

# Renal biopsy in diabetic patients: a meta-analysis and meta-regression of 48 studies

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**Introduction and aims:** The utility of renal biopsy (RB) in diabetics is object of debate (1). Diabetics with rapidly worsening renal function and/or unusual clinical features are often “clinically” labeled as having progressive forms of diabetic nephropathy (DN) while, in many cases, they are rather developing a non-diabetic renal disease (NDRD) or super-imposed conditions (DN + NDRD) (2). In this systematic review we aimed at clarifying the usefulness of RB in the diabetic setting by 1) defining the epidemiology spectrum of DN, NDRD and “mixed” forms in current literature and 2) analyzing the frequency of such diagnoses by a meta-analysis.

**Methods:** We performed a systematic search of potentially relevant articles in the PubMed and Ovid MEDLINE databases through focused, high sensitive search strategies. Studies were included if dealing with diabetics undergoing RB with available prevalence data on DN, NDRD or mixed forms (DN + NDRD). The meta-analysis was performed by using a random effect model. Heterogeneity was assessed by  $I^2$  (and P value) and factors explaining heterogeneity were investigated by meta-regression.

**Results:** We included 48 studies of 4876 diabetics undergoing RB (Fig.1). The most frequent indications to RB in these patients were a sudden appearance of nephrotic range proteinuria or renal function impairment, hematuria or rapidly declining renal function. The prevalence of DN diagnosis was highly variable, ranging from 6.5 to 94% ( $I^2=90\%$ ,  $P<0.001$ ) of the overall diagnoses, as well as that of NDRD (3 to 82.9%,  $I^2=88\%$ ,  $P<0.001$ ) and mixed forms (4 to 45.5%,  $I^2=86\%$ ,  $P<0.001$ ). IgA nephropathy was the most frequent NDRD with a frequency ranging from 3 to 59 %. The positive predictive values (PPVs) (pooled data) of clinical judgment for identifying DN, NDRD and mixed forms (as assessed by renal biopsy) were 50,1% (95% CI: 44.7 -55.2), 36,9% (95% CI: 32.3-41,8) and 19.7% (95% CI: 16.3-23.6), respectively (Fig.2). Meta-regression analysis identified systolic pressure ( $r= -0.53$ ,  $p=0.02$ ), HbA1c ( $r= -0.49$ ,  $p=0.02$ ), duration of diabetes ( $r= -0.36$ ,  $p=0.04$ ) and diabetic retinopathy ( $r= -0.59$ ,  $p=0.001$ ) as factors explaining heterogeneity among PPVs of clinical diagnosis for NDRD. The same analysis indicated serum creatinine ( $r=-0.42$ ,  $p=0.01$ ) as the only factor underlying heterogeneity among studies for DN and creatinine ( $r=0.52$ ,  $p=0.006$ ) and even more GFR ( $r=-0.73$ ,  $p=0.007$ ) as the only two factors elucidating heterogeneity among studies for mixed forms. Overall, the odds ratio (OR) of finding DN at renal biopsy was just 69% higher (OR: 1,71, 95% CI: 1.51-1.88) than that of NDRD (Fig.3).

**Conclusions:** NDRDs (either as single pictures or super-imposed to DN) are indeed highly prevalent in diabetic patients. Clinical judgment alone can lead to misleading diagnoses and, thus, wrong therapeutic approaches in a significant percentage of patients. Risk stratification of diabetics according to individual factors is needed for selecting patients who might benefit of RB for correct diagnosis assessment.

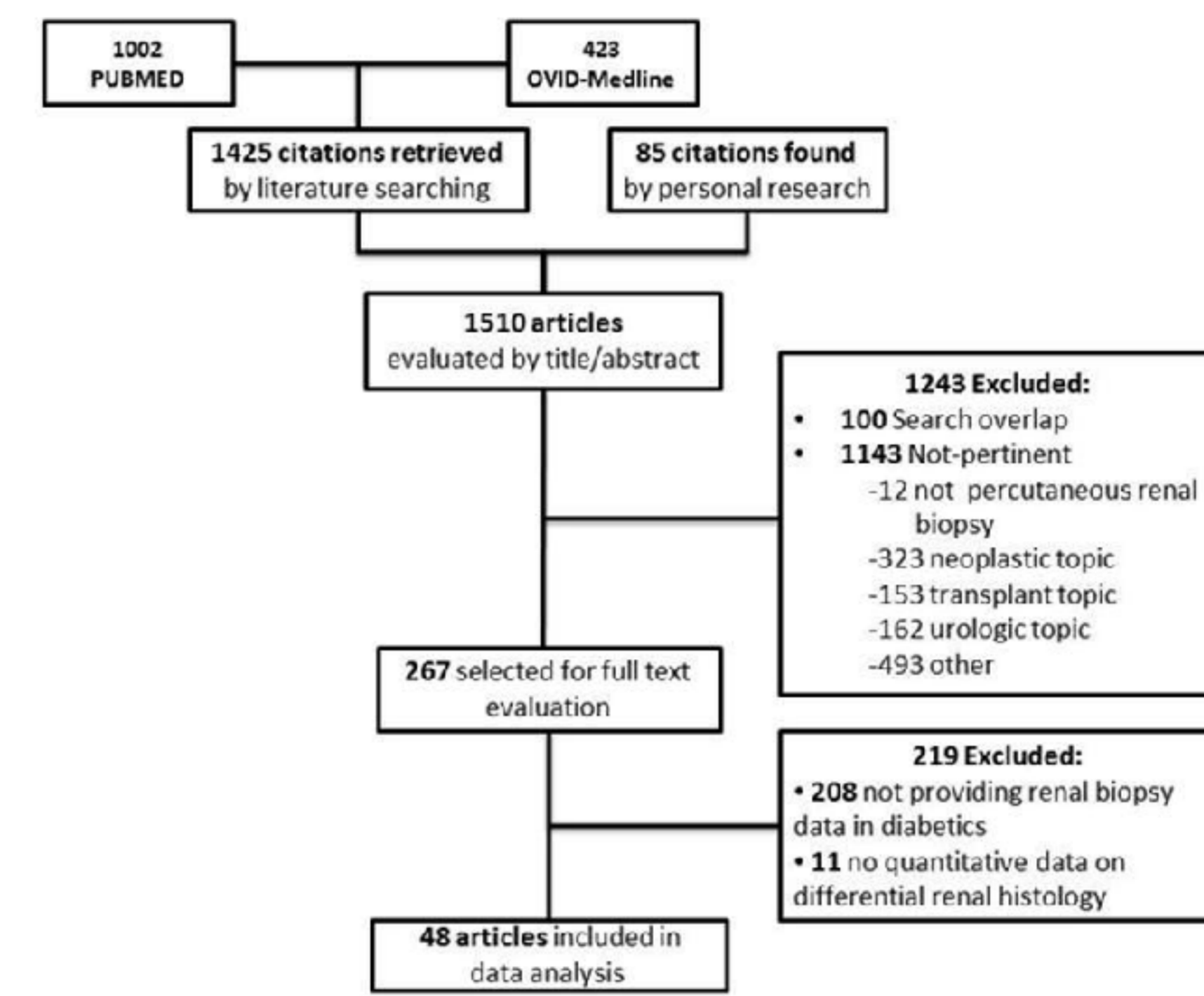
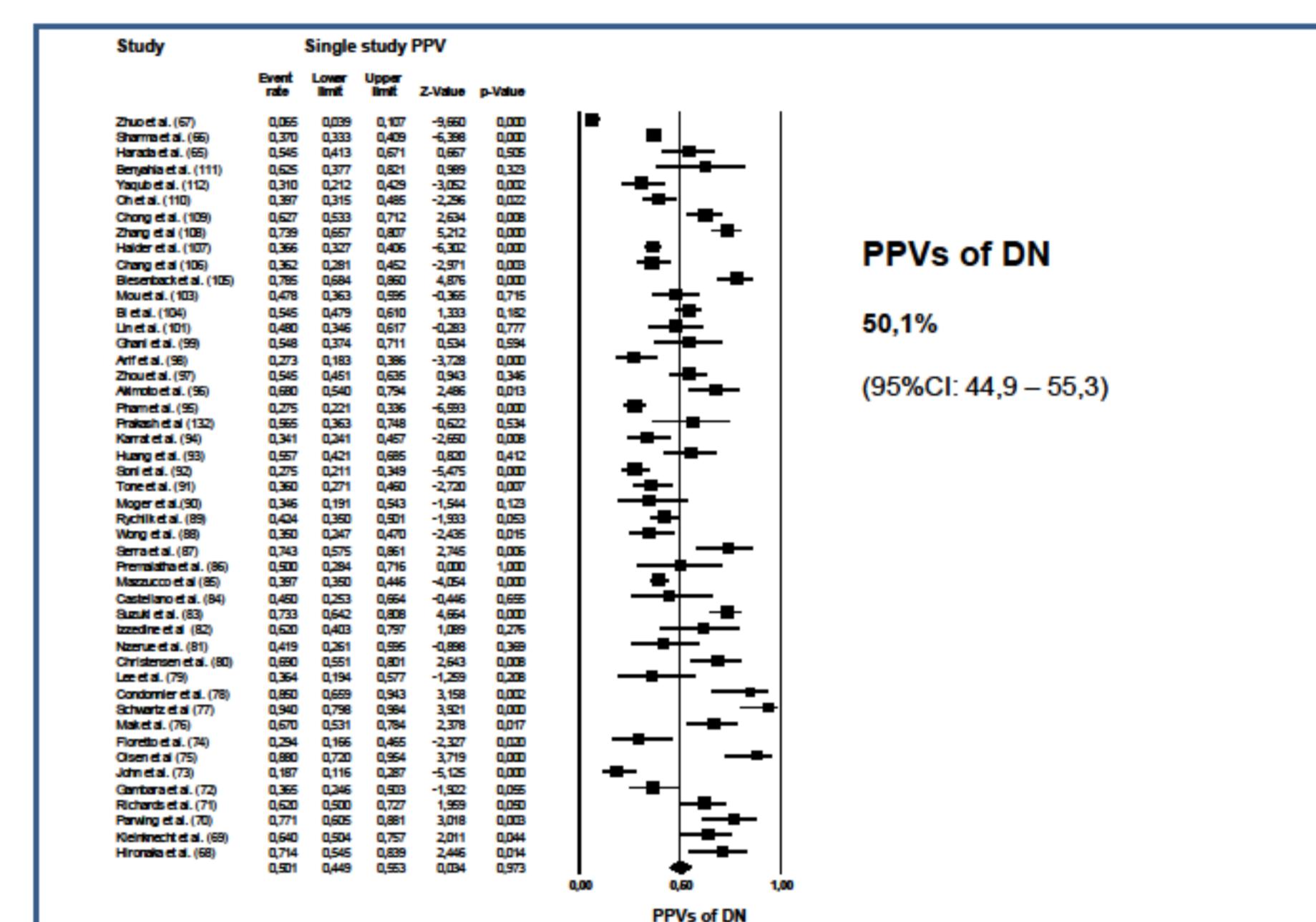
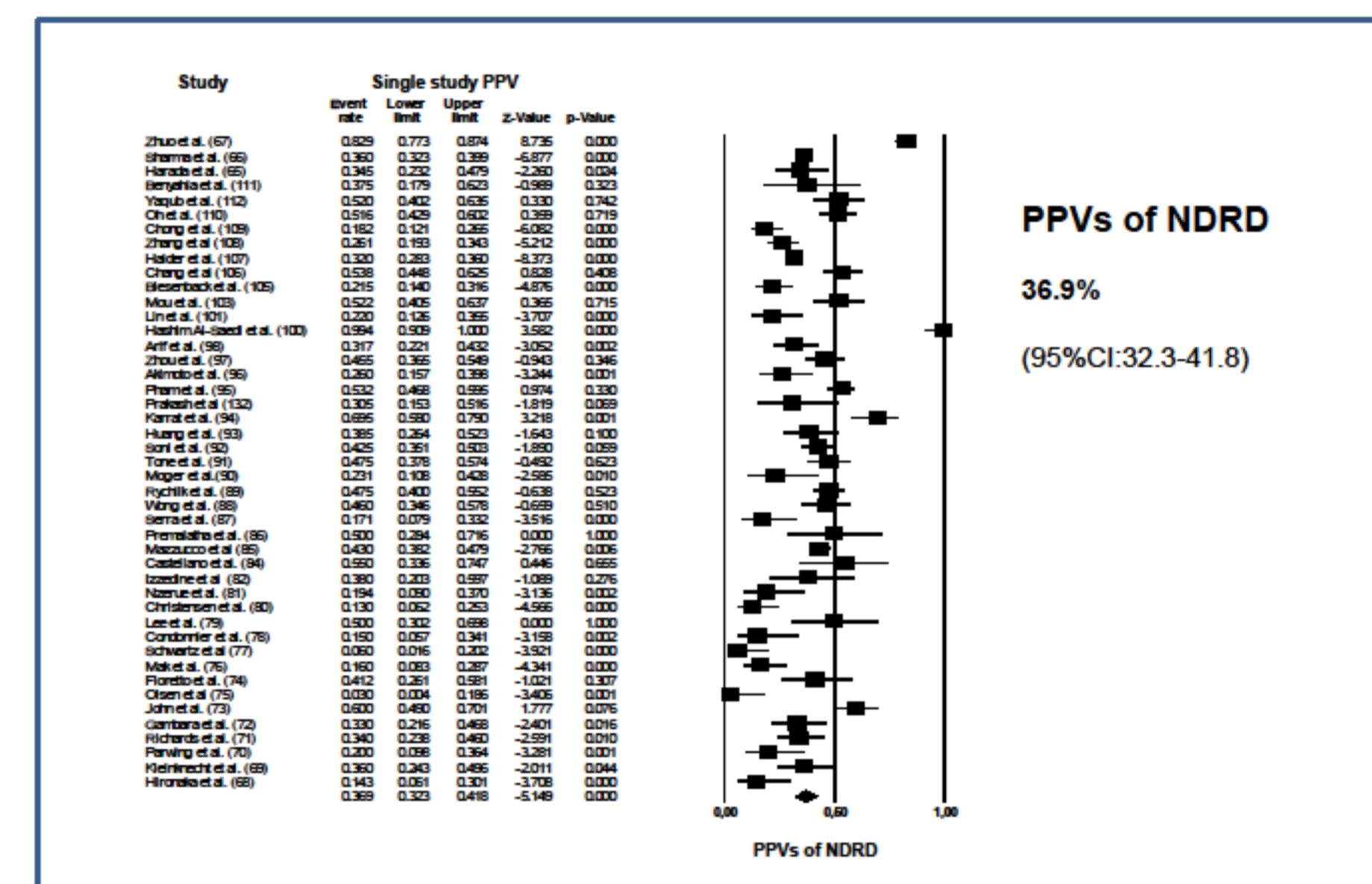


Fig.1: Flow of study selection process

2a



2b



2c

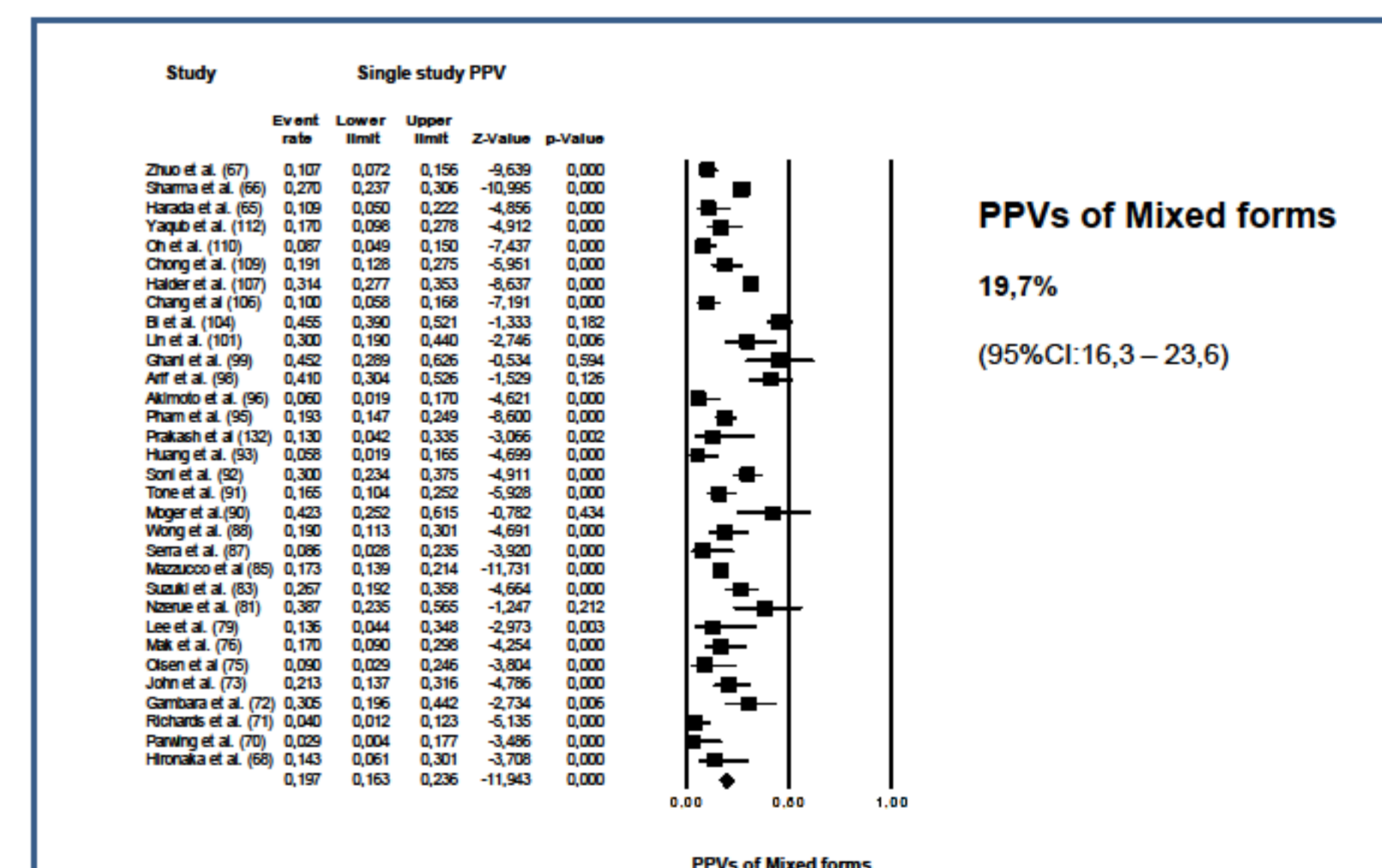


Fig.2: Positive predictive values (PPVs) of clinical judgment for the diagnosis of DN (2a), NDRD (2b) and mixed forms (2c) from pooled meta-analysis.

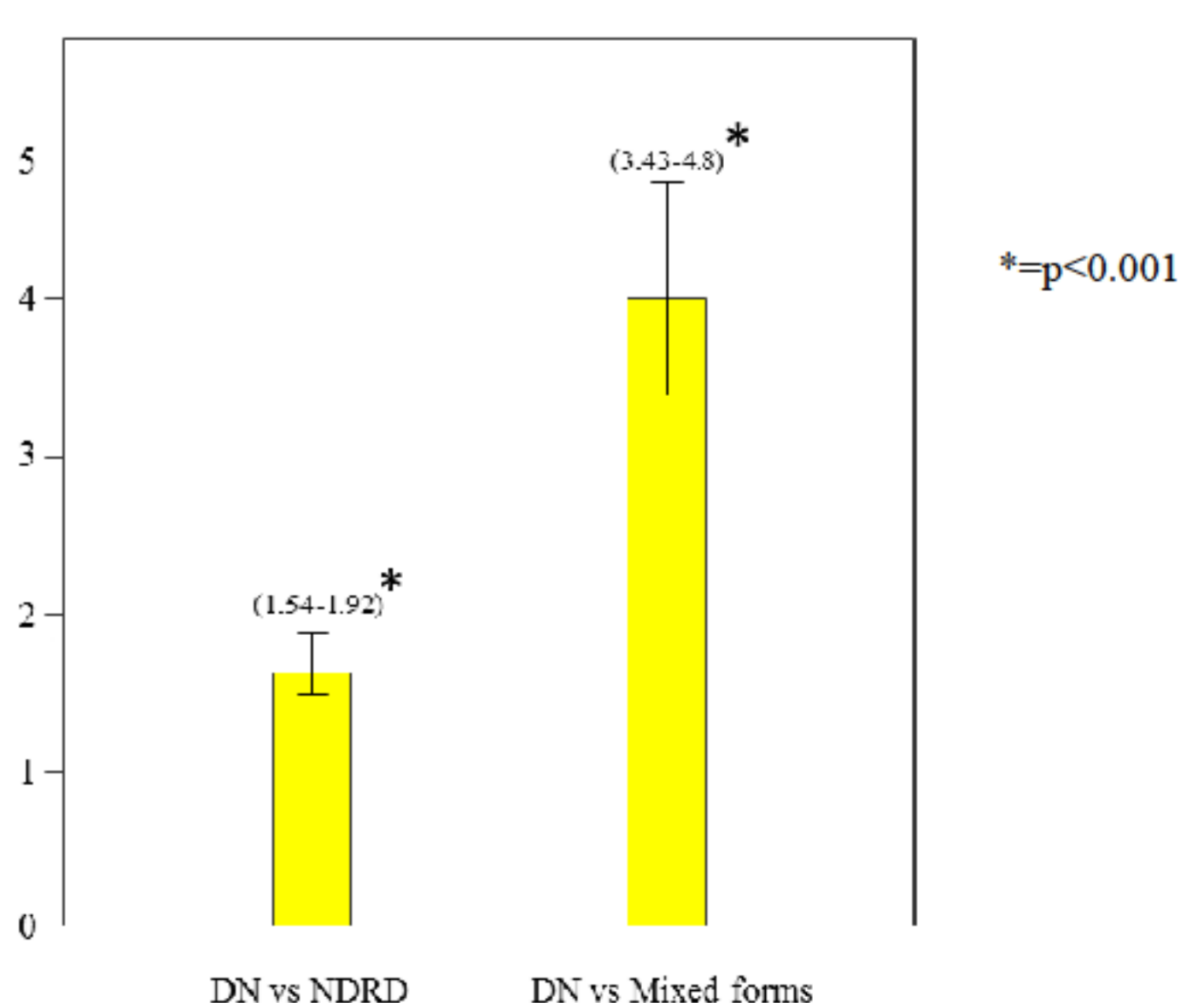


Fig.2: Odds ratio (95%CI) of DN diagnosis at renal biopsy compared with NDRD and mixed forms

**References:**

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