

# Peripheral blood cytokines in paediatric-onset inflammatory bowel disease - a systematic review and meta-analysis

S.Jansson<sup>1,2</sup>, A.Ehrström<sup>1,2</sup>, C.U.Rask<sup>3,4</sup>, J. Burisch<sup>2,5,6</sup>, M.E.Benros<sup>6,7</sup>, J.Seidelin<sup>6,8</sup>, M.Malham<sup>1,2,9,10</sup>, V.Wewer<sup>1,2,6</sup>

1) Department of Paediatrics and Adolescent Medicine, Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark 2) Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents, and Adults, Amager and Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark 3) Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Aarhus, Denmark 4) Department of Clinical Medicine, Aarhus University, Aarhus, Denmark 5) Gastro Unit, Medical Division, Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark 6) Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark 7) Copenhagen Research Centre for Biological and Precision Psychiatry, Mental Health Centre Copenhagen, Copenhagen University Hospital, Copenhagen, Denmark 8) Department of Digestive Diseases, Transplantation, and General Surgery, IBD section, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark 9) Department of Paediatric Gastroenterology and Nutrition, Royal Hospital for Children and Young People, Edinburgh, United Kingdom 10) Copenhagen Health Complexity Center, Department of Public Health, University of Copenhagen, Copenhagen, Denmark. Funding: S.Jansson and V.Wewer received funding from Aage and Johanne Louis Hansens Fond, Ferring Pharmaceuticals and Takeda Pharma A/S. The sponsors had no influence on study design, methodology or publication of results. E-mail: sabine.sophie.jansson@regionh.dk

## BACKGROUND

- Cytokines play a central role in the aetiology, disease severity and treatment of inflammatory bowel disease (IBD)
- Paediatric-onset IBD is an aggressive phenotype, but little is known about the cytokine levels in paediatric-onset IBD.

## AIM

- To summarize findings of cytokine levels in peripheral blood in patients with paediatric-onset IBD compared to healthy controls

## METHOD

PRISMA guidelines  
PROSPERO (ID: CRD42024579684)

Literature search on the 1st of August 2024  
Pubmed, EMBASE, Web of Science, Scopus

Paediatric, child, adolescent AND  
Crohn and ulcerative colitis, inflammatory bowel disease AND  
Cytokine, chemokine, interleukin, interferon, tumour necrosis factor

Patients with paediatric-onset IBD and healthy controls  
Cytokine levels in plasma or serum  
Method for measuring cytokine levels was described

Not stratifying for paediatric-onset IBD  
< 5 patients with paediatric-onset IBD  
Patients with other immune-mediated diseases

Pooled effect sizes of mean values were calculated using Hedges' g for any cytokine reported by two or more studies

☆☆☆ The Newcastle-Ottawa scale



## CONCLUSION

- IL-6 was increased in the peripheral blood of patients with paediatric-onset IBD
- Data on other cytokines were scarce.

## RESULTS

- Twenty-one studies met the inclusion criteria, including a total of 950 patients with paediatric-onset IBD, 481 healthy controls, and a total of 57 cytokines
- Interleukin-6 was increased in patients with paediatric-onset IBD compared to healthy controls (standardized mean difference 1.99, 95% confidence interval 1.12-2.85), Figure 3.
- Only two studies reported mean values of Tumour necrosis factor- $\alpha$ . Meta-analysis did not show a difference between patients and controls (standardized mean difference 0.36, 95% confidence interval -0.08-0.79)

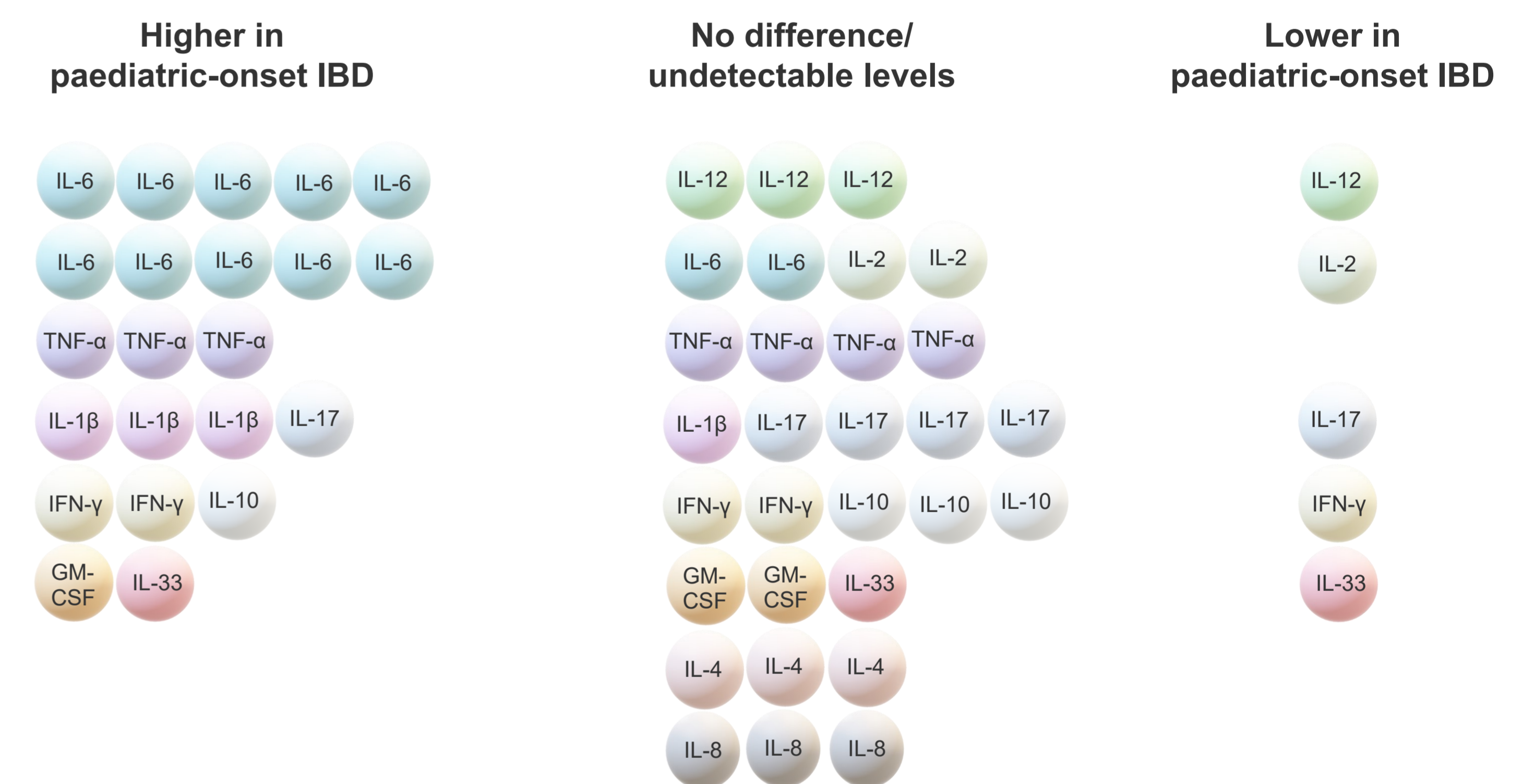


Figure 2: Number of studies reporting higher, lower or no difference of cytokine levels between patients with pediatric-onset IBD and controls (including all cytokines reported by three or more studies). One circle represents the findings from one study. IL: Interleukin, IFN: interferon, TNF: tumour necrosis factor, GM-CSF: Granulocyte-macrophage colony-stimulating factor

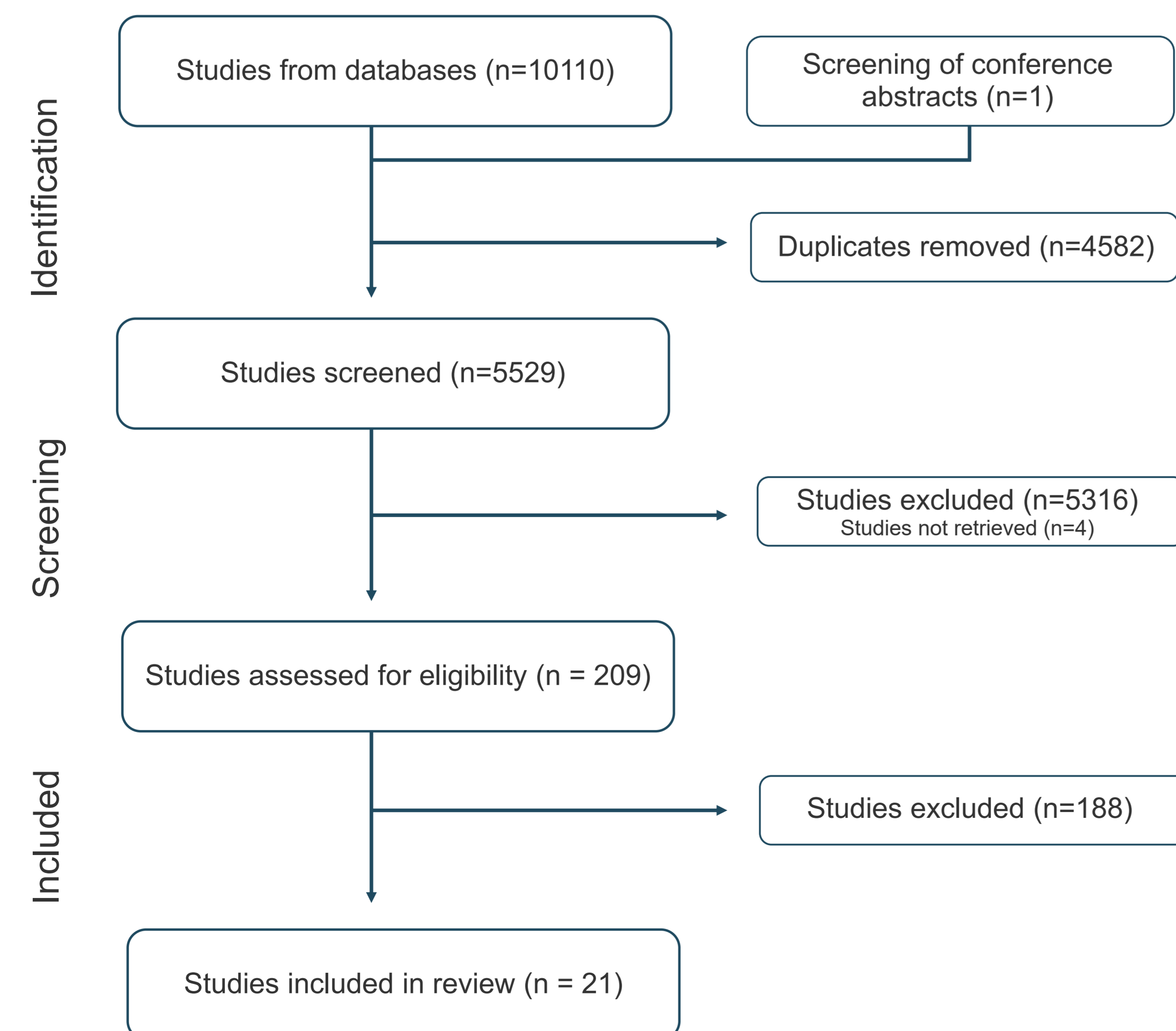


Figure 1: PRISMA flow chart of study selection

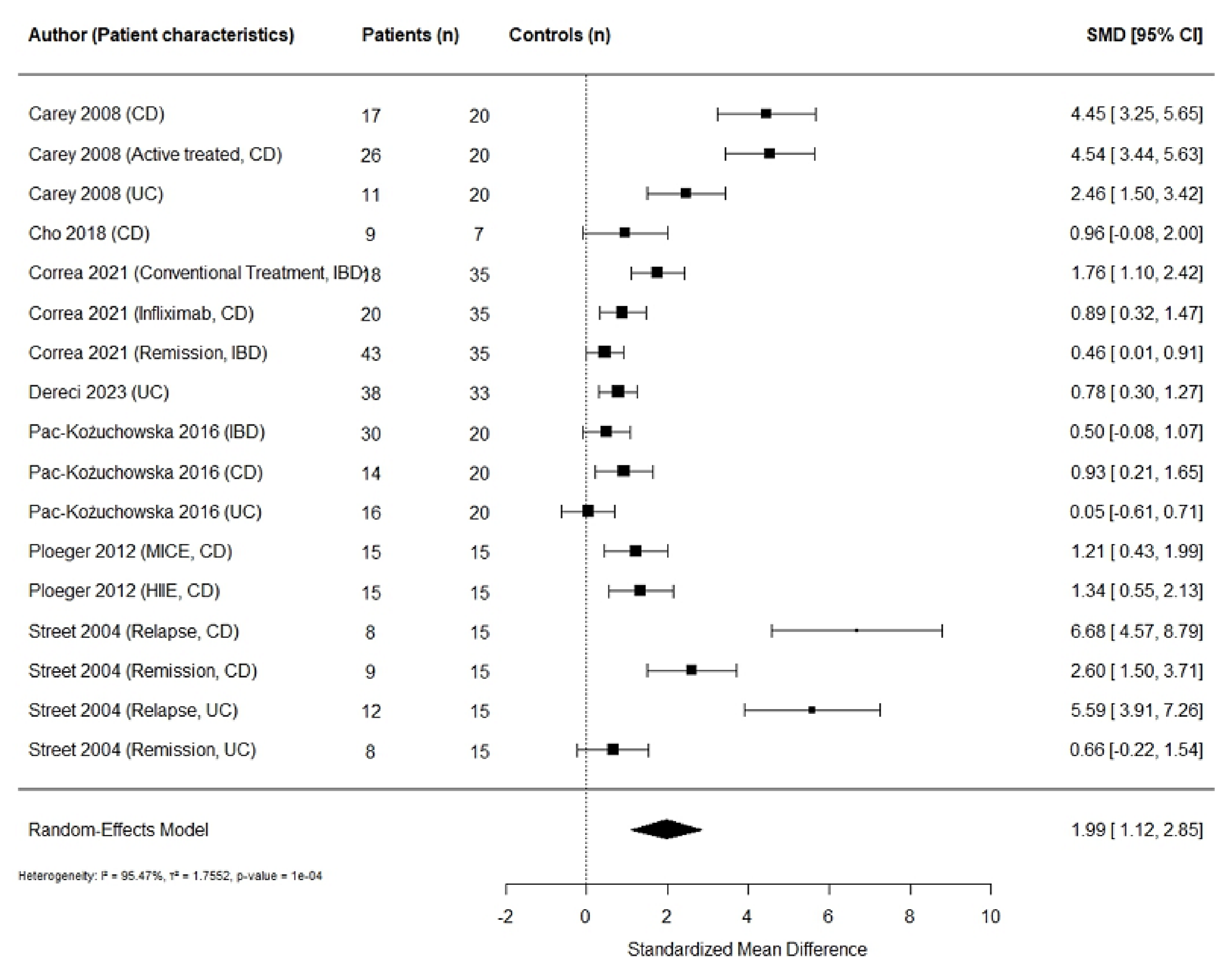


Figure 3: Meta-analysis of IL-6 levels  
SMD: standardized mean difference; CI: confidence interval; CD: Chron's disease; UC: ulcerative colitis; IBD: inflammatory bowel disease; MICE: moderate intensity continuous exercise, HIIE: high intensity intermittent exercise (Ploeger 2012 investigated the impact of exercise on cytokine levels).