



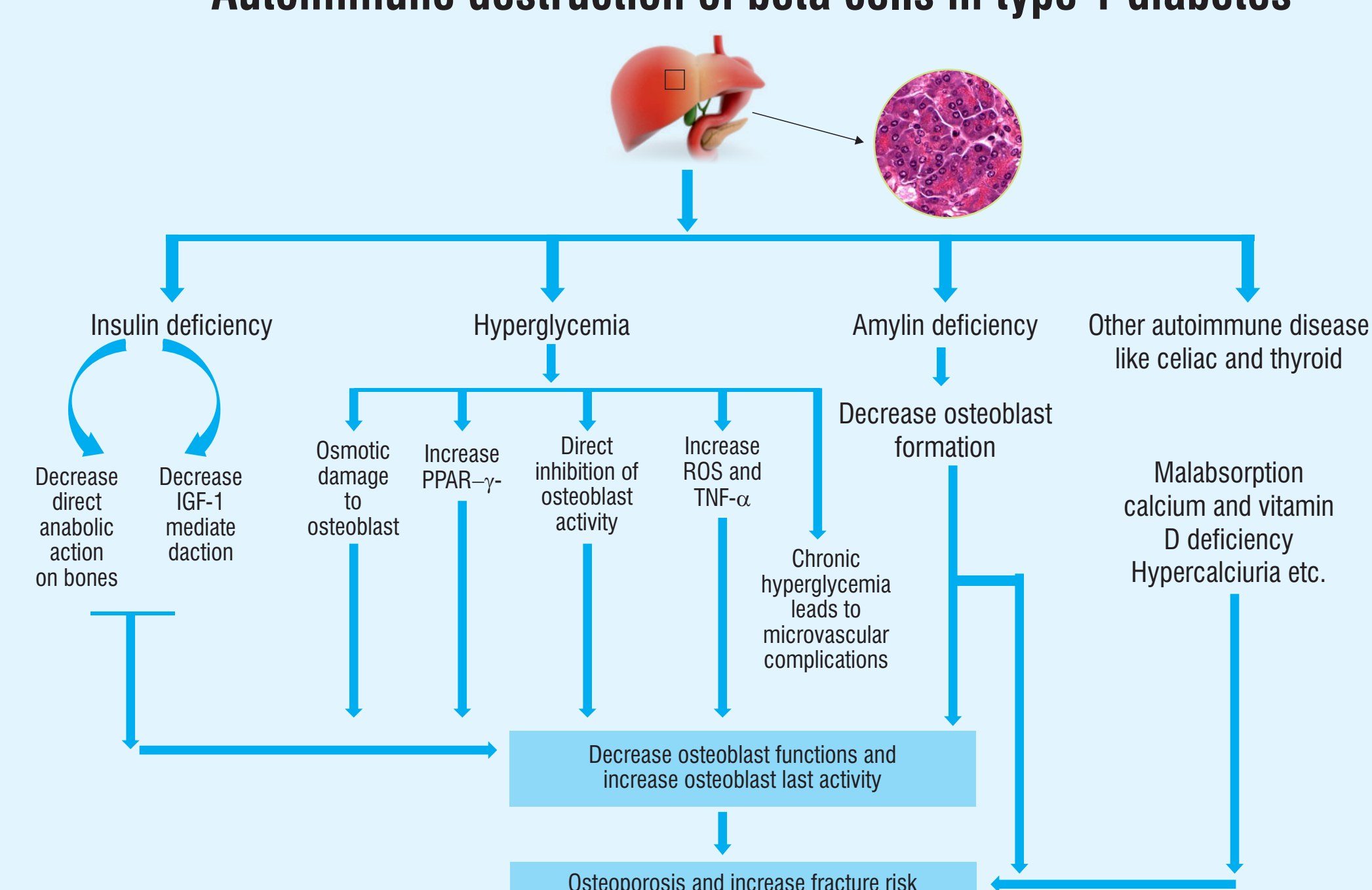
Association Between Bone Mineral Density and Type 1 Diabetes Mellitus: A Meta-analysis Of Observational Studies

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INTRODUCTION

- Various studies have reported that Bone Mineral Density (BMD) is reduced in patients with Type 1 Diabetes Mellitus (T1DM)¹
- In fact, osteopenia has been described in T1DM patients long ago, even before the availability of modern techniques to measure BMD¹
- However, the data is not consistent among all the reported studies¹
- Potential mechanisms leading to osteoporosis in patients with T1DM¹

Autoimmune destruction of beta cells in type 1 diabetes



OBJECTIVE

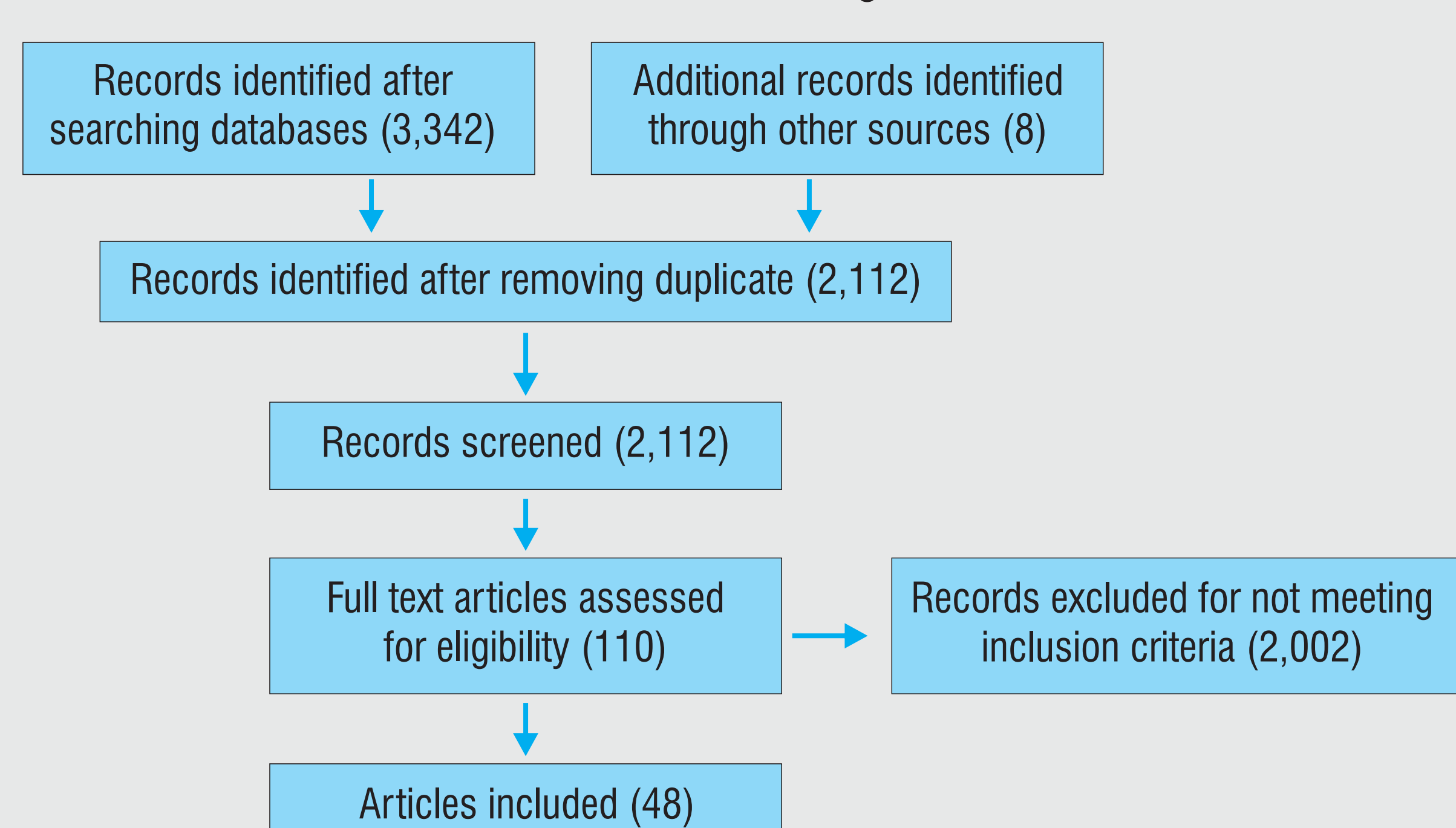
To perform a meta-analysis to estimate the difference in BMD between T1DM and non-diabetic populations

METHODOLOGY

- Eligibility Criteria**
 - Cases: T1DM patient (of any age group)
 - Control: Healthy subject (non diabetic)
 - BMD measurement:
 - BMD was measured by dual energy X-ray absorptiometry (DXA)
 - BMD measurements were expressed as an absolute value in g/cm²
 - Study design: All observational studies were included (case controlled and cohort studies)
- Literature Search:** Performed in PubMed and EMBASE for cross-sectional cohort and case-control studies pertaining to T1DM and osteoporosis
- Additional searches were conducted to include research abstracts, cross references and bibliography of individual articles
- Studies up to January 2014 were included
- Key Words:**
 - Type 1 Diabetes Mellitus
 - Bone Mineral Density
 - Dual energy X-ray absorptiometry (DEXA)
 - Assessment of studies was performed by two independent researchers
- A random effects was used to pool data in case of substantial heterogeneity among studies
- Heterogeneity and publication bias were assessed

RESULTS

PRISMA Flow Diagram



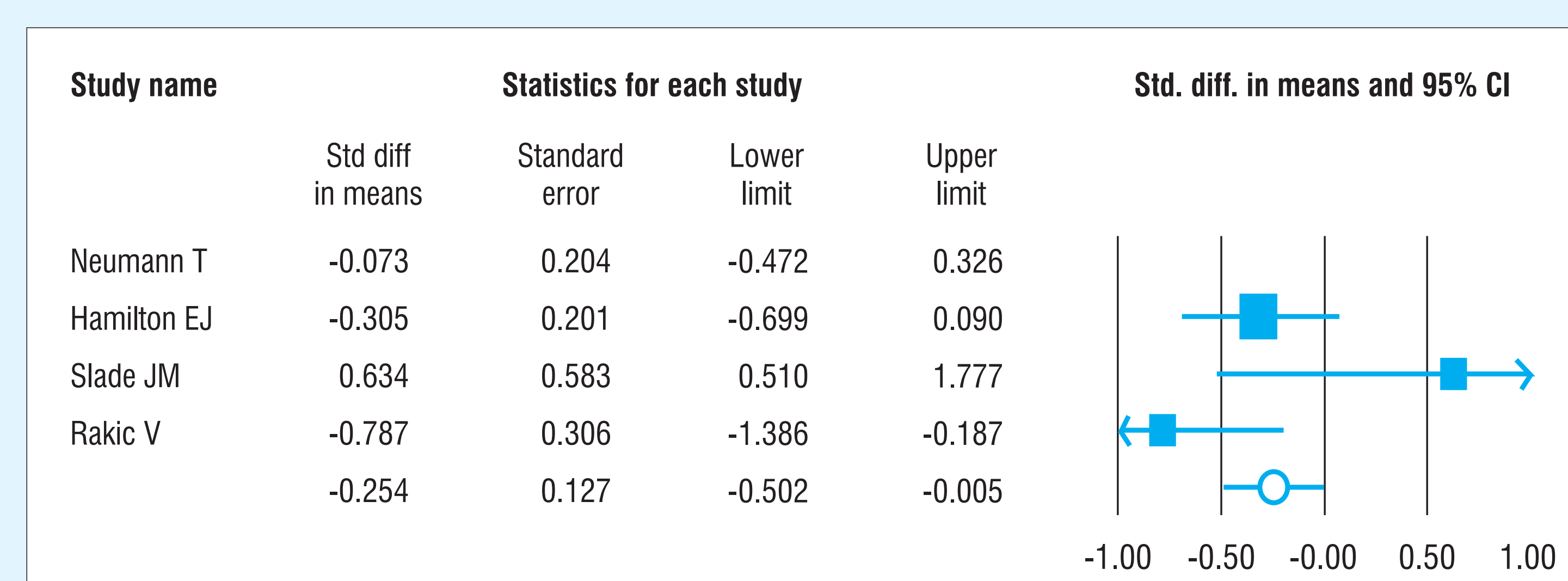
RESULTS

- Number of studies included: 48
- Number of patients involved:
 - Cases: 2,885
 - Controls: 4,814
- Meta-analysis showed that BMD in T1DM patients was significantly lower at many regions
- Pooled mean differences of BMD in patients with T1DM when compared with control:
 - Hip region:**
 - Women: -0.43 (95% Confidence interval [CI]: -0.69 to -0.17)
 - Men: -0.25 (95% CI: -0.50 to -0.005)
 - Spine region:**
 - Men: -0.30 (95% CI: -0.47 to -0.13)
 - Forearm region:**
 - Women: -0.21 (95% CI: -0.43 to 0.00)
 - Femoral neck: No significant difference was found in BMD (in both men and women)

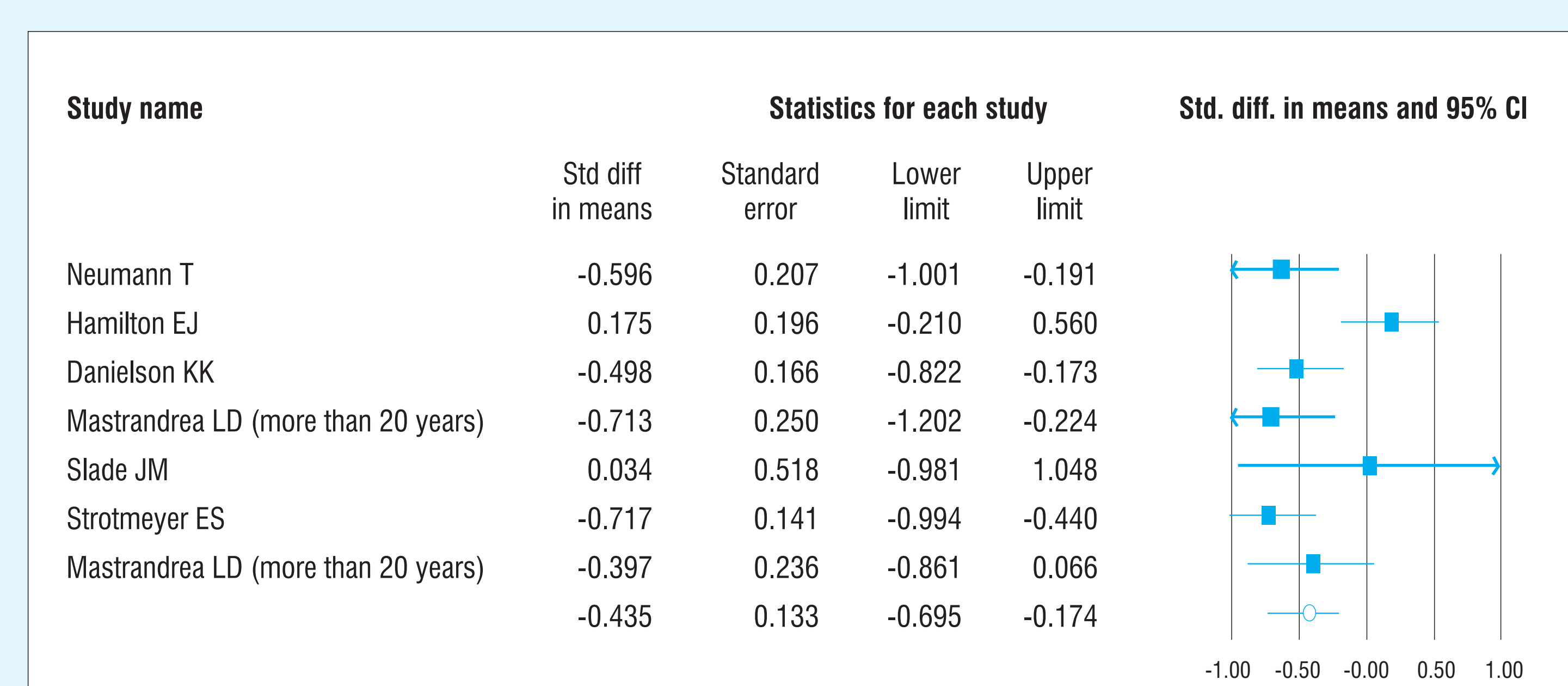
- Pooled mean differences of site-wise BMD in patients with T1DM when compared with control:

Site	Gender	Number of studies	Effect size (SMD)	95% CI	P value	I ² value
Spine	Male	9	-0.308	0.479 to -0.136	0.001*	0%
	Female	17	0.101	0.292 to 0.104	0.353	69%
Hip	Male	4	-0.254	0.502 to -0.005	0.045*	63%
	Female	7	-0.435	0.695 to -0.174	0.001*	51%
Femoral neck	Male	8	0.077	0.574 to 0.727	0.818	98%
	Female	11	0.170	0.779 to 1.119	0.725	93%
Forearm	Male	3	-0.069	0.332 to 0.195	0.609	0%
	Female	4	-0.218	0.437 to 0.002	0.052	49%

- Hip BMD in Male Subjects with Type 1 diabetes mellitus compared to healthy subjects

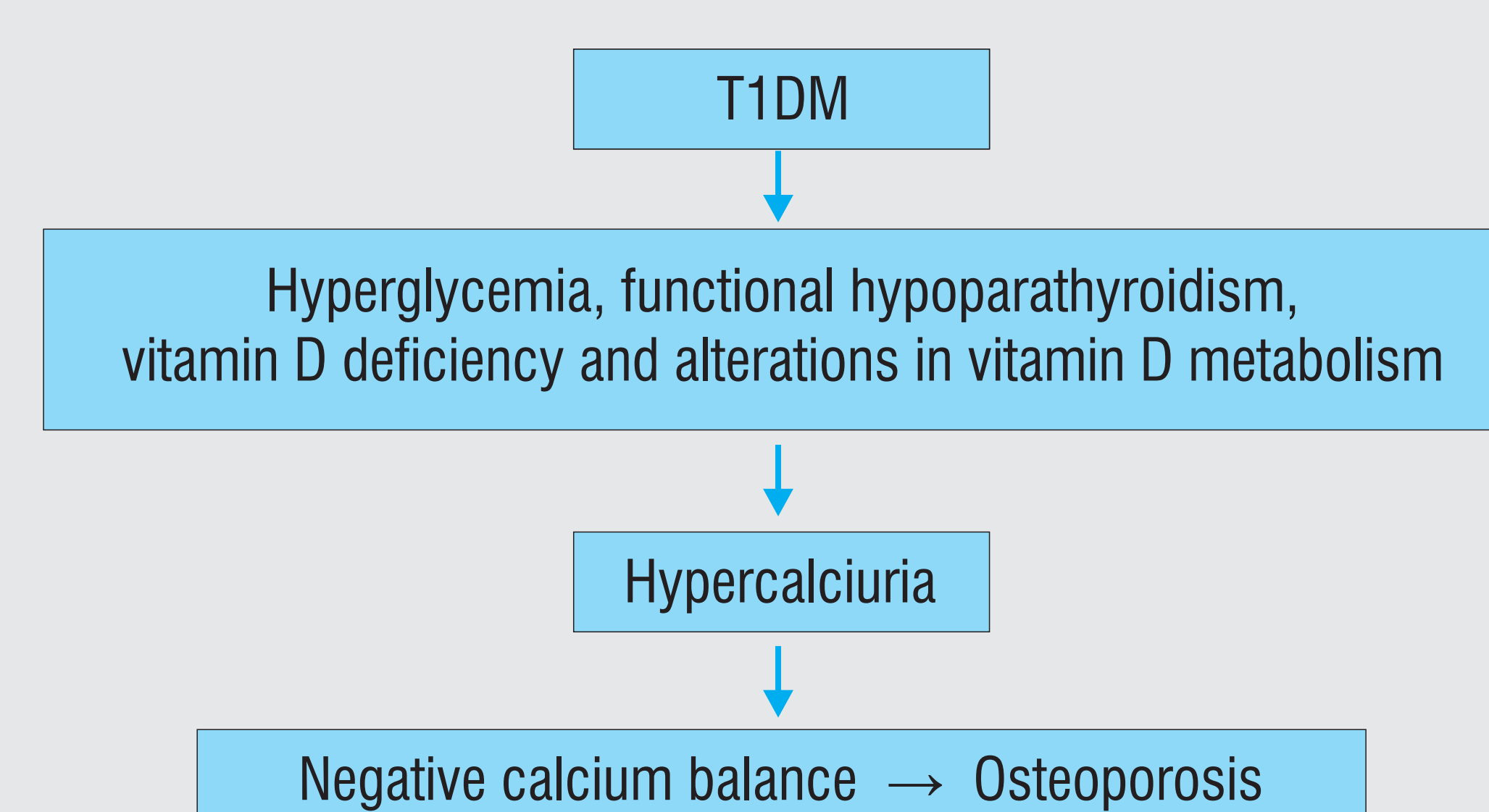
Fixed effect= SMD -0.254, 95% CI -0.502 to -0.005 (p value = 0.045), I²= 51%

- Hip BMD in Female Subjects with Type 1 diabetes mellitus compared to healthy subjects

Random effect model = SMD -0.435, 95% CI -0.695 to -0.174 (P value= 0.001), I²= 62.97

DISCUSSION

- Proposed pathogenic mechanisms behind reduced BMD in T1DM patients:²
 - Hyperglycemia
 - Autoimmune inflammation
 - Increased PPAR- γ activity increased marrow adiposity
 - Hypoinsulinemia and hypoamylinemia
 - Deficit of IGF-I and Vitamin D
 - Nonenzymatic glycosylation of type 1 collagen with subsequent formation of AGEs (advanced glycation end products)
- Factors influencing the bone in T1DM patients
 - Age of onset
 - Prepubertal onset T1DM: decreased bone formation and inadequate accrual peak bone mass osteopenia³
 - Gender
 - Men with T1DM are more prone to osteopenia than women⁴
 - Estrogen adequacy and/or use of estrogen-based oral contraceptive pills might be the reason for higher bone mass in women compared to men⁴
 - BMI
 - Lower BMI is associated with higher incidence of osteoporosis⁵
 - Adipose tissue \rightarrow adipocytokines \rightarrow increase in BMD⁵
 - T1DM patients \rightarrow lower BMI lower adipose tissues \rightarrow more prone to develop OP⁵
 - Poor glycemic control⁶
 - T1DM \rightarrow poor glycemic control \rightarrow microvascular complications (Retinopathy, Neuropathy, Nephropathy)
 - Retinopathy and neuropathy \rightarrow fall \rightarrow fractures
 - Nephropathy Hypercalciuria AND alter vitamin D metabolism vitamin D deficiency
 - Endocrine factors⁷



CONCLUSIONS

- Both men and women with T1DM have preponderance to have lower BMD levels
- Multiple factors can influence BMD in individuals with T1DM:
 - Age
 - Gender
 - Menopausal status
 - Bone type
- Large prospective epidemiological studies are required to confirm our findings

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