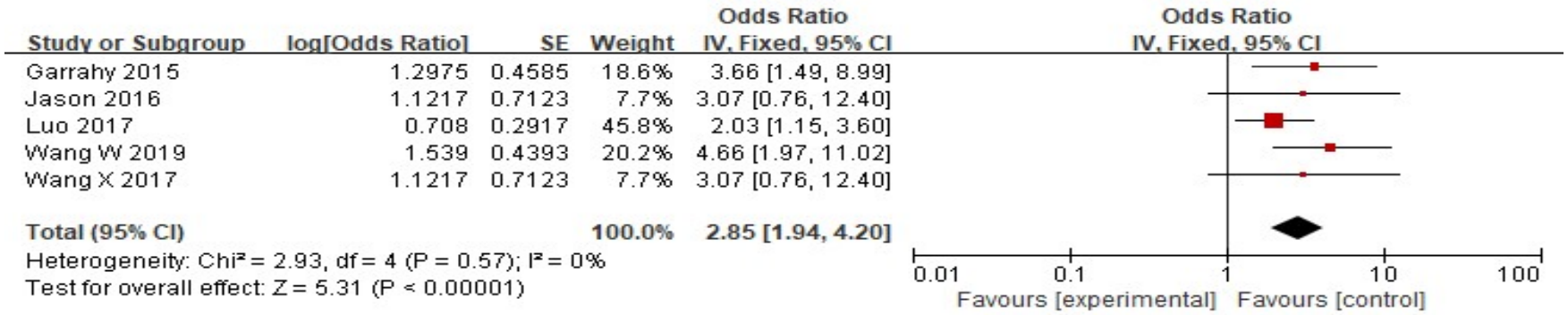
Test for overall effect: $Z = 14.91$ ($P < 0.00001$)



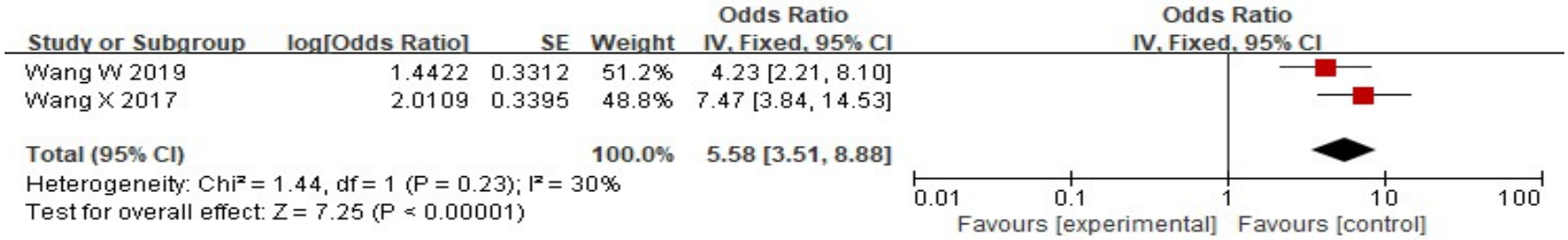
Preoperative vitamin D Figure 3



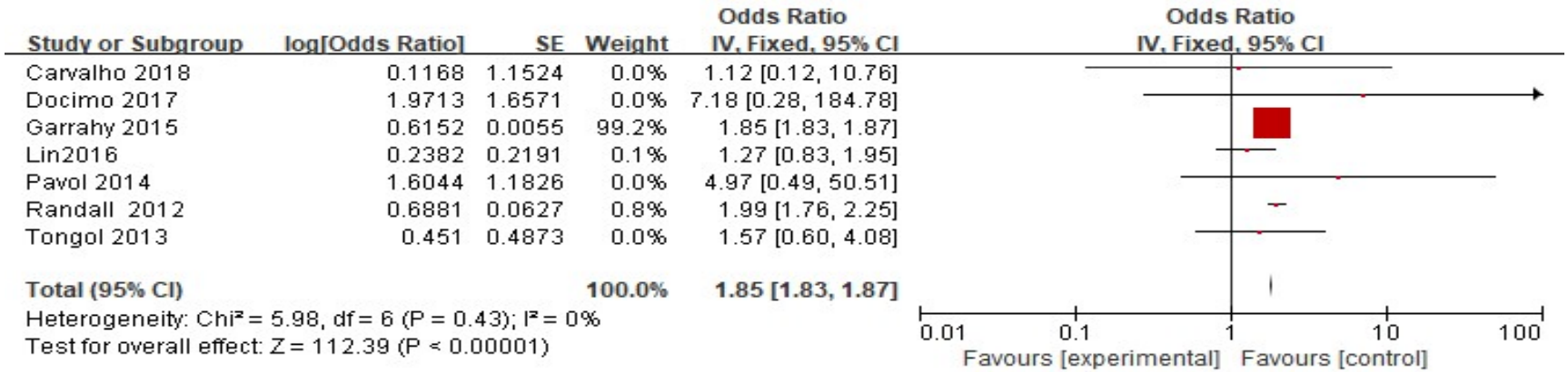
Hypomagnesemia Figure 4



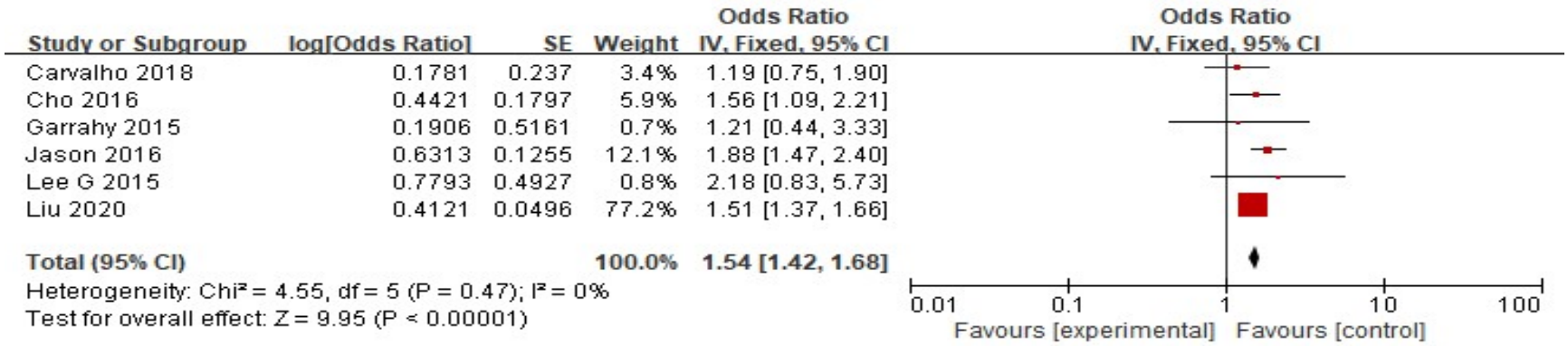
Hypoparathyroidism Figure 5



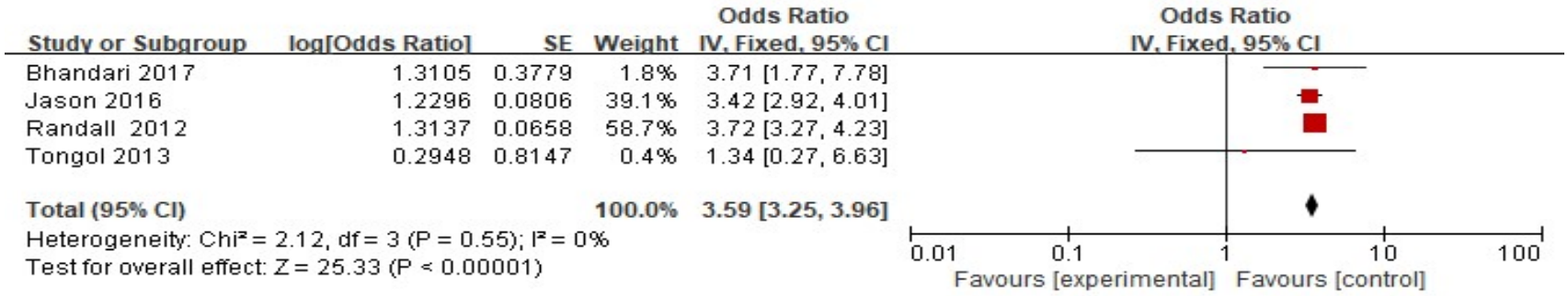
Thyriod malignancy Figure 6



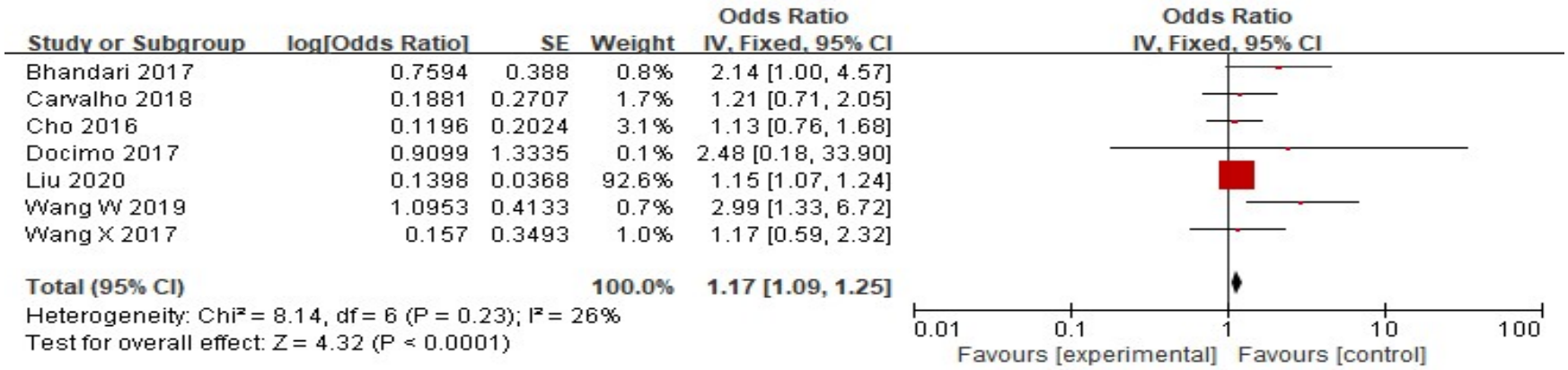
Central neck dissection(CND) Figure 7



Total thyroidectomy Figure 8



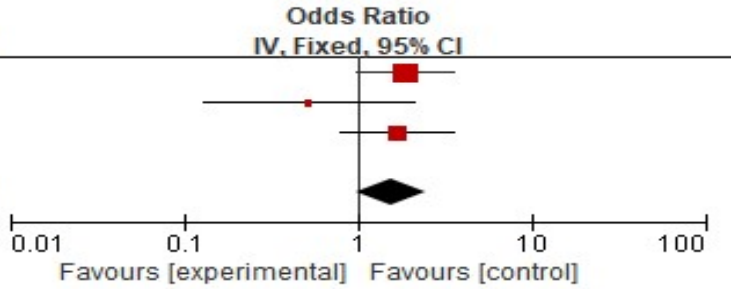
Central compartment neck dissection Figure 9



Modified radical neck dissection(MRND) Figure 10

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Cho 2016	0.6345	0.3268	51.1%	1.89 [0.99, 3.58]
Tongol 2013	-0.6506	0.709	10.9%	0.52 [0.13, 2.09]
Wang X 2017	0.5188	0.3785	38.1%	1.68 [0.80, 3.53]
Total (95% CI)			**100.0%**	**1.57 [0.99, 2.48]**

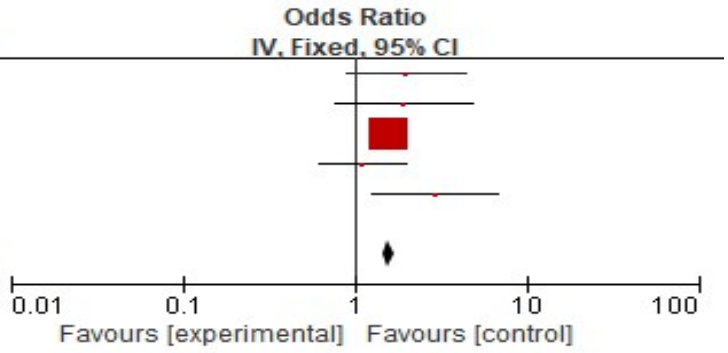
Heterogeneity: Chi² = 2.76, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 1.93 (P = 0.05)



Incidental parathyroidectomy Figure 11

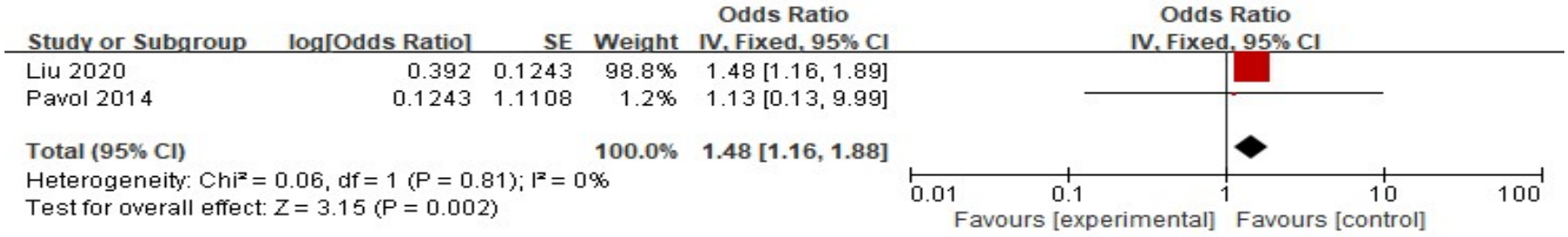
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Garrahy 2015	0.6931	0.4131	0.9%	2.00 [0.89, 4.49]
Lee G 2015	0.6627	0.4649	0.7%	1.94 [0.78, 4.83]
Liu 2020	0.4574	0.0403	95.8%	1.58 [1.46, 1.71]
Pavol 2014	0.0998	0.2981	1.8%	1.10 [0.62, 1.98]
Tongol 2013	1.0787	0.4357	0.8%	2.94 [1.25, 6.91]
Total (95% CI)			**100.0%**	**1.58 [1.47, 1.71]**

Heterogeneity: Chi² = 3.99, df = 4 (P = 0.41); I² = 0%
Test for overall effect: Z = 11.66 (P < 0.00001)

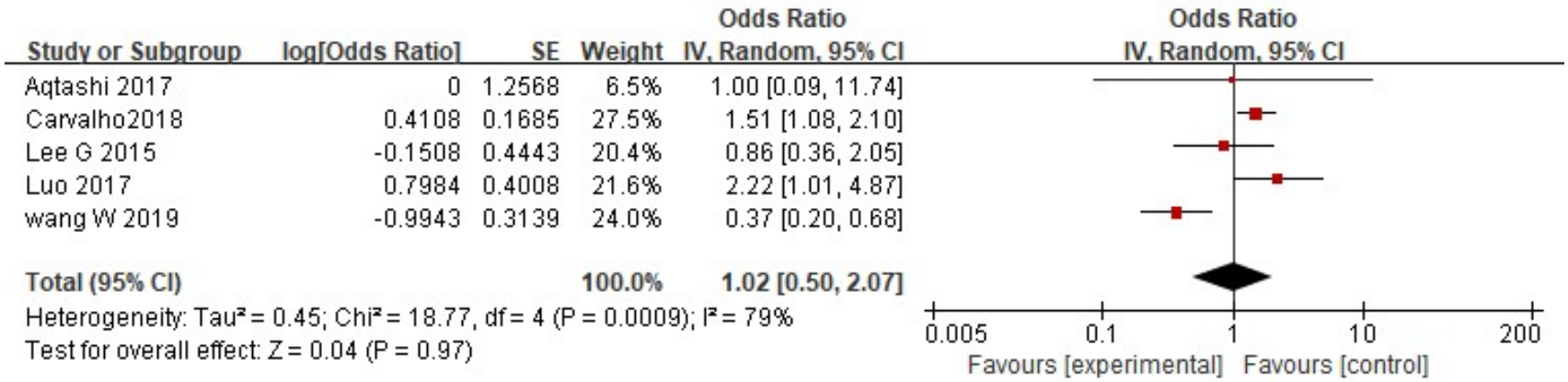


Multinodular goitre Figure 12

Thyroiditis Figure 13



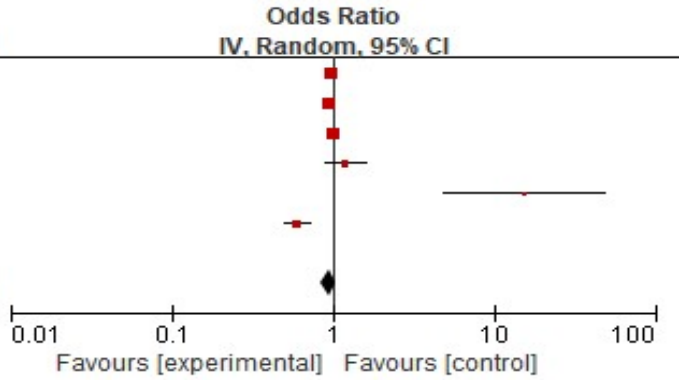
Preoperative calcium level Figure 14



Preoperative PTH Figure 15

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aqtashi 2017	-0.0212	0.0384	23.3%	0.98 [0.91, 1.06]
Bhandari 2017	-0.0661	0.0234	24.9%	0.94 [0.89, 0.98]
Lee G 2015	0.01	0.0102	25.7%	1.01 [0.99, 1.03]
Luo 2017	0.1773	0.1459	9.7%	1.19 [0.90, 1.59]
Servicio 2013	2.7344	0.5916	0.9%	15.40 [4.83, 49.10]
Talal 2014	-0.5108	0.093	15.5%	0.60 [0.50, 0.72]
Total (95% CI)			**100.0%**	**0.95 [0.85, 1.06]**

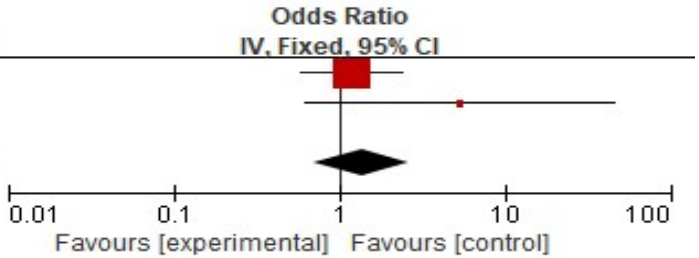
Heterogeneity: Tau² = 0.01; Chi² = 61.71, df = 5 (P < 0.00001); I² = 92%
Test for overall effect: Z = 0.97 (P = 0.33)



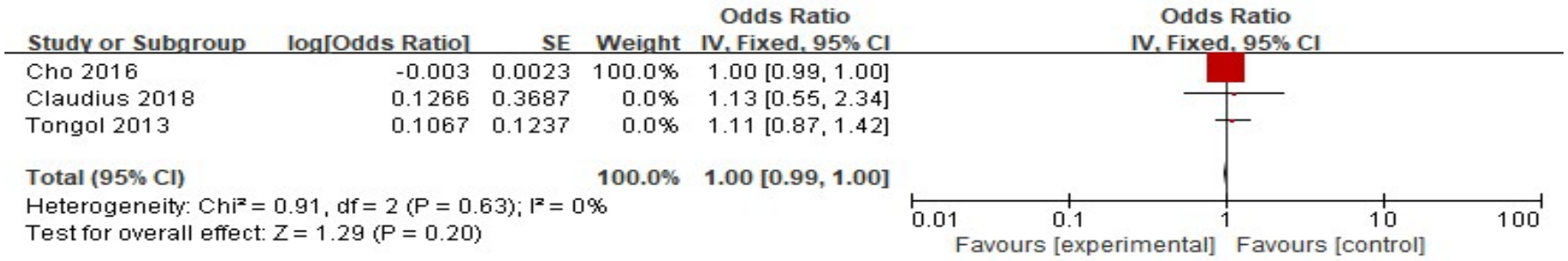
Graves diseases Figure 16

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Lin2016	0.1697	0.3558	90.4%	1.18 [0.59, 2.38]
Pavol 2014	1.6771	1.0914	9.6%	5.35 [0.63, 45.43]
Total (95% CI)			**100.0%**	**1.37 [0.71, 2.66]**

Heterogeneity: Chi² = 1.72, df = 1 (P = 0.19); I² = 42%
Test for overall effect: Z = 0.93 (P = 0.35)

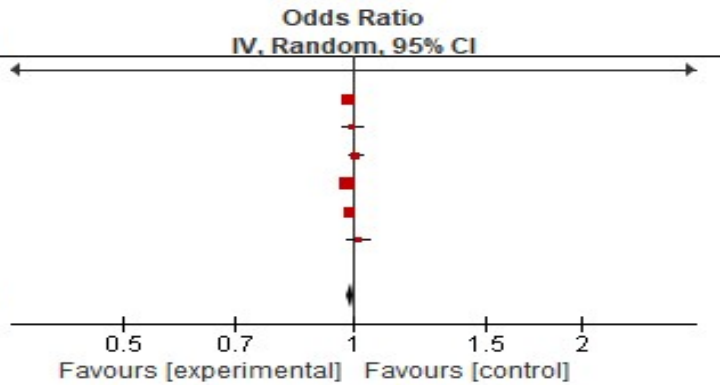


Surgery time Figure 17



Age Figure 18

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Carvalho 2018	-5.5215	4.2584	0.0%	0.00 [0.00, 16.86]
Cho 2016	-0.0121	0.0068	22.7%	0.99 [0.97, 1.00]
Lee G 2015	0	0.0155	7.0%	1.00 [0.97, 1.03]
Lin2016	0.01	0.01	14.0%	1.01 [0.99, 1.03]
Pavol 2014	-0.0141	0.0052	29.0%	0.99 [0.98, 1.00]
Randall 2012	-0.0101	0.007	22.0%	0.99 [0.98, 1.00]
Tongol 2013	0.0177	0.0183	5.3%	1.02 [0.98, 1.06]
Total (95% CI)			**100.0%**	**0.99 [0.98, 1.00]**

Heterogeneity: Tau² = 0.00; Chi² = 8.94, df = 6 (P = 0.18); I² = 33%

Test for overall effect: Z = 1.51 (P = 0.13)