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SAFETY AND EFFICACY OF AUGMENTATION THERAPY IN PATIENTS WITH ALPHA-1-ANTITRYPSIN DEFICIENCY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND & OBJECTIVE

- Alpha-1 antitrypsin deficiency (AATD) is an underdiagnosed genetic condition characterised by reduced level of alpha-1 antitrypsin enzyme which predisposes individuals to lung, liver, or other systemic diseases
- Augmentation therapy (AT) is the only licensed treatment for the patients with AATD associated lung diseases
- The purpose of this study was to perform a systematic literature review (SLR) and meta-analysis of publications evaluating the safety and efficacy of approved AT in AATD

METHODS

- An SLR was conducted from database inception to May 2022 by searching three major biomedical databases (Embase®, PubMed®, CENTRAL®) to identify relevant randomized control trials (RCT) evaluating AT versus placebo in AATD patients
- References of identified SLR/network meta-analyses (NMA) were investigated for validation
- The SLR followed two review and a quality control process for screening and data extractions
- The risk of bias assessment was performed using Cochrane's RoB-2 tool

RESULTS

- The SLR identified 9 RCTs assessing AT in AATD, of which only 3 RCTs met the inclusion criteria **[Fig 1]** and were included in the meta-analysis
- A PRISMA diagram for the screening process is presented in **Fig 2**
- The RCTs contributing to meta-analysis varied regarding the trial duration, ranging from two to three years
- ATs were associated with significantly better efficacy compared to placebo regarding the annual deterioration in lung density (random-effects, Sidik-Jonkman model, mean difference [MD]: 0.79; 95% CI: 0.29 to 1.28) **[Fig 3]**

- The other analysed efficiency outcomes (annual % predicted FEV1 and diffusing capacity of the lungs for carbon monoxide) were comparable (non-significant) between AT and placebo **[Fig 4, 5]**
- In terms of safety outcomes i.e., any adverse events (AE), any serious AEs, and upper respiratory tract infections, the results of meta-analysis were also comparable between AT and placebo **[Fig 6, 7, 8]**

Figure 1: Prespecified PICOS eligibility criteria for selection of evidence

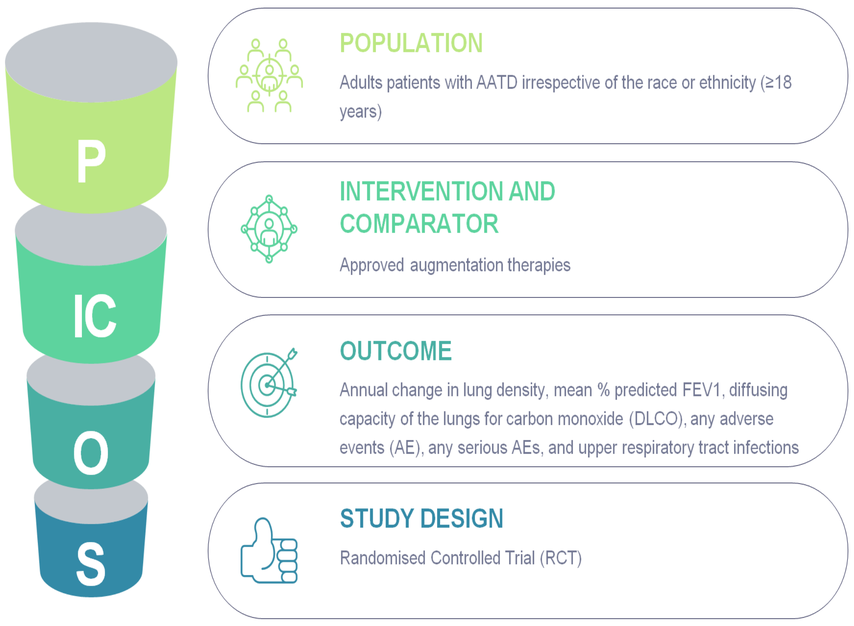


Figure 2: PRISMA diagram for the screening process

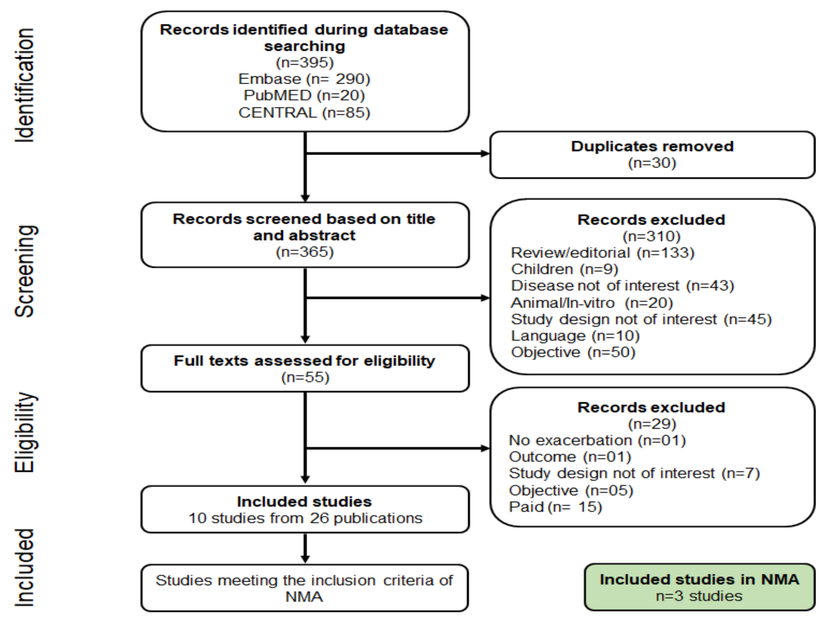


Figure 3: Forest plot of comparison between AT vs. Placebo for mean annual change in lung density

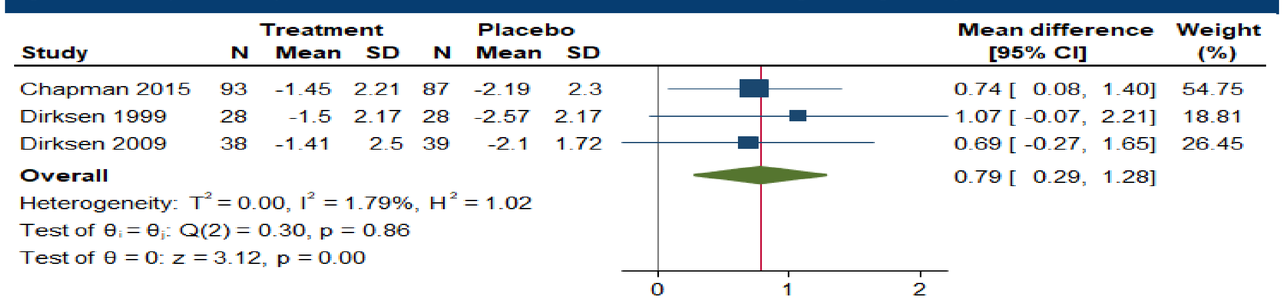


Figure 4: Forest plot of comparison between AT vs. Placebo for mean % predicted FEV1

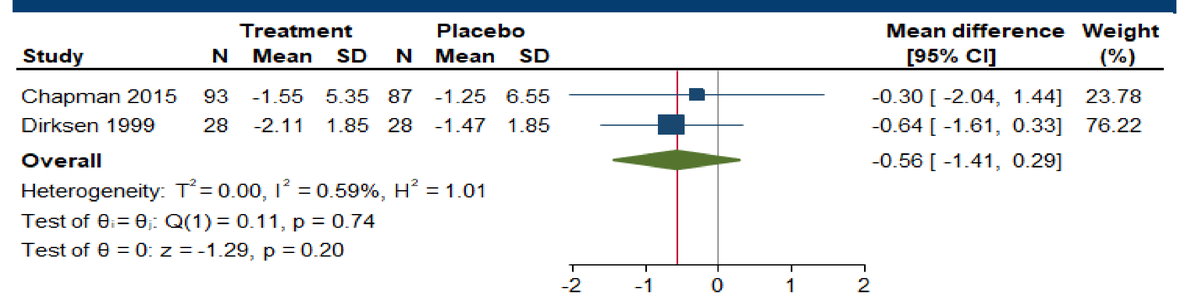


Figure 5: Forest plot of comparison between AT vs. Placebo for mean change in DLCO

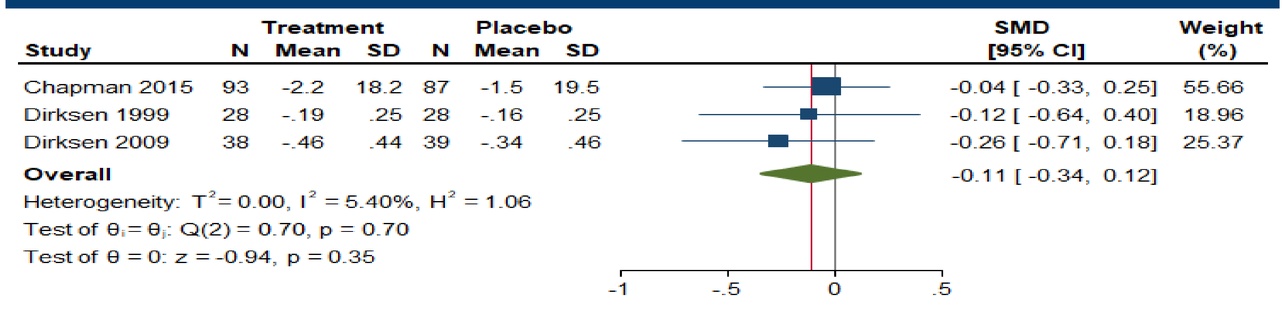


Figure 6: Forest plot of comparison between AT vs. Placebo for any adverse event

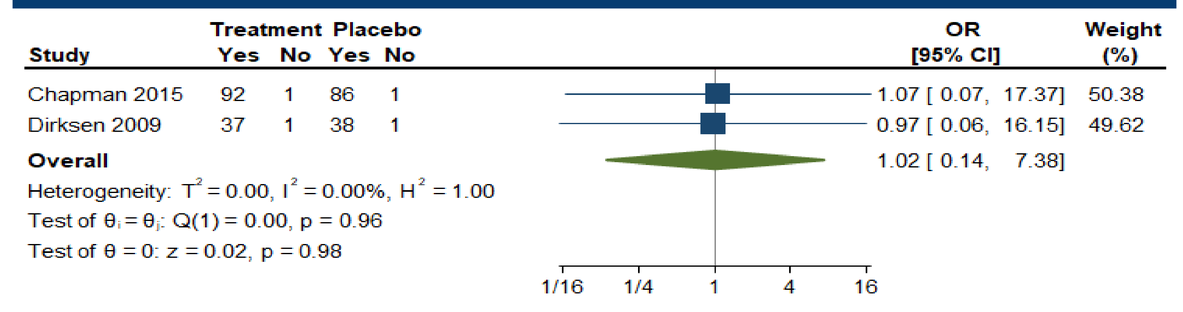


Figure 7: Forest plot of comparison between AT vs. Placebo for any serious adverse event

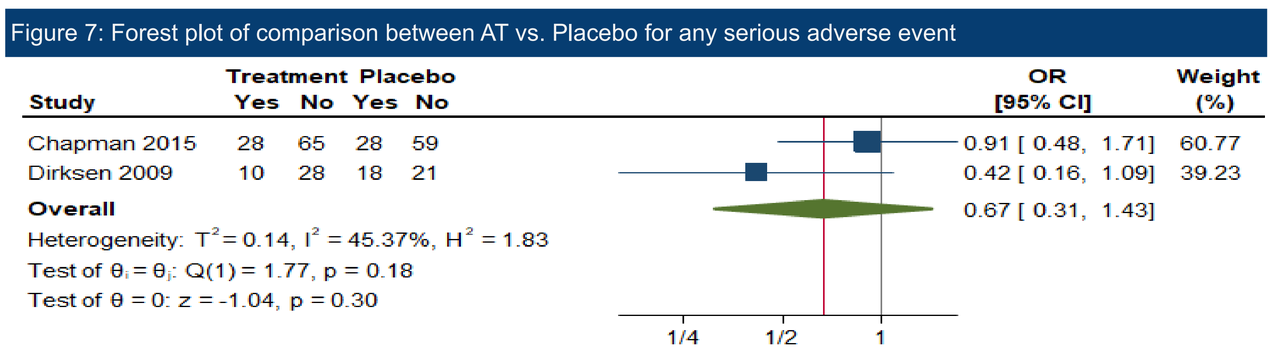
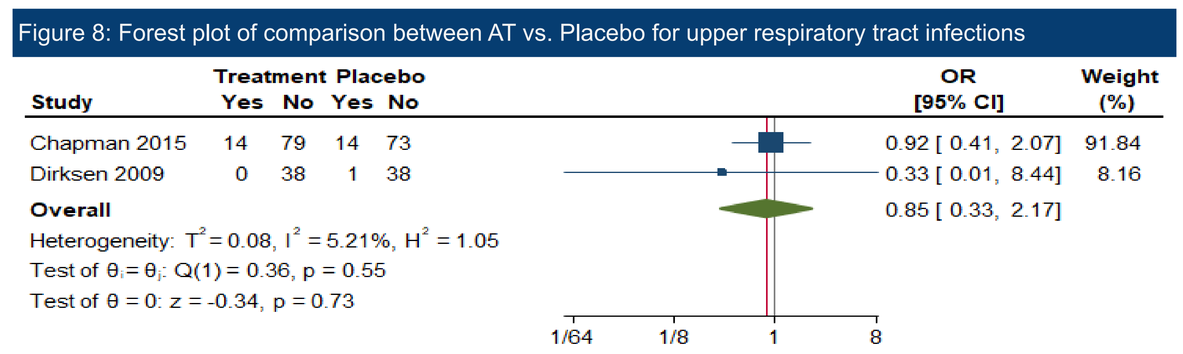


Figure 8: Forest plot of comparison between AT vs. Placebo for upper respiratory tract infections



CONCLUSIONS

- The SLR and meta-analysis highlight the favourable efficacy of AT for the treatment of AATD in terms of lung density, indicating reduction in emphysema progression
- The evidence base for AT in AATD is scarce, hence, more studies examining AT are warranted for the treatment of adult patients with AATD

REFERENCES

1. Dirksen, A., Dijkman, J.H., et al. A randomized clinical trial of alpha1-antitrypsin augmentation therapy. Am J Respir Crit Care Med. 1999;160(5 Pt I):1468–1472
2. Dirksen, A., Piitulainen, E., et al. Exploring the role of CT densitometry: a randomised study of augmentation therapy in alpha1-antitrypsin deficiency. Eur Respir J. 2009;33(6):1345–1353\
3. Chapman, K.R., Burdon, J.G., et al. Intravenous augmentation treatment and lung density in severe alpha1 antitrypsin deficiency (RAPID): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;386(9991):360–368.

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Disclosure
BS, PR, GB, AS, the authors, declare that they have no conflict of interest

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