Bicarbonate defective CFTR variants in chronic pancreatitis: A meta-analysis.

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INTRODUCTION

Cystic fibrosis transmembrane conductance regulator (CFTR) plays a central role in pancreatic ductal secretory functions by carrying Cl^- and HCO^{3-} ions across the apical membrane. Two **CFTR mutations that eliminate effective chloride conductance cause cystic fibrosis**. It has been hypothesized, that a group of mutations that cause **selective bicarbonate defect in CFTR channel function ($CFTR^{BD}$)** may play a role in the development of **chronic pancreatitis (CP)**. Although functional studies support this notion, large genetic association studies are lacking to confirm this association.

AIMS

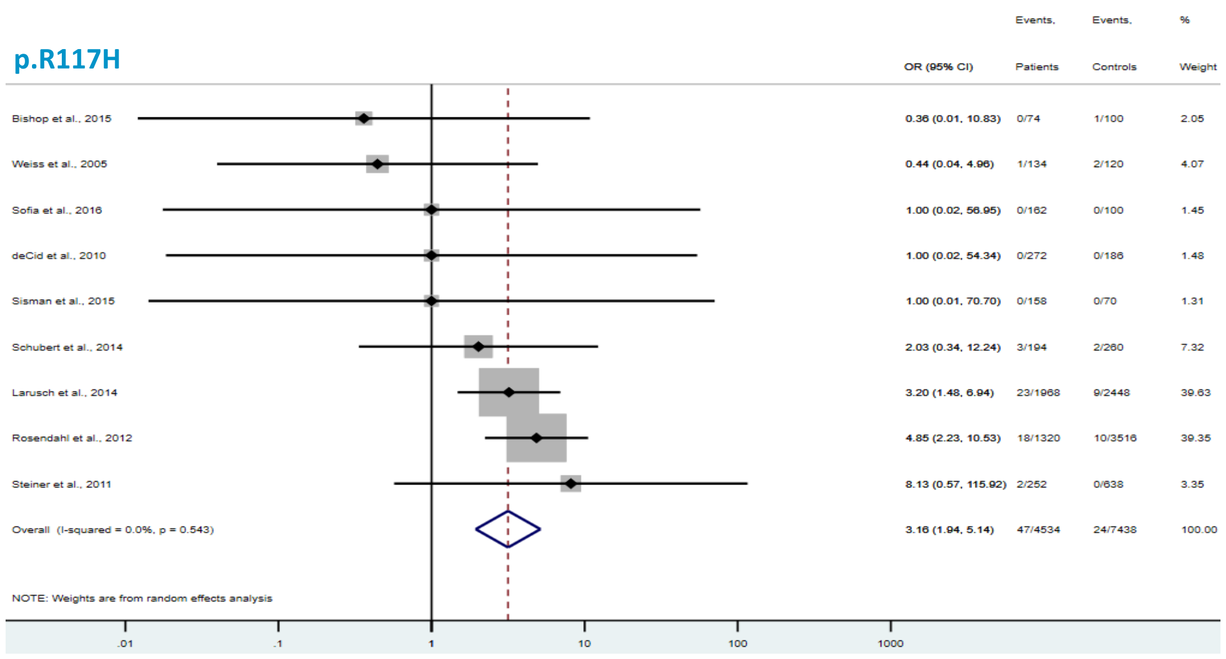
To investigate the **role of $CFTR^{BD}$** variants in **chronic pancreatitis**.

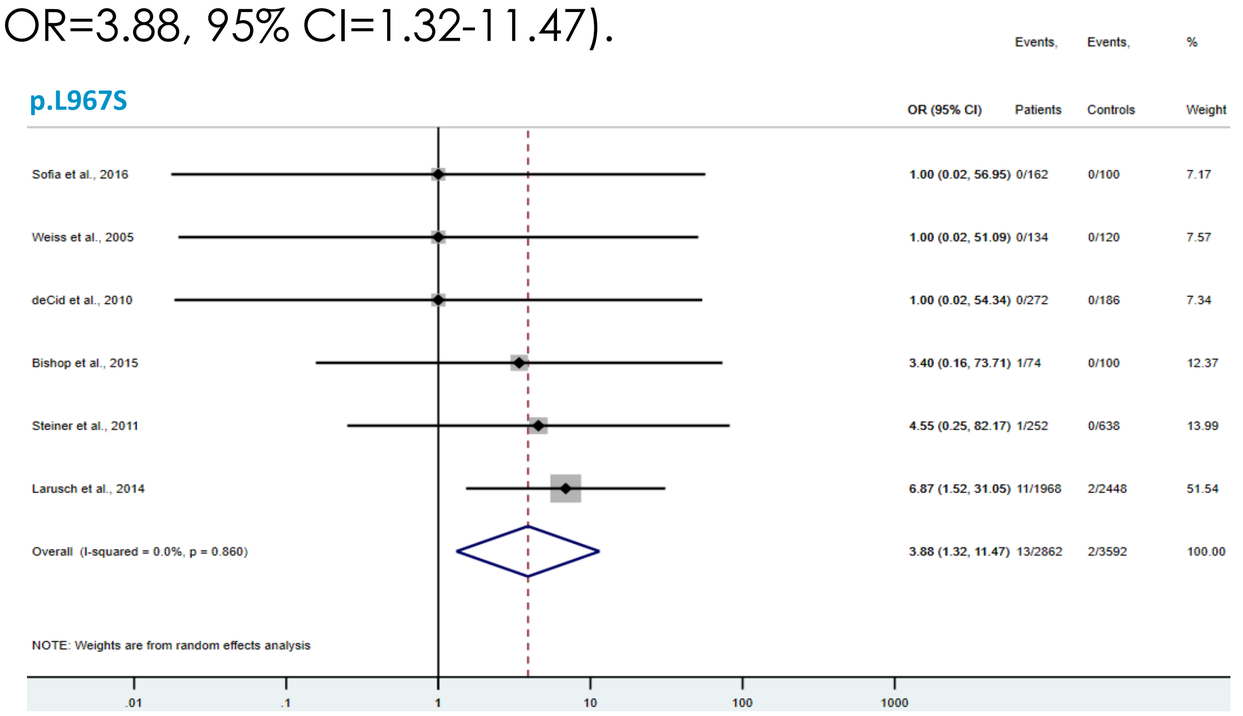
METHODS

A **systematic search** was conducted in 4 databases to identify **case-control studies** where the **nine $CFTR^{BD}$ variants (p.R74Q, p.R75Q, p.R117H, p.R170H, p.L967S, p.L997F, p.D1152H, p.S1235R, p.D1270N)** in pancreatitis were investigated. **Twenty-one articles** were eligible for qualitative synthesis. As these variants are rare in Asian and African populations, **cohorts with European ancestry** were analyzed further.

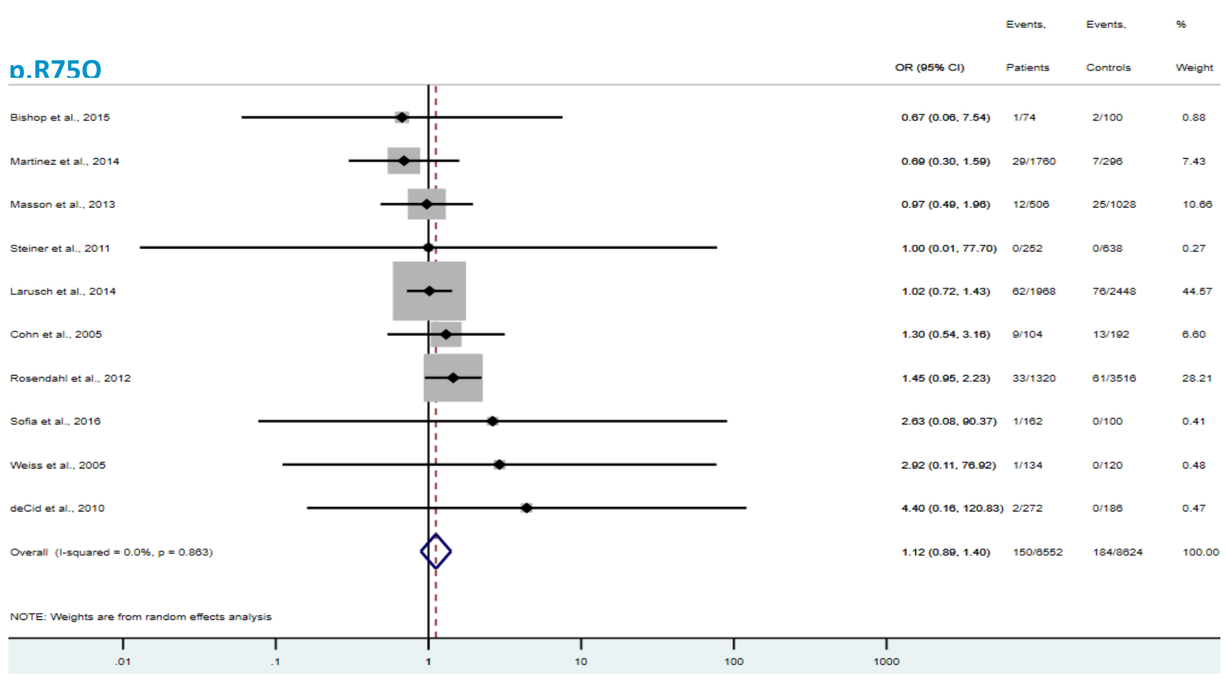
RESULTS

Variants **p.R117H and p.L967S** were **significantly overrepresented in pancreatitis cases** relative to controls (OR=3.16, 95% CI=1.94-5.14 and OR=3.88, 95% CI=1.32-11.47).

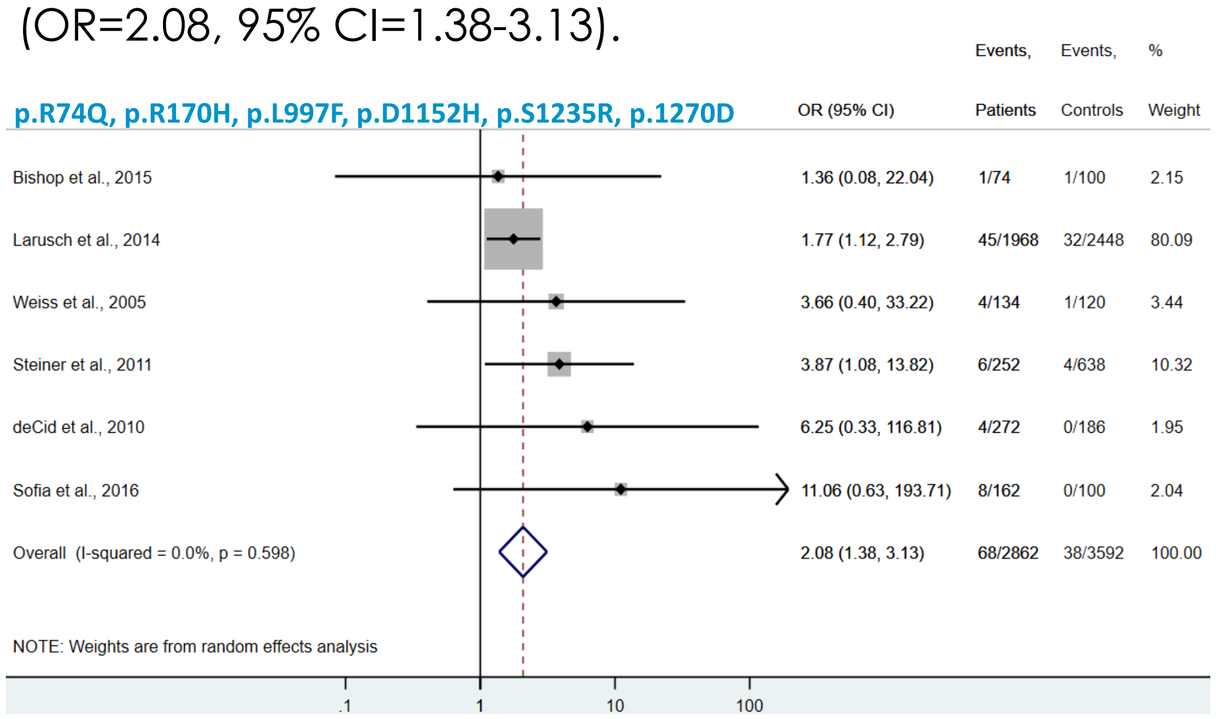




There was **no enrichment** of the relatively frequent **p.R75Q** mutation in patients compared to controls (OR=1.12, 95% CI=0.89-1.40).



Due to the rarity and/or inconclusive effect of **p.R74Q, p.R170H, p.L997F, p.D1152H, p.S1235R and p.1270D variants,** their cumulative analysis has been performed (OR=2.08, 95% CI=1.38-3.13).



CONCLUSIONS

Despite their similar functional effect on bicarbonate permeability and conductance, **$CFTR^{BD}$ variants affect chronic pancreatitis risk heterogeneously**. While there is **no relation between p.R75Q and CP**, variants **p.R117H and p.L967S significantly increase CP risk** and should be considered as risk factors for CP.

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