

Risk of Fracture in Type 2 Diabetes Mellitus Patients: Meta-analysis of Observational Studies

Chirag Shah¹, Romil Shah², Garima Kinra¹, Shivaprasad Singuru¹, Murthy VSN¹, Amit Dang¹¹MarksMan Healthcare Solutions LLP (HEOR and RWE Consulting), Navi Mumbai, India ²S.J.M. College of Pharmacy, Chitradurga, India

INTRODUCTION

- Diabetes mellitus (DM) affects almost one third of people aged 65 and above, and thus is a major public health problem¹
- Various studies done in patients with type 1 DM and type 2 DM have shown that this population is at an increased risk of developing fractures²
- The risk of fractures is significantly greater in patients with T1DM when compared to the general population³
- T1DM patients have a higher risk of developing fractures of the hip, spine, and proximal humerus⁴
- Similarly, even in T2DM, some studies suggest an increased fracture risk⁴
- However, there is inconsistent association between T2DM and increased fracture risk
- Some studies suggest that the fracture risk in patients with T2DM is lower than, or is similar to that in the general population⁴
- To clarify this confusion, we performed this systematic review of observational studies

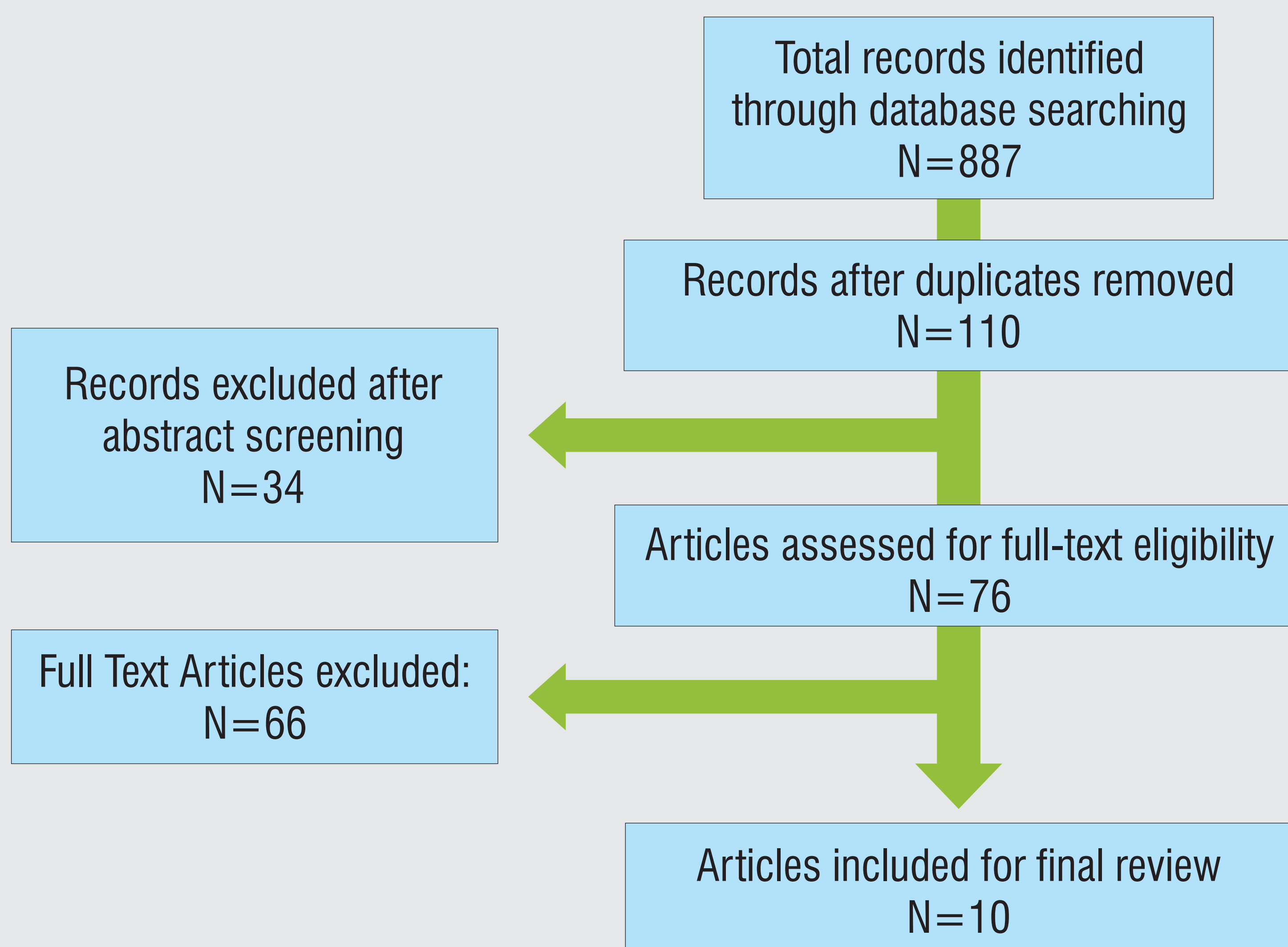
OBJECTIVE

- To assess the association between T2DM and fracture risk

MATERIALS AND METHODS

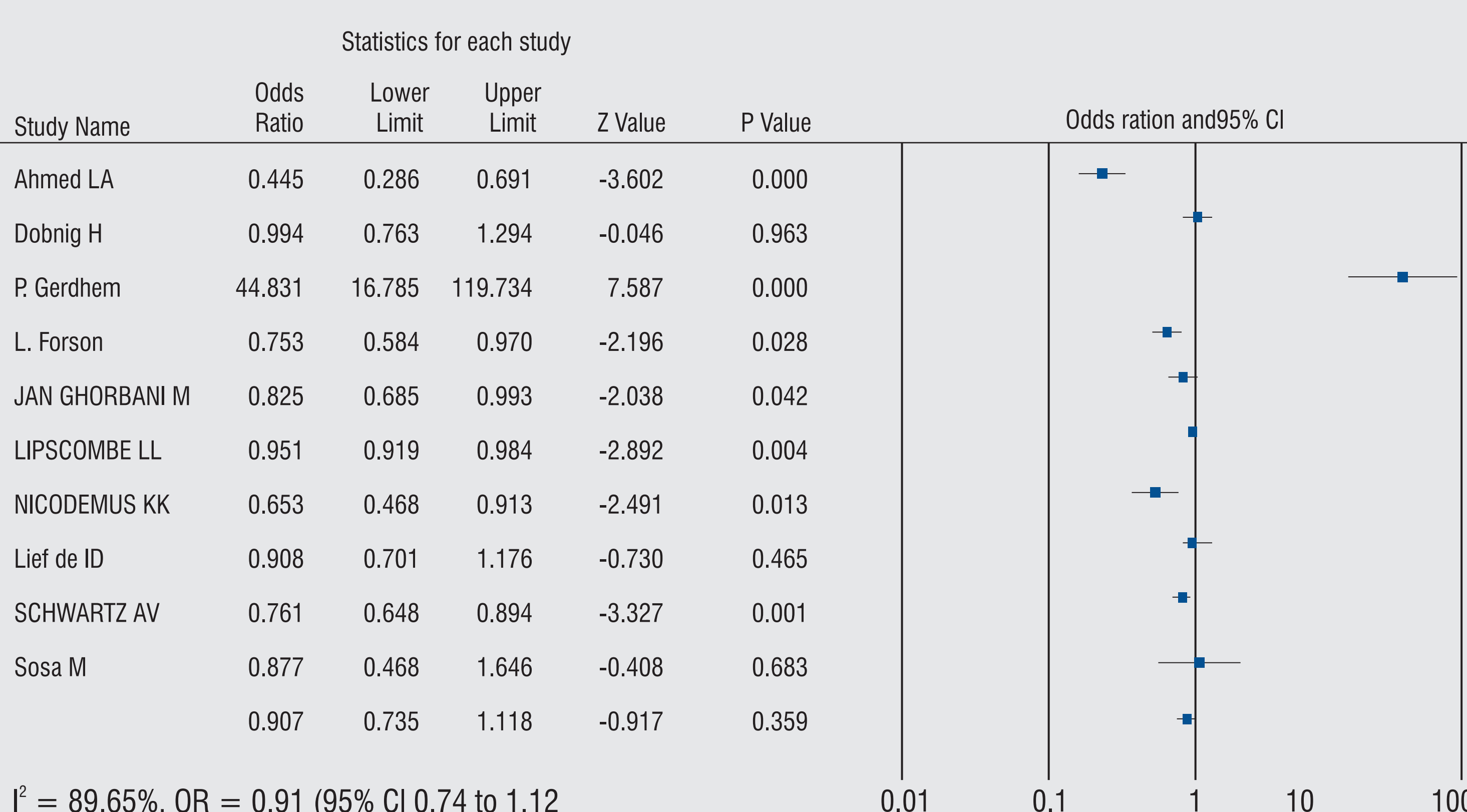
- A systematic literature search was performed in Medline and EMBASE databases
- Abstracts from annual scientific meeting of various diabetes and bone and mineral societies were also searched to identify relevant studies
- Studies reporting fracture risk in subjects with T2DM in comparison with subjects without diabetes were included
- Heterogeneity was calculated by performing I² statistics
- Summary relative risk (RR) estimates and 95% confidence intervals (CIs) were calculated using random-effects model

RESULTS



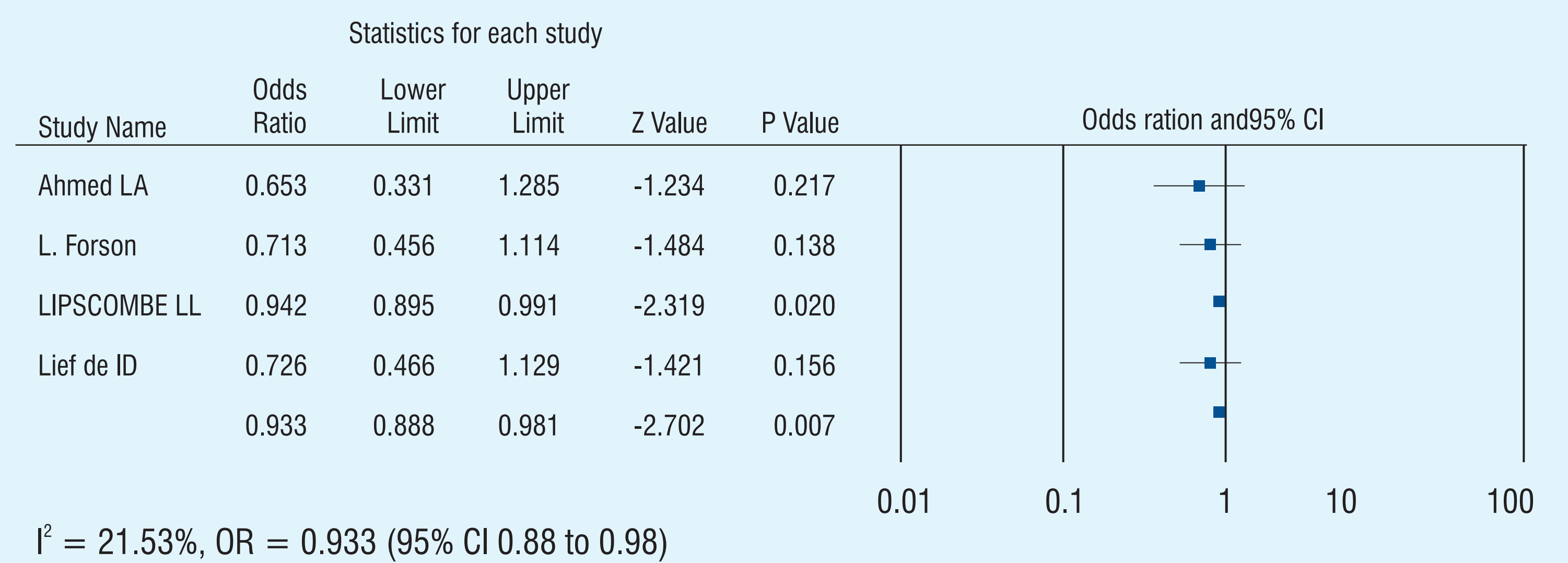
- We analyzed 10 studies covering 25,848 fracture events among 6,12,748 subjects without diabetes (4.2%) and 8570 fracture events among 2,12,011 subjects with T2DM (4.0%)
- The pooled relative risk (RR) of any fracture in subjects with T2DM was 0.91 (95% CI 0.75–1.11, p=0.375)

RESULTS: FRACTURE-T2DM ASSOCIATION IN WOMEN



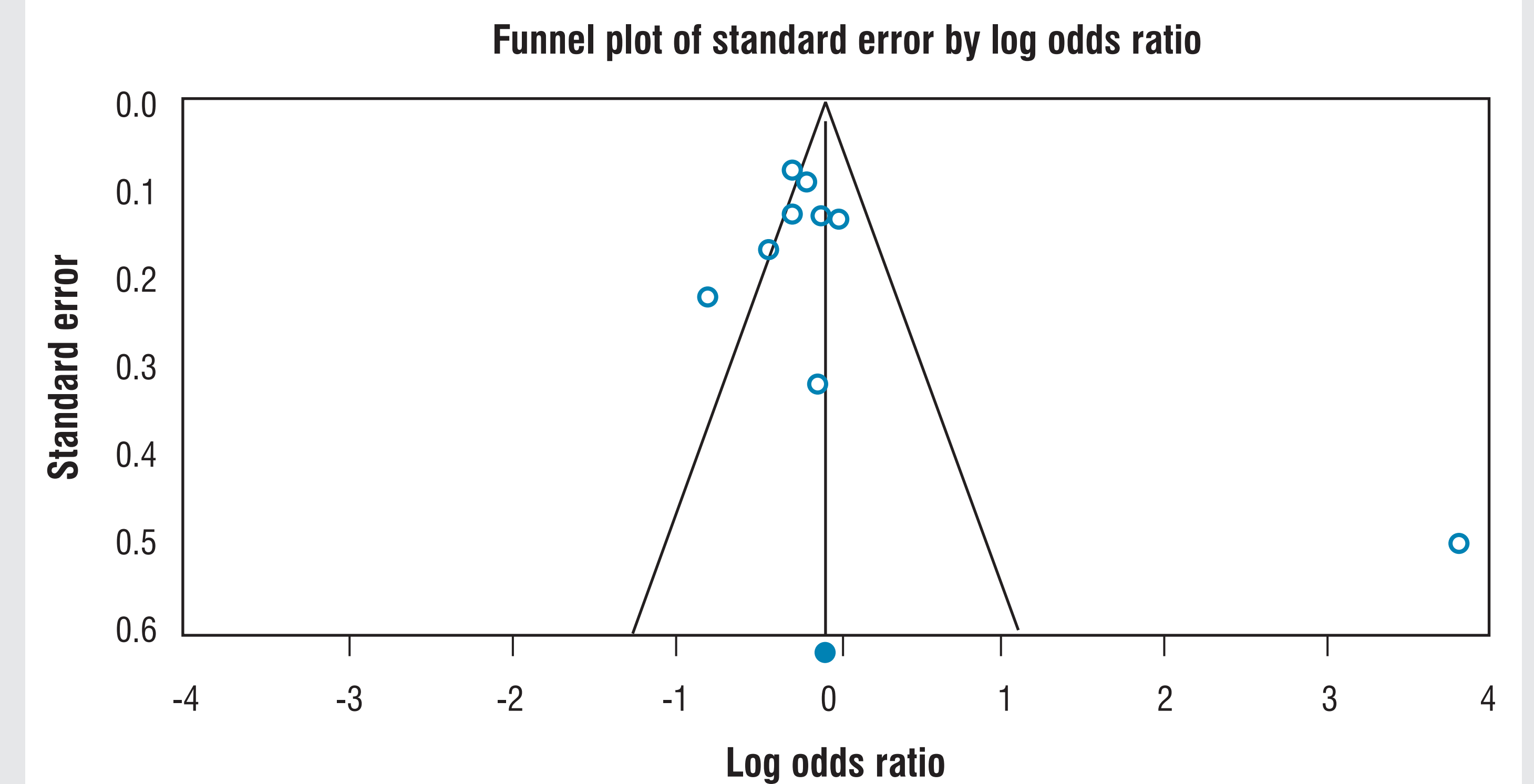
- The pooled RR for any fractures in women with T2DM was 0.907 (95% CI 0.735- 1.118, 10 studies) compared to subjects without diabetes

RESULTS: FRACTURE-T2DM ASSOCIATION IN MEN



- The pooled RR for any fractures in men with T2DM was 0.93 (95% CI 0.88 to 0.98, four studies) compared to subjects without diabetes, demonstrating significant reduction (7%) of fracture risk in men with T2DM.

- Sensitivity analysis demonstrated stability of result after removing outliers.
- No publication bias was observed on visual analysis of funnel plot.



DISCUSSION

- Patients with T2DM have an increased Bone mineral density (BMD) even after adjustment for obesity⁵
- Despite this increased BMD, patients with T2DM (specially those with longer duration of disease) are not protected from fractures⁶
- Patients with T1DM have a decreased BMD⁷
- However, impaired bone quality rather than impaired bone density appears to be the main contributor to the increased fracture risk seen in diabetes⁸
- Other factors contributing to increased fracture risks in diabetic patients are peripheral and autonomic neuropathy, recurrent hypoglycemic events, vitamin D deficiency, and thiazolidinedione therapy⁴
- Longer disease duration, the presence of diabetic complications, inadequate glycemic control, insulin use and increased risk for falls are all reported to increase fracture risk⁹
- Despite these factors, the association between T2DM and fractures is inconsistent⁴
- Our study found that men with T2DM were protected from risk of any type of fracture compared to non diabetic men

CONCLUSIONS

- Our meta-analysis suggests that patients of T2DM are not at increased risk of incidence of fractures as compared to non diabetic subjects.
- Male patients with T2DM are mildly protected from incidence of fracture compare to non diabetic male subjects.

REFERENCE

- Cowie CC et al. Diabetes Care 2009;32:287–94
- Janghorbani M et al. Am J Epidemiol 2007;166:495–505.
- Janghorbani M et al. Diabetes Care 2006;29:1573–8.
- Khazai NB et al. Curr Opin Endocrinol Diabetes Obes 2009;16(6):435-45
- van Daele PL et al. Ann Intern Med 1995;122:409–14.
- Vestergaard P. Osteoporos Int 2007;18:427–44.
- Ahmed LA et al. Osteoporos Int 2006;17:495–500.
- Vestergaard P. Curr Opin Endocrinol Diabetes Obes 2009;16:125–31.
- Dede AD et al. Metabolism 2014;63(12):1480-90