

Supplementary Material:

	Randomization Domain					Overall
	D1	D2	D3	D4	D5	
Iseri et al. 2019	+	+	+	+	+	+

Domains:

D1: Randomization Process

D2: Deviations from the intended intervention

D3: Missing Outcome Data

D4: Measurement of the Outcome

D5: Selection of the reported result

Judgement:

⊕ Low risk

⊕ Some concerns

⊕ High Risk

Supplementary Figure 1 Risk of bias in RCTs.

Study ID	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Chen et al 2014	⊕	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Chen et al 2015	⊕	⊕	⊕	⊕	⊕	⊕	⊕	⊕

Domains:

D1: Bias due to confounding

D2: Bias due to selection of participants

D3: Bias in classification of interventions

D4: Bias due to deviation from intended interventions

D5: Bias due to missing data

D6: Bias in measurement of outcomes

D7: Bias in selection of reported results

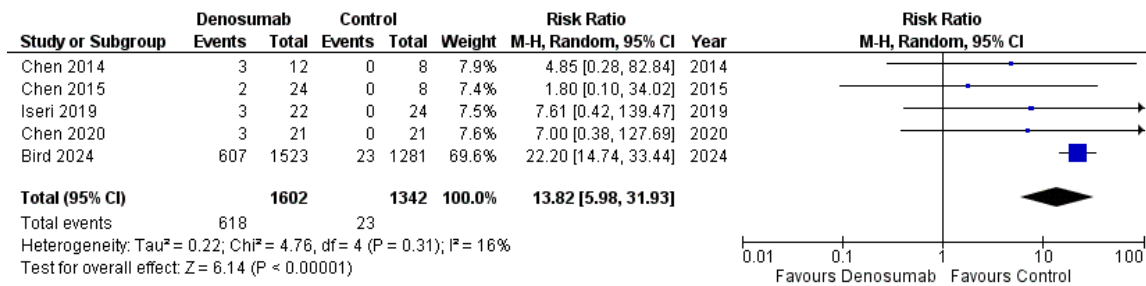
Judgement:

⊕ Low risk

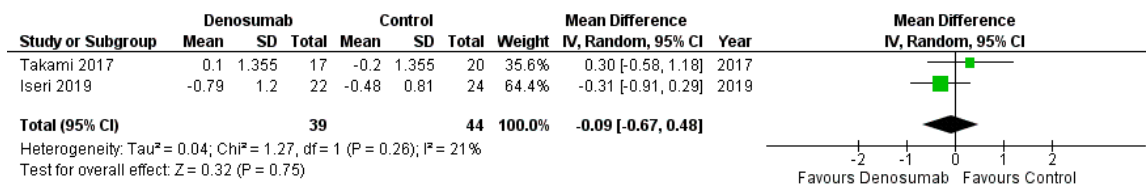
⊕ Some concerns

⊕ High Risk

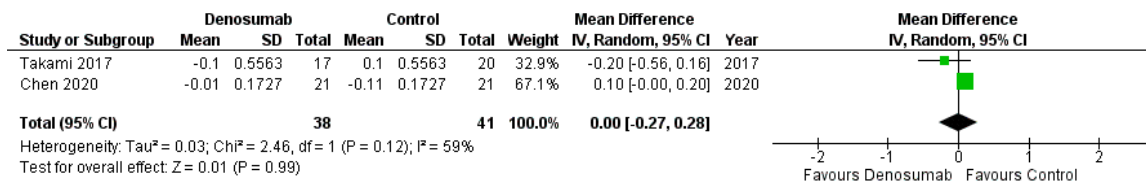
Supplementary Figure 2 Risk of bias in non-randomized open label trials.



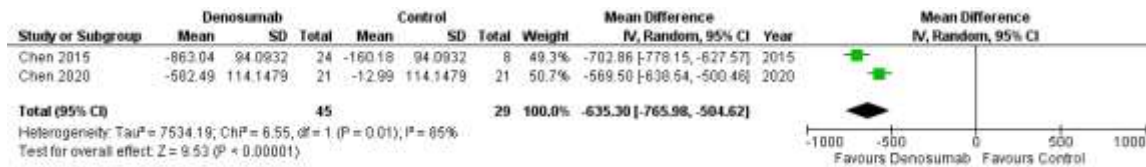
Supplementary Figure 3 Sensitivity analysis forest plot of severe hypocalcemia outcome.



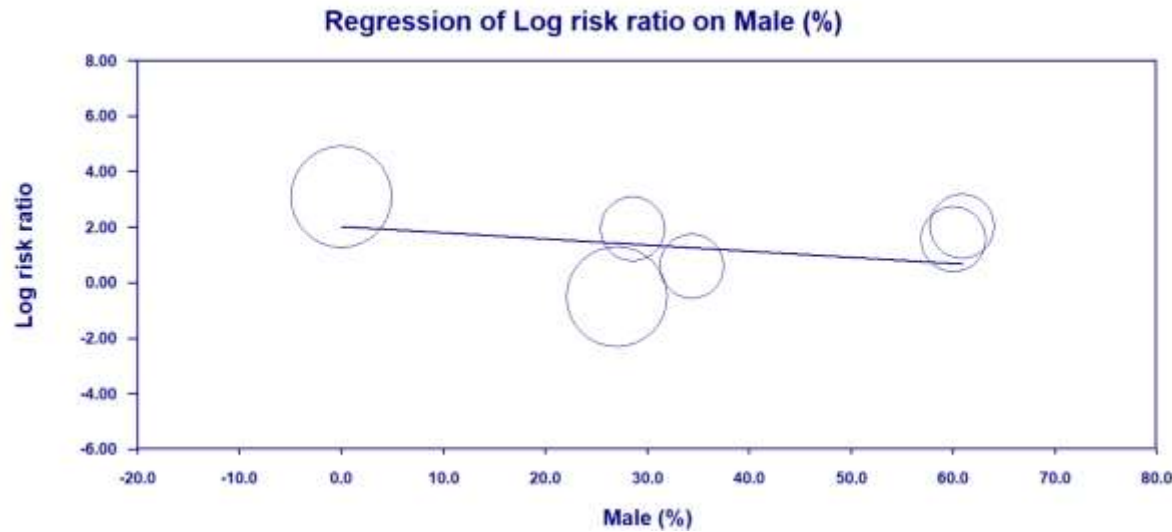
Supplementary Figure 4 Sensitivity analysis forest plot of change in serum phosphate



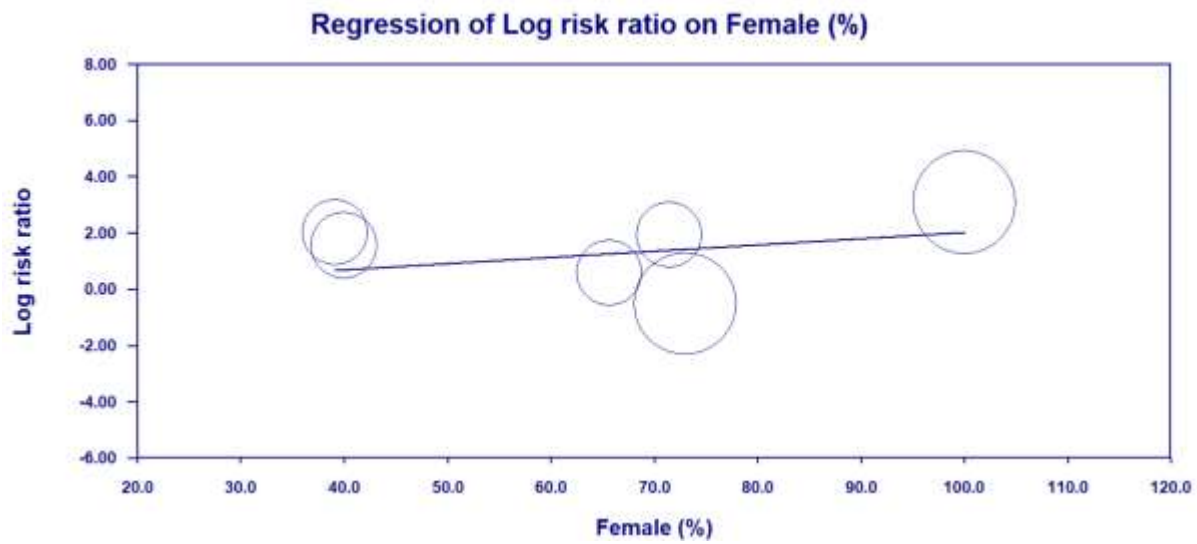
Supplementary Figure 5 Sensitivity analysis forest plot of change in serum calcium



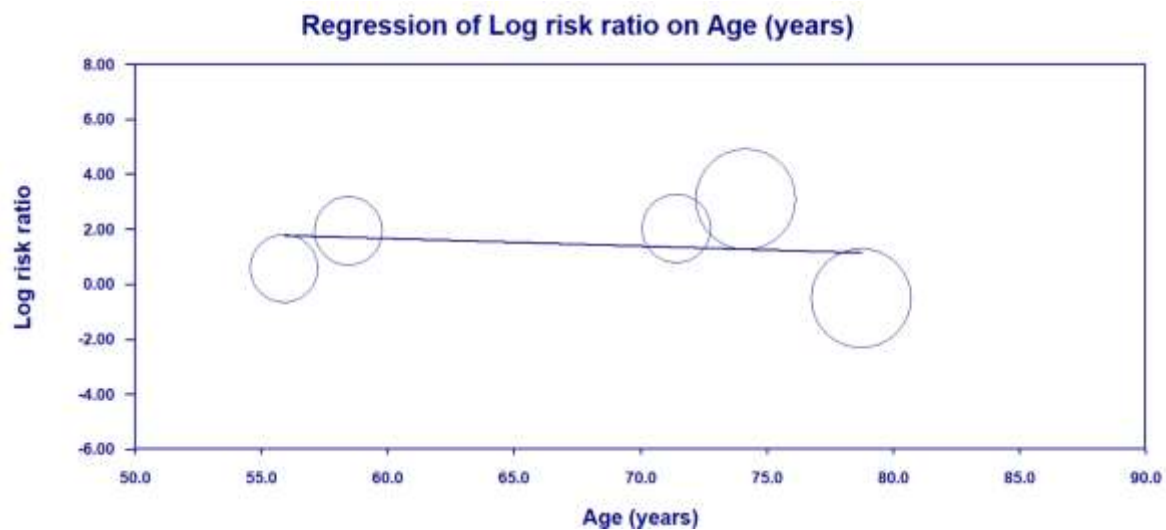
Supplementary Figure 6 Sensitivity analysis forest plot of change in serum iPTH



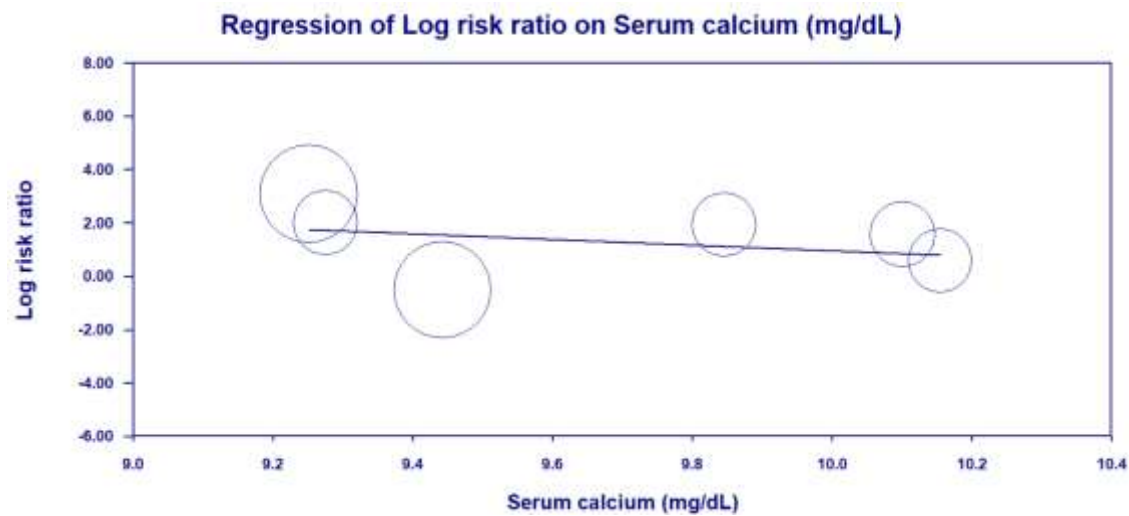
Supplementary Figure 7 Meta-regression on male (%) for severe hypocalcemia.



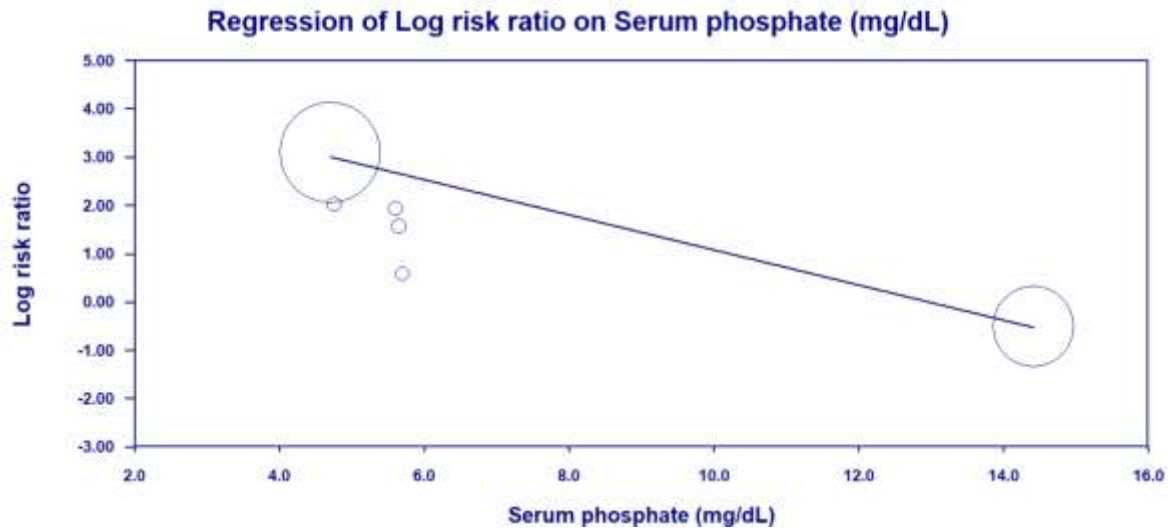
Supplementary Figure 8 Meta-regression on female (%) for severe hypocalcemia.



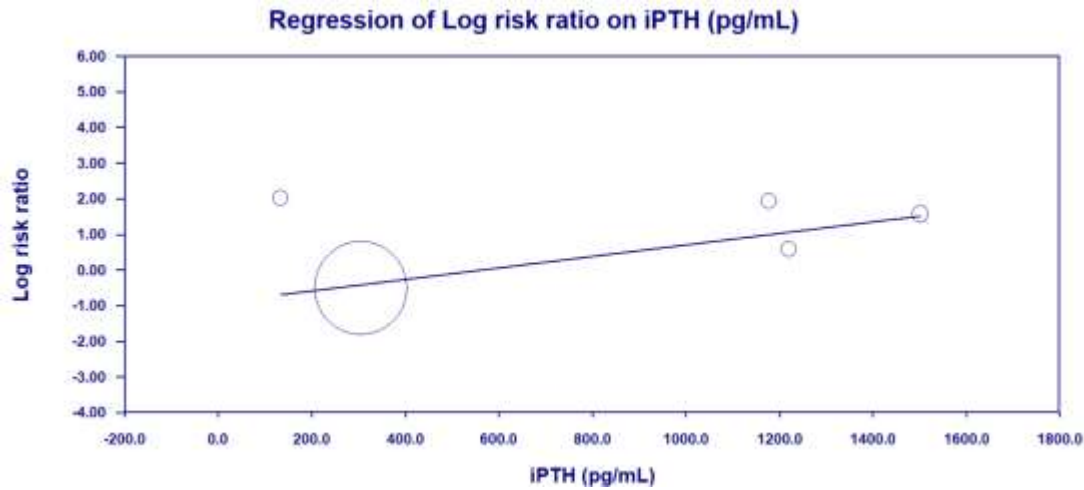
Supplementary Figure 9 Meta-regression on age (years) for severe hypocalcemia.



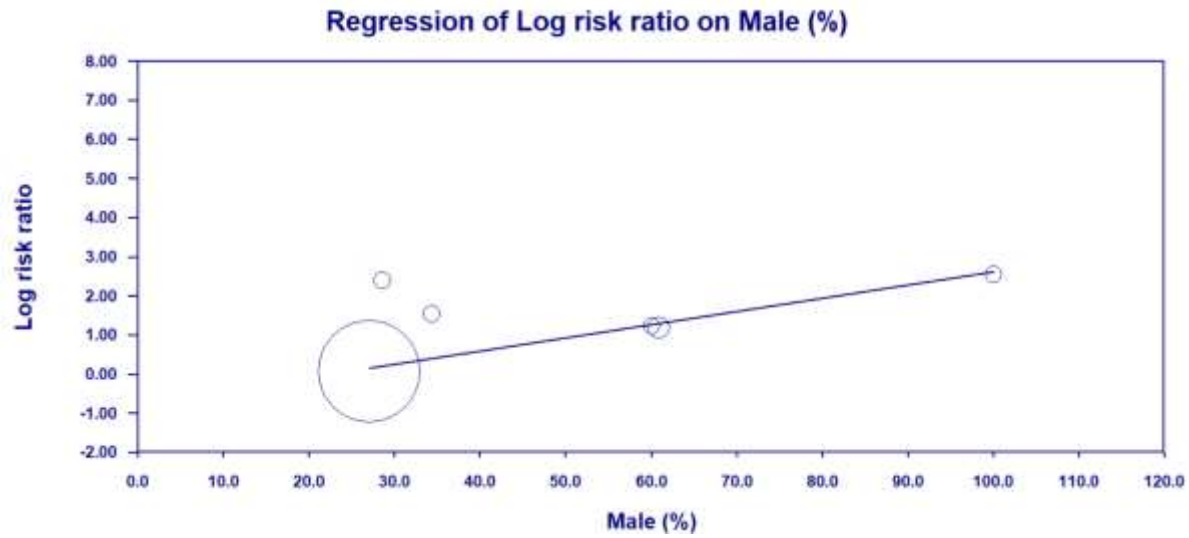
Supplementary Figure 10 Meta-regression on serum calcium (mg/dL) for severe hypocalcemia.



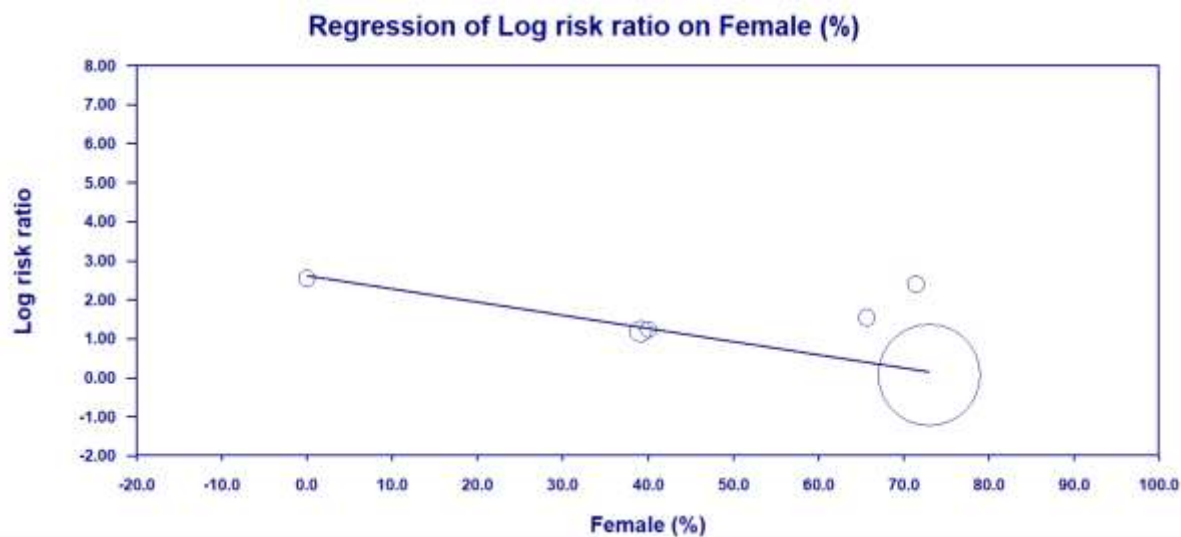
Supplementary Figure 11 Meta-regression on serum phosphate (mg/dL) for severe hypocalcemia.



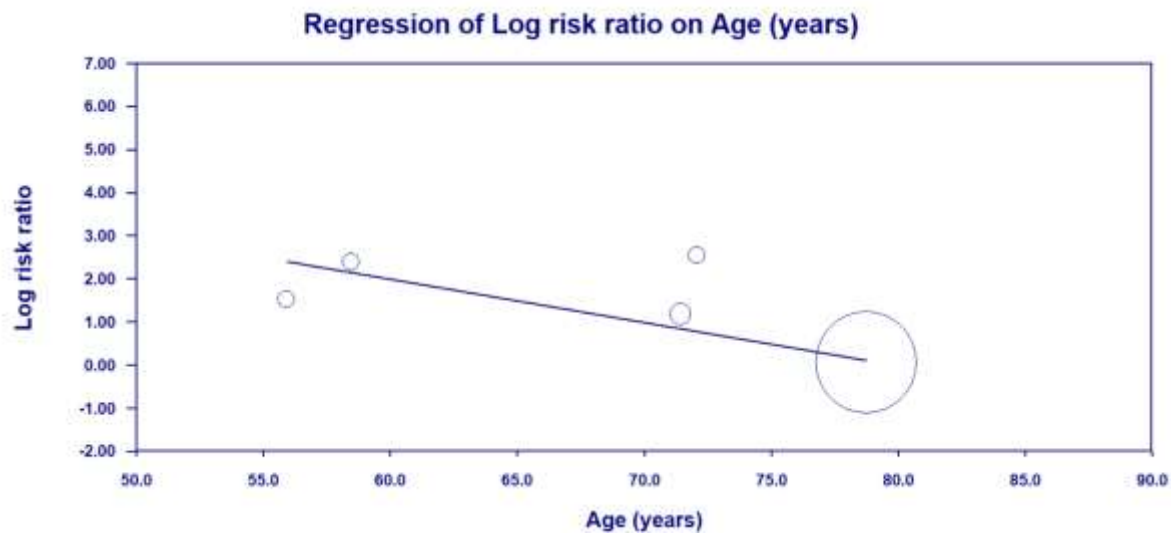
Supplementary Figure 12 Meta-regression on iPTH (pg/dL) for severe hypocalcemia.



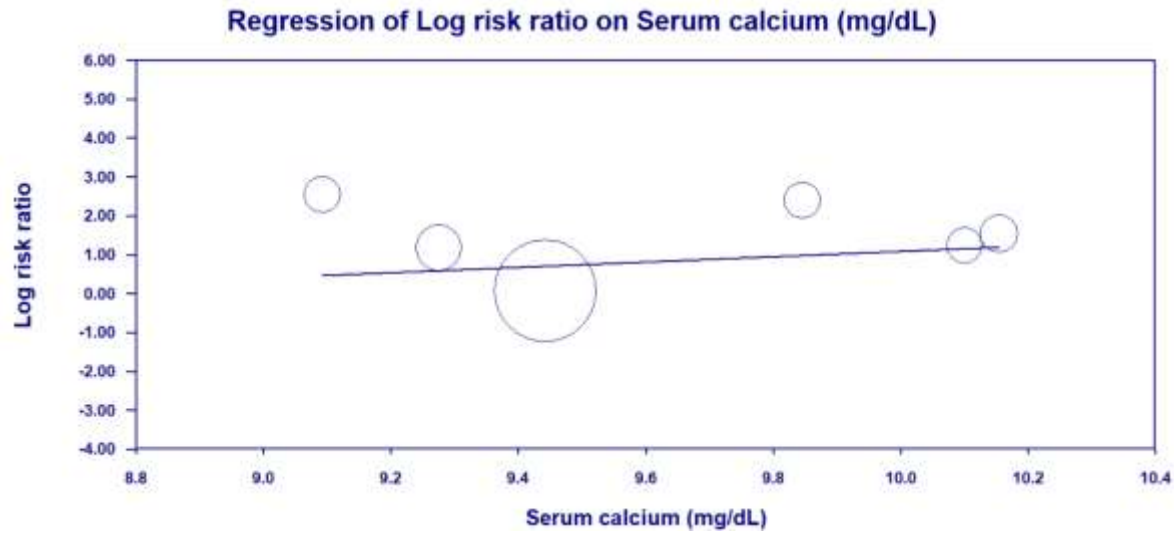
Supplementary Figure 13 Meta-regression on male (%) for mild hypocalcemia.



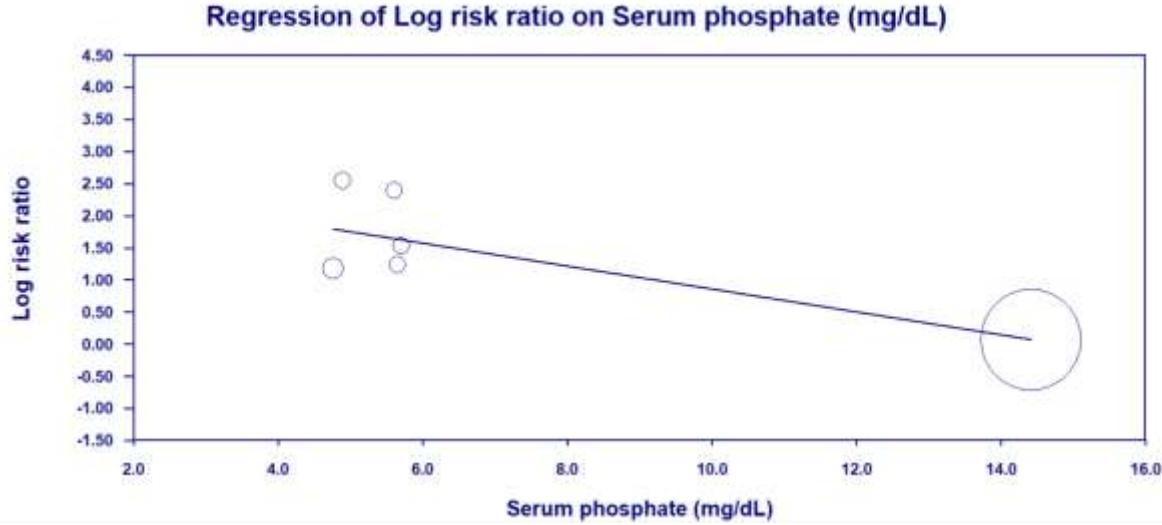
Supplementary Figure 14 Meta-regression on female (%) for mild hypocalcemia.



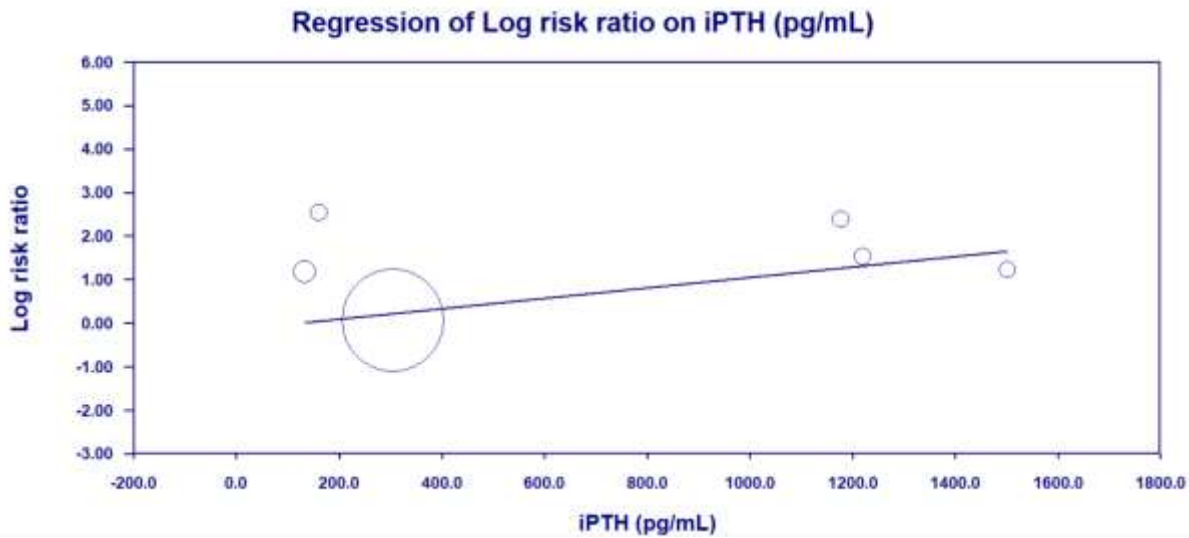
Supplementary Figure 15 Meta-regression on age (years) for mild hypocalcemia.



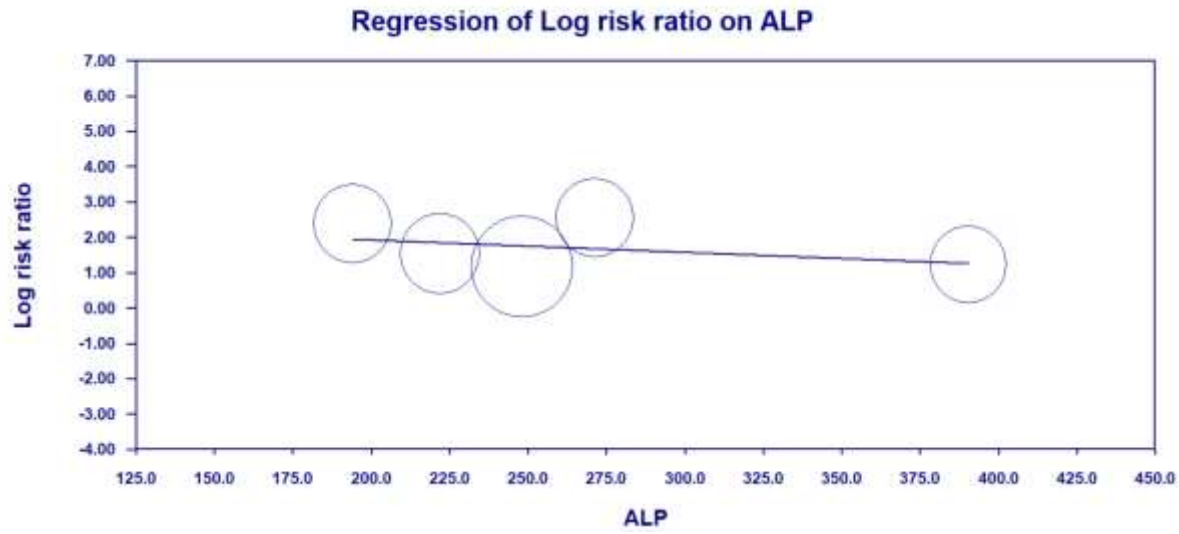
Supplementary Figure 16 Meta-regression on serum calcium (mg/dL) for mild hypocalcemia.



Supplementary Figure 17 Meta-regression on serum phosphate (mg/dL) for mild hypocalcemia.



Supplementary Figure 18 Meta-regression on iPTH (pg/dL) for mild hypocalcemia.



Supplementary Figure 19 Meta-regression on ALP (IU/L) for mild hypocalcemia.

Supplementary Table 1 Detailed search strategy

Database	Search terms
Scopus (<i>n</i> = 53)	(Denosumab) AND (hypocalcemia) AND (dialysis OR "end stage renal disease")
PubMed (<i>n</i> = 44)	("denosumab"[MeSH Terms] OR "denosumab"[All Fields] OR "denosumab s"[All Fields]) AND ("hypocalcaemia"[All Fields] OR "hypocalcemia"[MeSH Terms] OR "hypocalcemia"[All Fields] OR "hypocalcemias"[All Fields]) AND ("dialysance"[All Fields] OR "dialysances"[All Fields] OR "dialysation"[All Fields] OR "dialysator"[All Fields] OR "dialysators"[All Fields] OR "dialyse"[All Fields] OR "dialysed"[All Fields] OR "dialyser"[All Fields] OR "dialysers"[All Fields] OR "dialysing"[All Fields] OR "dialysis solutions"[Pharmacological Action] OR "dialysis solutions"[MeSH Terms] OR ("dialysis"[All Fields] AND "solutions"[All Fields]) OR "dialysis solutions"[All Fields] OR "dialysate"[All Fields] OR "dialysates"[All Fields] OR "dialyzate"[All Fields] OR "dialyzates"[All Fields] OR "dialysis"[MeSH Terms] OR "dialysis"[All Fields] OR "dialyses"[All Fields] OR "dialyzability"[All Fields] OR "dialyzable"[All Fields] OR "dialyzation"[All Fields] OR "dialyze"[All Fields] OR "dialyzed"[All Fields] OR "dialyzer"[All Fields] OR "dialyzer s"[All Fields] OR "dialyzers"[All Fields] OR "dialyzing"[All Fields] OR "renal dialysis"[MeSH Terms] OR ("renal"[All

	Fields] AND "dialysis"[All Fields]) OR "renal dialysis"[All Fields] OR ("kidney failure, chronic"[MeSH Terms] OR ("kidney"[All Fields] AND "failure"[All Fields] AND "chronic"[All Fields]) OR "chronic kidney failure"[All Fields] OR ("end"[All Fields] AND "stage"[All Fields] AND "renal"[All Fields] AND "disease"[All Fields]) OR "end stage renal disease"[All Fields]))
Cochrane Library (<i>n</i> = 7)	(Denosumab) AND (hypocalcemia) AND (dialysis OR end stage renal disease OR ESRD)
Embase (<i>n</i> = 98)	(Denosumab) AND (hypocalcemia) AND (dialysis OR end stage renal disease OR ESRD)

Supplementary Table 2 Risk of bias in cohort studies

	Selection				Comparability	Outcome			
Ref.	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome was not PRESENT at start of study	Comparability of groups on the basis of analysis	Assessment of outcome	Was follow up long enough for outcomes to occur?	Adequacy of follow up of cohorts	Total score
Bird <i>et al</i> , 2024	1	1	1	1	1	1	1	1	8
Cowan <i>et al</i> , 2023	1	1	1	1	1	1	1	1	8

Supplementary Table 3 Risk of bias in case control studies

	e clearly stated?	a case definition?				implemented consistently across all study participants?				and poor)
	Y	Y	Y	Y	Y	Y	Y	Y	Y	GOOD

Supplementary Table 5: Meta regression values for severe hypocalcemia

Baseline Characteristics for Severe Hypocalcemia	Coefficient	<i>P</i> value
Male (%)	-0.0222	0.4559
Female (%)	0.0222	0.4559
Age (years)	-0.0266	0.7615
Serum calcium (mg/dL)	-1.0425	0.5827
Serum phosphate (mg/dL)	-0.3634	0.0000
iPTH (pg/mL)	0.0016	0.0654

Supplementary Table 6 Meta regression values for mild hypocalcemia

Baseline Characteristics for Mild Hypocalcemia	Coefficient	P value
Male (%)	0.0336	0.0421
Female (%)	-0.0336	0.0421
Age (years)	-0.1003	0.0290
Serum calcium (mg/dL)	0.6697	0.6365
Serum phosphate (mg/dL)	-0.1784	0.0124
iPTH (pg/mL)	0.0012	0.1560
ALP (IU/L)	-0.0034	0.7229