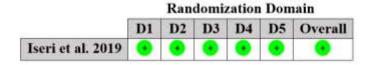
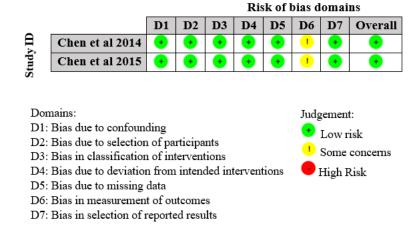
Supplementary Material:



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

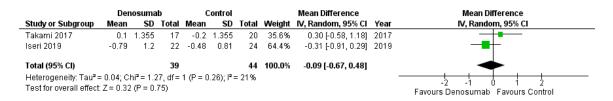
Supplementary Figure 1 Risk of bias in RCTs.



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

	Denosu	mab	Conti	rol		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Chen 2014	3	12	0	8	7.9%	4.85 [0.28, 82.84]	2014	1 -
Chen 2015	2	24	0	8	7.4%	1.80 [0.10, 34.02]	2015	5
Iseri 2019	3	22	0	24	7.5%	7.61 [0.42, 139.47]	2019	
Chen 2020	3	21	0	21	7.6%	7.00 [0.38, 127.69]	2020) -
Bird 2024	607	1523	23	1281	69.6%	22.20 [14.74, 33.44]	2024	·
Total (95% CI)		1602		1342	100.0%	13.82 [5.98, 31.93]		•
Total events	618		23					
Heterogeneity: Tau ² =	= 0.22; Chi	² = 4.76	df = 4 (F)	P = 0.31); I ^z = 169	%		
Test for overall effect	: Z= 6.14 (P < 0.00	0001)					0.01 0.1 1 10 100 Favours Denosumab Favours Control

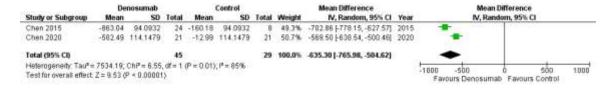
Supplementary Figure 3 Sensitivity analysis forest plot of severe hypocalcemia outcome.



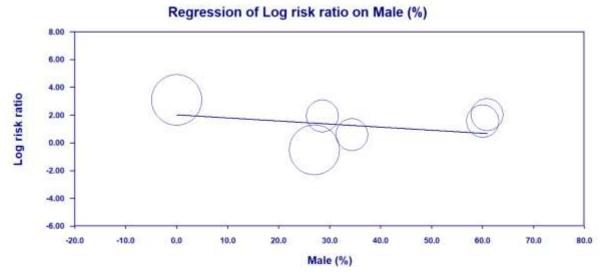
Supplementary Figure 4 Sensitivity analysis forest plot of change in serum phosphate

	De	nosumal)		Control			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Takami 2017	-0.1	0.5563	17	0.1	0.5563	20	32.9%	-0.20 [-0.56, 0.16]	2017	
Chen 2020	-0.01	0.1727	21	-0.11	0.1727	21	67.1%	0.10 [-0.00, 0.20]	2020	•
Total (95% CI)			38			41	100.0%	0.00 [-0.27, 0.28]		+
Heterogeneity: Tau ² :				(P = 0.1)	12); I² = 5	9%				-5 -1 1 1 2
Test for overall effect	: Z = 0.01	(P = 0.9	9)							Favours Denosumab Favours Control

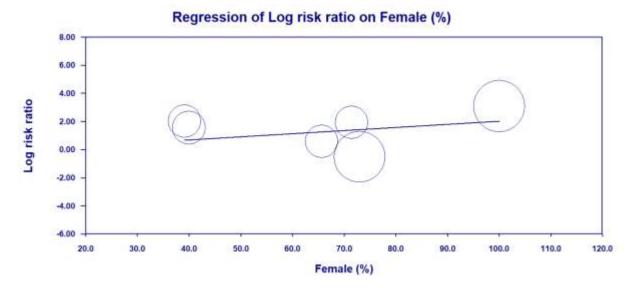
Supplementary Figure 5 Sensitivity analysis forest plot of change in serum calcium



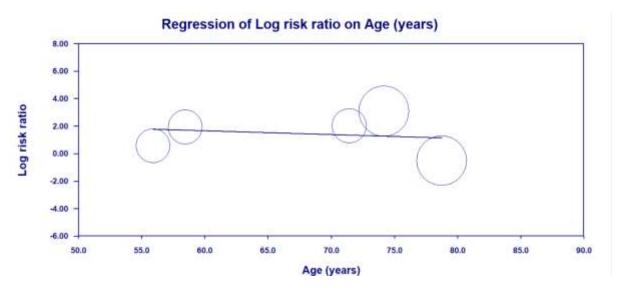
Supplementary Figure 6 Sensitivity analysis forest plot of change in serum iPTH



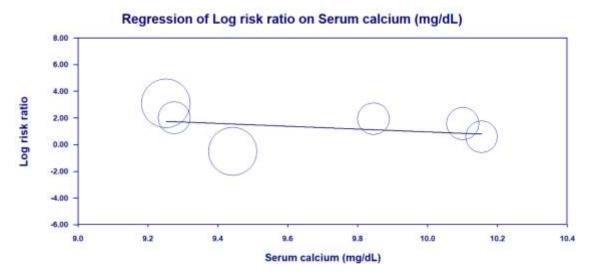
Supplementary Figure 7 Meta-regression on male (%) for severe hypocalcemia.



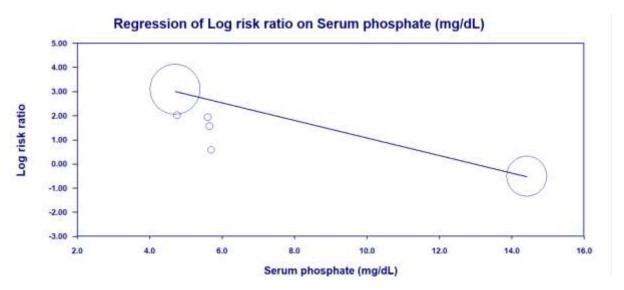
Supplementary Figure 8 Meta-regression on female (%) for severe hypocalcemia.



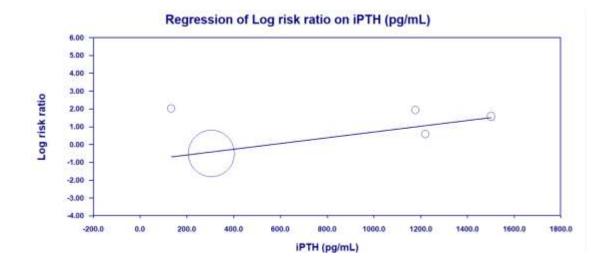
Supplementary Figure 9 Meta-regression on age (years) for severe hypocalcemia.



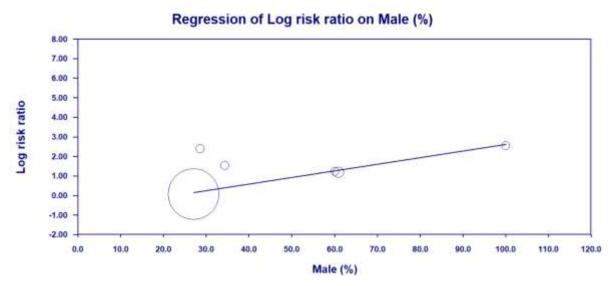
Supplementary Figure 10 Meta-regression on serum calcium (mg/dL) for severe hypocalcemia.



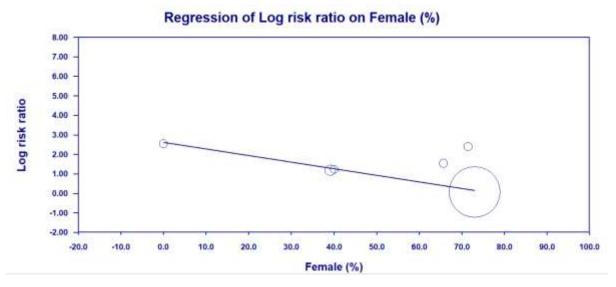
Supplementary Figure 11 Meta-regression on serum phosphate (mg/dL) for severe hypocalcemia.



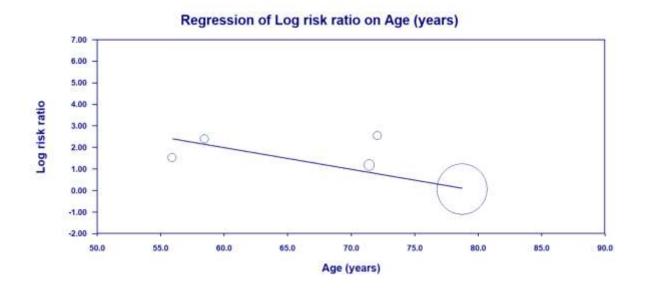
Supplementary Figure 12 Meta-regression on iPTH (pg/dL) for severe hypocalcemia.



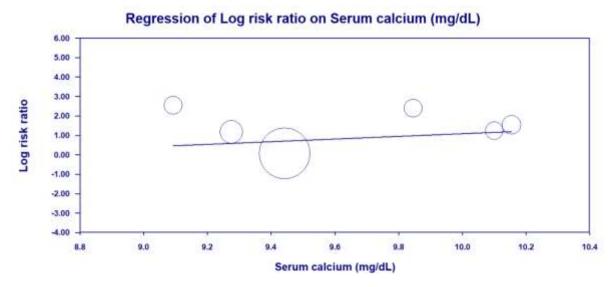
Supplementary Figure 13 Meta-regression on male (%) for mild hypocalcemia.



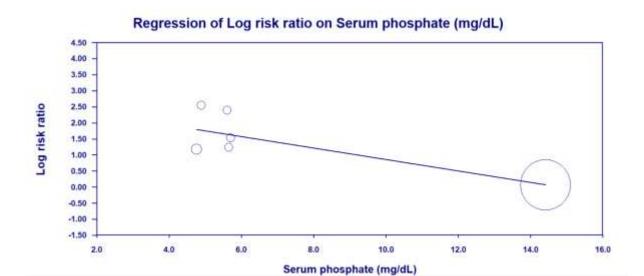
Supplementary Figure 14 Meta-regression on female (%) for mild hypocalcemia.



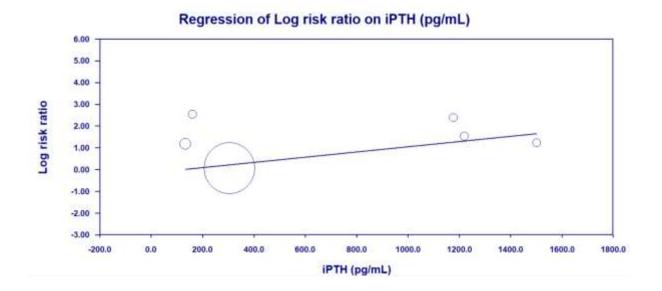
Supplementary Figure 15 Meta-regression on age (years) for mild hypocalcemia.



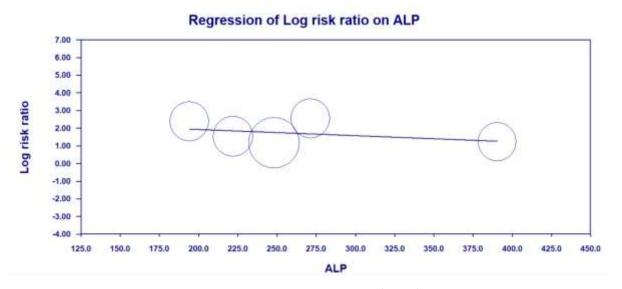
Supplementary Figure 16 Meta-regression on serum calcium (mg/dL) for mild hypocalcemia.



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 $(n = 98)$	(Denosumab) AND (hypocalcemia) AND (dialysis OR end stage renal
	disease OR ESRD)

Supplementary Table 2 Risk of bias in cohort studies

	Selection				Comparabili	Outcome			
					ty				
Ref.	Representative	Selecti	Ascertainm	Demonstrati	Comparabili	Assessme	Was	Adequa	Tot
	ness of the	on of	ent of	on that	ty of groups	nt of	follow	cy of	al
	exposed cohort	non-	exposure	outcome	on the basis	outcome	up long	follow	scor
		expose		was not	of analysis		enough	up of	e
		d		PRESENT at			for	cohorts	
		cohort		start of			outcom		
				study			es to		
							occur?		
Bird	1	1	1	1	1	1	1	1	8
et al,									
2024									
Cowa	1	1	1	1	1	1	1	1	8
n et al,									
2023									

Supplementary Table 3 Risk of bias in case control studies

	Selection				Comparabilit	Exposure				
					у	y				
Autho	Is the	Representativen	Selectio	Definitio	Comparabilit	Ascertainme	Same	Non-	Tota	
r, year	case	ess of the cases	n of	n of	y of cases and	nt of	method of	respons	1	
	definitio		Control	Controls	controls on	exposure	ascertainme	e rate	scor	
	n		s		the basis of		nt of cases		e	
	adequat				design or		and controls			
	e				analysis					
Takam	1	1	1	1	2	1	1	1	8	
i et al.										
2017										

Supplementary Table 4 Risk of bias in case series

	1. Was	2. Was the	3. Were the	4. Were the	5. Was the	6. Were the	7. Was	8. Were	9. Were	10.
	the	study	cases	subjects	interventio	outcome	the	the	the results	Qualit
Stud	study	populatio	consecutive	comparable	n clearly	measures	length of	statistical	well	y
Stud	questio	n clearly	?	?	described?	clearly	follow-	methods	described	rating
y	n or	and fully				defined,	up	well	?	(good,
	objectiv	described,				valid,	adequate	described		fair,
		including				reliable, and	?	?		

e clearly	a case				implemente				and
stated?	definition				d				poor)
	?				consistently				
					across all				
					study				
					participants?				
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	P 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