Supplemental Table of Contents

Table S1 – Inclusion and Exclusion Criteria for the Systematic Review

Question Component	Inclusion Criteria	Exclusion Criteria
Population	• Adult patients (> 18 years) • Renal transplant (deceased or living donor kidney transplantation) • Outcome data available > 1 year post-renal transplantation	• Patients with other organ transplants, including kidney-pancreas transplantation
Intervention	• Use of any bisphosphonate (oral or IV) post-renal transplant, alone or in combination with other agents (calcium, vitamin D, etc.)	
Outcomes	Primary: • Change in BMD from baseline Secondary: • Fracture incidence • Other confounding variables (i.e. immunosuppression, BMI, smoking)	• Trials that did not provide information either on BMD or fracture incidence
Study Design	• Randomized trials • Observational studies (cohort, case-control)	• Case series • Case reports • Review articles (systematic, meta-analysis, descriptive)

Figure S1 – Sample Search Strategy – Ovid MEDLINE 2016

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

#	Searches	Results	Type
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Figure S2 – Bias Assessment for Randomized Control Trials using the Cochrane Risk of Bias Tool Criteria [27]

	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias
	Random Sequence Generation	Allocation Concealment	Participants and Personnel Blinding	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Sánchez-Escuredo, 2015	-	-	-	-	+	+	-
Okamoto, 2014	-	-	-	-	+	+	-
Walsh, 2009	+	+	+	+	+	+	?
Lan, 2008	-	-	-	-	?	-	-
Schwarz, 2004	-	-	+	+	+	+	-
Fan, 2003	-	-	-	-	+	+	?
Jeffery, 2003	?	?	-	-	+	?	-
Koc, 2002	-	-	-	-	+	?	-

Table S2 – Cochrane Risk of Bias Table for RCTs [27]

Cochrane Risk of Bias Tool Criteria								
	Selection Bias		**Performance Bias**	**Detection Bias**	**Attrition Bias**	**Reporting Bias**	**Other Bias**	**Total**
Study	*Random Sequence Generation*	*Allocation Concealment*	*Blinding of Participants & Personnel*	*Blinding of Outcome Assessment*	*Incomplete Outcome Data*	*Selective Reporting*	*Other Sources of Bias*	
Sánchez-Escuredo, et al. 2015	0	0	0	0	2	2	0	4
Okamoto, et al. 2014	0	0	0	0	2	2	0	4
Walsh, et al. 2009	2	2	2	2	2	2	1	13
Lan, et al. 2008	0	0	0	0	1	0	0	1
Schwartz, et al. 2004	0	0	2	2	2	2	0	8
Fan, et al. 2003	0	0	0	0	2	2	1	5
Jeffrey, et al. 2003	1	1	0	0	2	1	0	5
Koc, et al. 2002	0	0	0	0	2	1	0	3

0 = high risk
1 = unclear

2 = low risk

Figure S3 – Risk of Bias Graph for Observational Studies using the Newcastle-Ottawa Criteria [28]

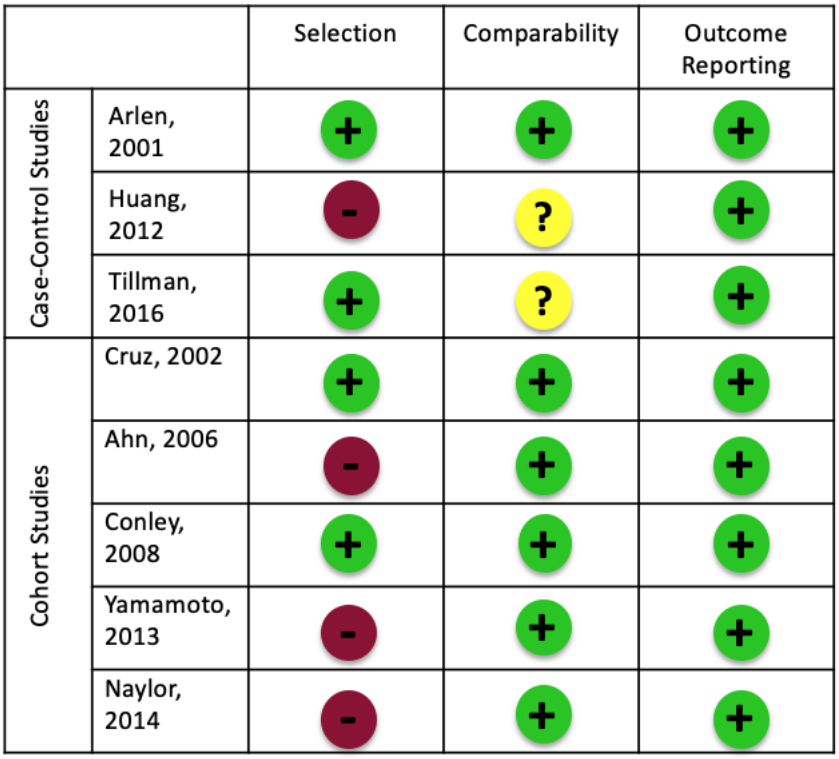

Table S3 – Newcastle-Ottawa **Risk of Bias Table for Observational Studies**

Newcastle-Ottawa Criteria Case-Control Studies				
	Selection (/1)	**Comparability of Cohorts (/2)**	**Outcome (/1)**	**TOTAL SCORE (/4)**
Study	• Cases and controls clearly defined • Representativeness of sample	• Demographic characteristics • Potential confounding factors	• Ascertainment of exposure • Non-response rate	
Arlen, 2001	1	2	1	4
Huang, 2012	0	1	1	2
Tillman, 2016	1	1	1	3

Newcastle-Ottawa Criteria Cohort Studies				
	Selection (/1)	**Comparability of Cohorts (/2)**	**Outcome (/1)**	**TOTAL SCORE (/4)**
Study	• Ascertainment of exposure • Representativeness of exposed and unexposed cohorts • Outcome not present at study start	• Demographic characteristics • Potential confounding factors	• Assessment method • Blinding • Follow-up length • Losses to follow-up accounted for	
Cruz, 2002	1	2	1	4
Ahn, 2006	0	2	1	3
Conley, 2008	1	2	1	4
Yamamoto, 2013	0	2	1	3
Naylor, 2014	0	2	1	3

Figure S4 – Funnel Plot of Reported Outcomes

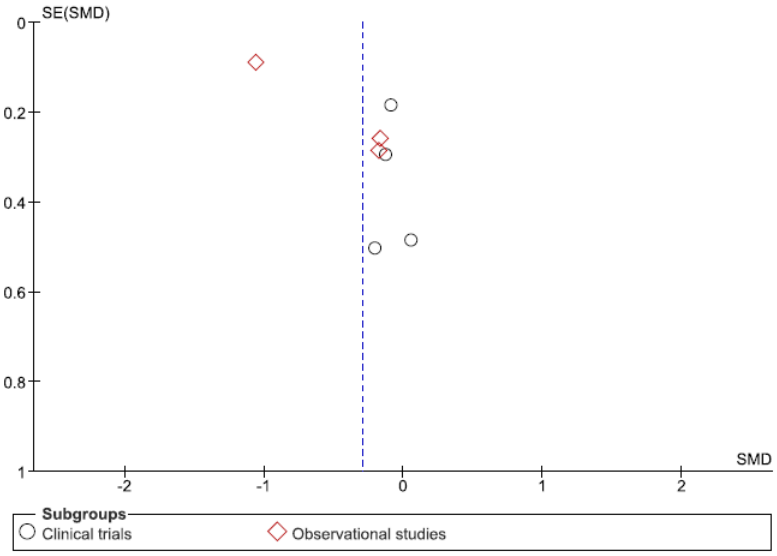

Table S3 - Confounding Factors Affecting Bone Mineral Density in Post Renal Transplant Patients Between Bisphosphonate And Control Groups

Steroid Use	**Description**	**Findings**
Jeffery, et al. (2003) [37]	From baseline (n=211): • Cumulative prednisone dose = 43.0±35.8g	• Prednisone correlated with decreased BMD at femur (univariate, $p<0.001$) • Prednisone was an independent predictor of low BMD (multivariate, $p<0.01$)
Ahn, et al. (2006) [44]	Mean change in T-score (spine) over first year post-transplant: • Double IS regimen (CsA, tacrolimus, steroid)-0.57±0.70 ($p = 0.26$) • Triple IS regimen (CsA, tacrolimus, steroid and mycophenolate mofetil): -0.46±0.66 ($p = 0.26$)	No significant difference in change in BMD over first year post-transplant based on IS regimens including steroid
Huang, et al. (2012) [42]	Patients stratified based on baseline bone health into 3 groups: normal/osteopenic/osteoporotic. The osteoporotic group was treated with Fosamax • Osteoporotic group received a greater cumulative steroid dose than the osteopenic group (1326.5 mg vs. 724.5 mg; $p<0.01$)	Increase in lumbar spine BMD greater in the osteoporotic group than osteopenic group (0.033 g/cm^2 vs. 0.009 g/cm^2; $p<0.05$)
	To detect a difference in BMD at follow-up due to the use of IS agents, patients were divided into osteoporotic vs. non-osteoporotic based on their 1st follow-up BMD results. • Cumulative dose of prednisolone in non-osteoporotic/osteoporotic: 872±730mg/ 1326.5±961mg ($p<0.01$)	Prednisolone showed a positive association in patients with osteoporosis at follow-up BMD (univariate, OR 5.18; 95% CI 1.6–16.4, $p<0.01$)
Naylor, et al. (2014) [40]	β for glucocorticoid exposure in predictors of BMD model: between no previous osteoporosis/previous osteoporosis groups: • L-spine: -0.008 ($p=0.22$)/-0.001 ($p=0.82$) • Total hip: -0.010 ($p=0.08$)/0.005 ($p=0.28$) • Femoral neck: -0.004 ($p=0.56$)/0.010 ($p=0.09$)	Greater glucocorticoid exposure was not associated with significant change in BMD, regardless of prior osteoporosis treatment status ($p>0.05$)
Cyclosporine Use	**Description**	**Findings**
Ahn, et al. (2006) [44]	Mean change in T-score spine over first year post-transplant: (Cyclosporine /tacrolimus) -0.51±0.64/-0.41±0.76 ($p=0.24$)	No significant difference in change in BMD over first year post-transplant based on cyclosporine use
Huang, et al. (2012) [42]	Cyclosporine use (in 100 mg tablets) between osteoporotic and osteopenic groups 119.20±210.85/ 131.12±177.79 ($p>0.05$)	No significant difference in change in BMD between osteoporotic and osteopenic groups based on cyclosporine use at 1 year follow-up.
Gender	**Description**	**Findings**
Jeffery, et al. (2003) [37]	From baseline (n=211): (Male/female = 149/62)	Female gender correlated with decreased overall BMD (univariate, $p<0.05$)
Ahn, et al. (2006) [44]	Mean change in T-score spine over first year post-transplant: • Male/female: -0.49±0.67/-0.47±0.66 ($p=0.83$)	Mean femoral T-score lower among female recipients ($p<0.001$). However gender did not influence change in BMD

		overall in first year post-transplant (p=0.83)
Tillmann, et al. (2016) [39]	Control: • Males: LS: 4.5±7.8 %; FN: 1.7±10.7% • Females: LS: 5.3±8.2%; FN: 5.8±14.7% Mann-Whitney U: LS: p = 0.94; FN: p = 0.56	No gender-specific effect on BMD (p>0.05)
	Ibandronate: • Males: LS: 7.2±6.8%; FN: 3.0±9.8% • Females: LS: 5.8±8.9%; FN: 6.4±15.1% Mann-Whitney U: LS: p = 0.60; FN: p = 0.70	No gender-specific effects on BMD (p>0.05)
Huang, et al. (2012) [42]	Overall BMD difference values were not different (p>0.05)	No significant gender-related differences in bone turnover during 14-month period of mean follow-up (p>0.05).
	Fosamax increased the BMD at the lumbar spine and the hip in males (p<0.05), but only at the lumbar spine in females (p<0.05).	Sites of action of Fosamax differ between genders
Naylor, et al. (2014) [40]	β for male gender in predictors of BMD model: between no previous osteoporosis/previous osteoporosis groups: • L-spine: 0.003 (p=0.46)/0.008 (p<0.01)* • Total hip: 0.002 (p=0.53)/0.002 (p=0.38) • Femoral neck: 0.005 (p=0.08)/-0.002 (p=0.55)	No overall clinically significant gender-related differences in BMD
BMI (kg/m^2)	**Description**	**Findings**
Jeffery, et al. (2003) [37]	Raw baseline data from patients not provided	Low body weight (p<0.001) and low BMI (p<0.01) correlated with reduced lumbar and femoral BMD (univariate)
Ahn, et al. (2006) [44]	Mean change in T-score spine over first year post-transplant: • <18.5 = -0.5±0.67 • 18.5 – 24.9 = -0.5±0.67 • ≥25 = -0.34±0.60	Spine and femoral T-scores lower in patients with lower BMI. However BMI did not influence change in BMD in first year post-transplant (p=0.40)
Naylor, et al. (2014) [40]	β for baseline BMI in predictors of BMD model: between no previous osteoporosis/previous osteoporosis groups: • L-spine: 0.0001 (p=0.95)/-0.000007 (p=1.0) • Total hip: 0.0005 (p=0.70)/-0.0004 (p=0.71) • Femoral neck: 0.0004 (p=0.76)/-0.001 (p=0.36) β for change in BMI across scans in predictors of BMD model: between no previous osteoporosis/previous osteoporosis groups: • L-spine: 0.000 (p=0.88)/ 0.001 (p=0.28) • Total hip: 0.002 (p<0.05)*/0.00007 (p=0.84) • Femoral neck: 0.002 (p<0.05)*/-0.001 (p=0.34)	Greater increases in BMI in the no prior osteoporosis treatment group were associated with significant increase in BMD at total hip and femoral neck (p<0.05)
Diabetes	**Description**	**Findings**
Jeffery, et al. (2003) [37]	From baseline participant characteristics (n=211): • Pre-transplant diabetes = 29/211	• Pre-transplant diabetes correlated with decreased BMD (univariate, p<0.001) • Pre-transplant diabetes was an independent predictor of low BMD (multivariate, p<0.001)

Ahn, et al. (2006) [44]	Mean change in T-score spine over first year post-transplant: • No DM/DM: -0.52±0.67/-0.15±0.50 ($p<0.01$)	Low BMD significantly correlated with being in non-diabetes group ($p<0.01$)
Huang, et al. (2012) [42]	N=12/76 were diabetic (osteoporotic = 5, non-osteoporotic = 7)	Binary logistic regression did not identify DM as significant factor in BMD (OR = ~0.6)
HD Duration	**Description**	**Findings**
Ahn, et al. (2006) [44]	Mean change in T-score spine over first year post-transplant: • HD <12 months: -0.39±0.57 ($p=0.001$) • HD ≥12 months: -0.67±0.79	Low BMD significantly correlated to longer period (≥12 months) of HD pre-transplant ($p=0.001$)
Smoking	**Description**	**Findings**
Huang, et al. (2012) [42]	N=10/76 were smokers (all male); 5 had normal baseline BMD, 5 had osteoporosis at baseline BMD	Binary logistic regression did not identify smoking as significant factor in BMD (OR = ~0.8)

Abbreviations: BMD- Bone Mineral Density; HD – Hemodialysis; CsA – Cyclosporine; IS - immunosuppression; LS lumbar spine; FN – femoral neck