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Introduction

Hyperglycemic states are known to have a bidirectional relationship with pancreatic disorders. The literature remains limited in discussing the role of prediabetic states on intermediate or long-term risk of having pancreatic cancer. Therefore, we conducted this updated meta-analysis to evaluate the risk of Pancreatic cancer among individuals with Prediabetes or impaired fasting glucose.
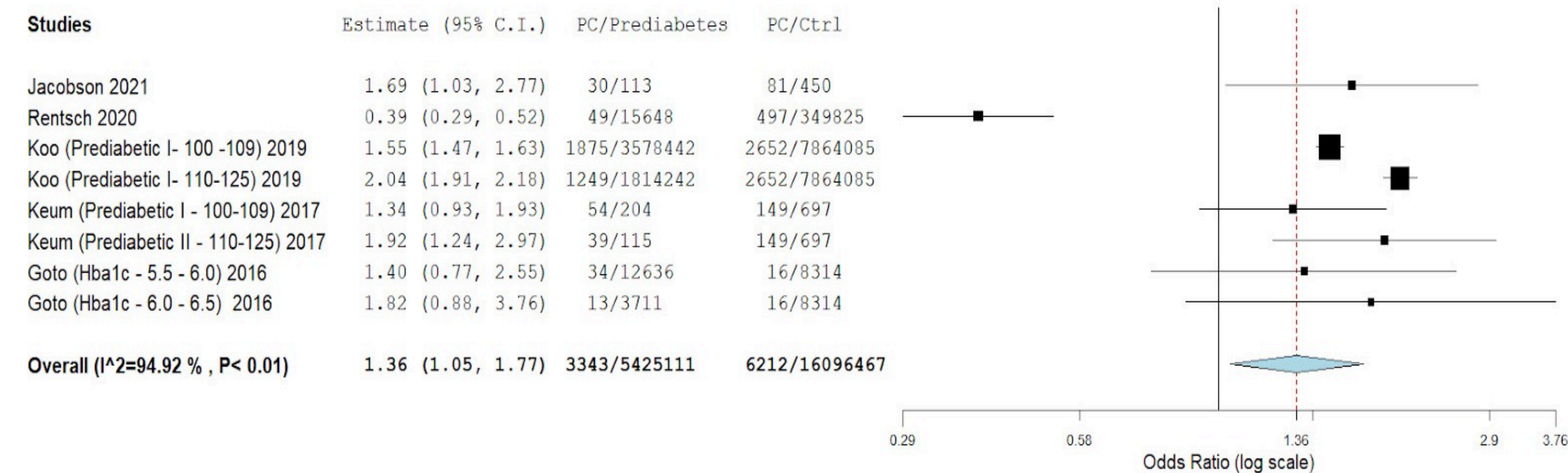
Methods and Materials

We systematically searched PubMed/Medline, EMBASE, Scopus, and Google Scholar to ascertain prospective studies describing pancreatic cancer in prediabetes between May 1, 2012 to May 1, 2022. Random-effects models were used to perform meta-analysis and subgroup analyses. I2 statistics was used to assess heterogeneity. Sensitivity analysis was done using the leave-one-out method.

Figure 1

a. Unadjusted OR - - Prediabetes vs Normoglycemia

Studies	Estimate (95% C.I.)	PC/Prediabetes	PC/Ctrl
Jacobson 2021	1.69 (1.03, 2.77)	30/113	81/450
Rentsch 2020	0.39 (0.29, 0.52)	49/15648	497/349825
Koo (Prediabetic I- 100 -109) 2019	1.55 (1.47, 1.63)	1875/3578442	2652/7864085
Koo (Prediabetic I- 110-125) 2019	2.04 (1.91, 2.18)	1249/1814242	2652/7864085
Keum (Prediabetic I - 100-109) 2017	1.34 (0.93, 1.93)	54/204	149/697
Keum (Prediabetic II - 110-125) 2017	1.92 (1.24, 2.97)	39/115	149/697
Goto (Hba1c - 5.5 - 6.0) 2016	1.40 (0.77, 2.55)	34/12636	16/8314
Goto (Hba1c - 6.0 - 6.5) 2016	1.82 (0.88, 3.76)	13/3711	16/8314
Overall (I^2=94.92 % , P< 0.01)	1.36 (1.05, 1.77)	3343/5425111	6212/16096467

b. Adjusted OR - - Prediabetes vs Normoglycemia

Studies	Estimate (95% C.I.)	Pancreatic Cancer/Prediabetes	Pancreatic Cancer/Ctrl
Jacobson 2021	1.77 (1.05, 2.98)	30/113	81/450
Koo (Prediabetic I- 100 -109) 2019	1.22 (1.15, 1.29)	1875/3578442	2652/7864085
Koo (Prediabetic I- 110-125) 2019	1.42 (1.33, 1.52)	1249/1814242	2652/7864085
Keum (Prediabetic I - 100-109) 2017	1.32 (0.91, 1.91)	54/204	149/697
Keum (Prediabetic II - 110-125) 2017	1.90 (1.22, 2.96)	39/115	149/697
Goto (Hba1c - 5.5 - 6.0) 2016	1.70 (0.92, 3.14)	34/12636	16/8314
Goto (Hba1c - 6.0 - 6.5) 2016	2.29 (0.99, 5.30)	13/3711	16/8314
Overall (I^2=66.13 % , P< 0.01)	1.40 (1.23, 1.59)	3294/5409463	5715/15746642

c. Leave one out Sensitivity Analysis

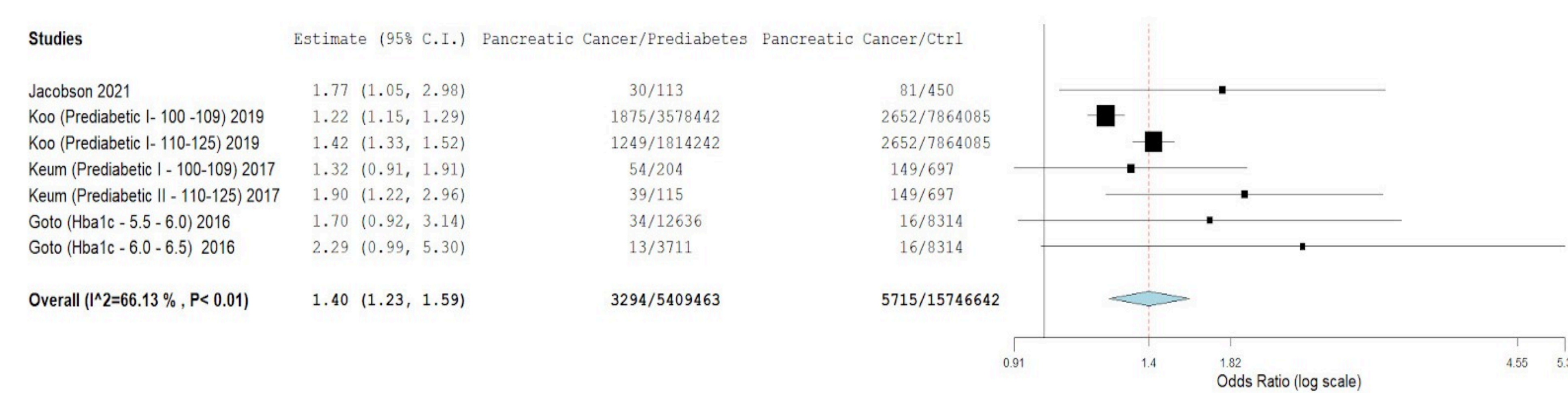| Studies	Estimate (95% C.I.)
Overall	1.40 (1.23, 1.59)
- Jacobson	1.38 (1.21, 1.58)
- Koo (Prediabetic I- 100 -109)	1.44 (1.35, 1.53)
- Koo (Prediabetic I- 110-125)	1.47 (1.19, 1.80)
- Keum (Prediabetic I - 100-109)	1.42 (1.23, 1.63)
- Keum (Prediabetic II - 110-125)	1.37 (1.20, 1.55)
- Goto (Hba1c - 5.5 - 6.0)	1.39 (1.22, 1.59)
- Goto (Hba1c - 6.0 - 6.5)	1.38 (1.22, 1.57)

Results

Five studies (1 USA, 1 UK, 1 Sweden, 1 Korea, 1 Japan) comprising 5,425,111 Prediabetics (mean age 59.3 years) and 16,096,467 normoglycemic patients with a median follow-up of 8.5 years were included in this study. A total of 3343 (0.06%) pancreatic cancer events were noted in the prediabetic group whereas 6212 (0.04%) pancreatic cancer events took place in the normoglycemic group. The unadjusted OR is 1.36 (95%CI 1.05-1.77, p 0.02) (fig 1a) and when adjusted for confounders like age, sex, etc, the overall estimated OR reported was 1.40 (1.23-1.59, p< 0.01) (fig 1b). Sensitivity analysis using the leave one out method did confirm equivalent results(fig 1c). Heterogeneity analysis for unadjusted OR had considerable heterogeneity with an overall I^2 of 94.92% with a P value < 0.01 and for adjusted OR had moderate heterogeneity with an overall I^2 of 66.13% with a p value< 0.01. Subgroup analysis by age showed that studies with older participants of mean/median ages 60 and above had higher odds of 1.83 (95%CI 1.28-2.62, p< 0.01) when compared to studies with relatively younger participants with mean/median ages < 60 years which reported odds of 1.35 (95%CI 1.18-1.55, p< 0.01). The risk of pancreatic cancer among pre diabetics was higher in studies from Japan (OR 1.89, 95%CI 1.15-3.10, p< 0.01) as compared to USA (OR 1.32; 95%CI 1.13-1.53, p< 0.01).
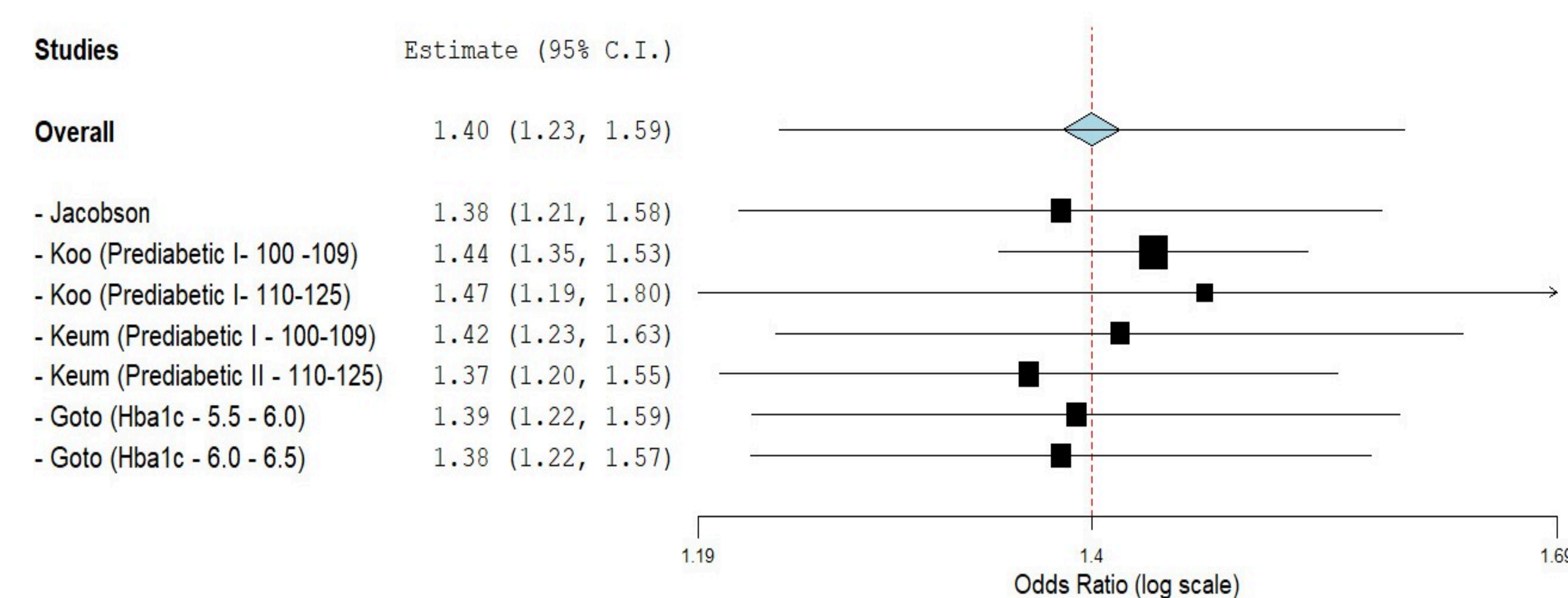
Discussion

This meta-analysis showed a 40% higher risk of pancreatic cancer in patients with prediabetes over a long-term median follow-up of over 8 years. A special screening protocol is warranted for pancreatic cancer screening which could lessen the disease burden including morbidity and mortality in high-risk patients.