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**Predictors of response to low-dose amitriptyline for irritable bowel syndrome**

**Wright-Hughes A, Ow P, Alderson S, *et al*. Predictors of response to low-dose amitriptyline for irritable bowel syndrome and efficacy and tolerability according to subtype: post hoc analyses from the ATLANTIS trial. *Gut* 2025; 74(5): 728-739. doi: 10.1136/gutjnl-2024-334490.**

The ATLANTIS trial (AmitripTyline at Low-dose ANd Titrated for Irritable bowel syndrome as Second-line treatment) was a randomised, double-blind, superiority trial enrolling 463 adults with IBS (irritable bowel syndrome). It demonstrated that low-dose amitriptyline (10-30 mg/day) was more effective than placebo in terms of improvement in IBS-severity scoring system (SSS) score at six months. In this exploratory sub-analysis, Wright-Hughes et al., aimed to determine any predictors of amitriptyline response among all patients randomised to the trial medication (intention-to-treat). They investigated whether baseline patient characteristics (i.e., effect modifiers) influenced the response to amitriptyline but using clinically relevant cut-offs or median values. They examined a broad range of modifiers including age, sex, socioeconomic status (based on Index of Multiple Deprivation), IBS subtype, PHQ-12 somatic symptom score, anxiety and depression scores, and IBS severity. They assessed these modifiers in terms of their effect on total IBS-SSS score, subjective global assessment (SGA) of relief of symptoms, and ≥30% improvement in abdominal pain. While subgroup effects were broadly consistent in direction, significant interaction p-values indicated that older age (≥50 years) and greater deprivation were associated with stronger treatment effects. Larger effects were observed in men, those with IBS-D (IBS-diarrhoea), and individuals with higher somatic symptom scores across all outcomes but this did not reach significance. Tolerability of amitriptyline was broadly similar across IBS subtypes based on descriptive data from the antidepressant side effect checklist (ASEC), with no evidence of worsening symptoms in any group, including those with IBS-C (IBS-constipation) or mixed bowel habits. Ultimately, Wright-Hughes et al. demonstrate through the sub-analysis of the ATLANTIS trial, that amitriptyline is a well-tolerated second-line treatment across all IBS subtypes, and characteristics including age and deprivation index may be associated with an enhanced treatment response.