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## BACKGROUND

Prescribing for heart failure (HF) patients may not always reflect the recommendations of international guidelines. Tools have been developed for assessing guideline adherence in HF. The Guideline Adherence Index (GAI) is the most frequently used and applied quantitative tool for this purpose. The aim of this work is to perform a meta-analysis of studies utilising the GAI to assess adherence to HF prescribing guidelines, the effect of guideline adherence on clinical outcomes and clinical associates of guideline adherence measured by GAI.

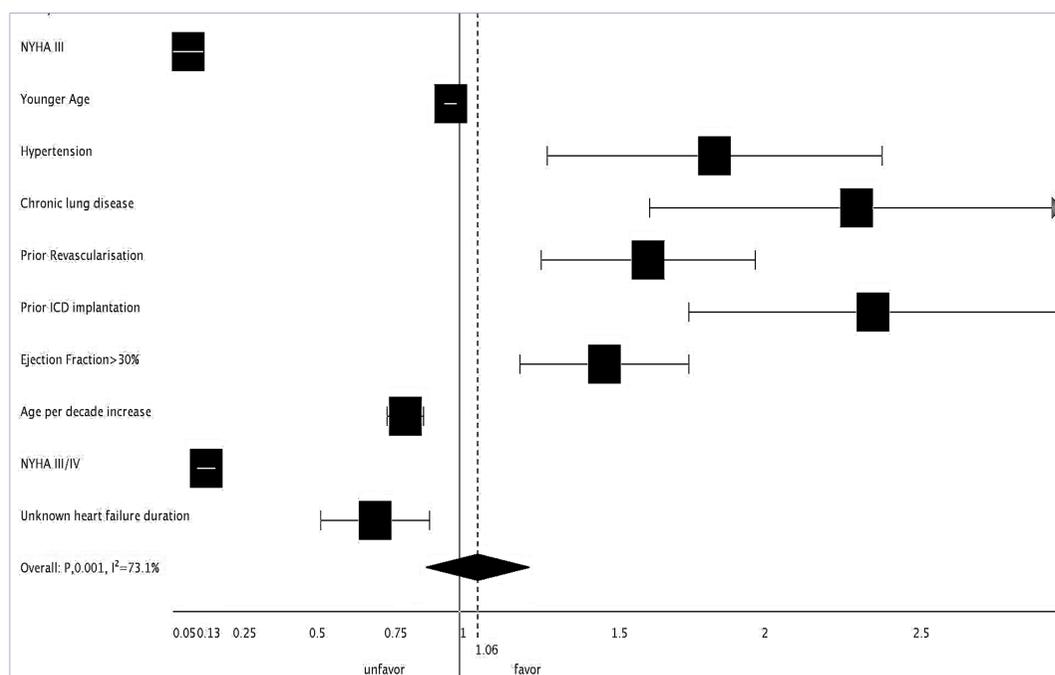
## METHODS

A systematic search of 11 electronic databases was performed to identify all quantitative studies reporting the GAI as a tool to measure guideline adherence in HF patients aged  $\geq 18$  years. All full-text GAI-based studies were included. The GAI considers patient eligibility for the indicated therapy regarding the top three (GAI-3) recommended HF medications (ACE inhibitor/ARB, beta-blocker, aldosterone antagonist). High GAI is defined as prescription of  $\geq 2$  recommended agents while Low GAI is defined as prescription of  $< 2$  agents. Pooled odd ratios (OR) and respective 95% confidence intervals (CIs) were displayed using the forest plot generator of DistillerSR<sup>®</sup> software. Hazard ratios (HR) and respective 95% CIs were pooled using NCSS<sup>®</sup> Statistical Software v11. Risk of bias was assessed using the GRACE checklist.

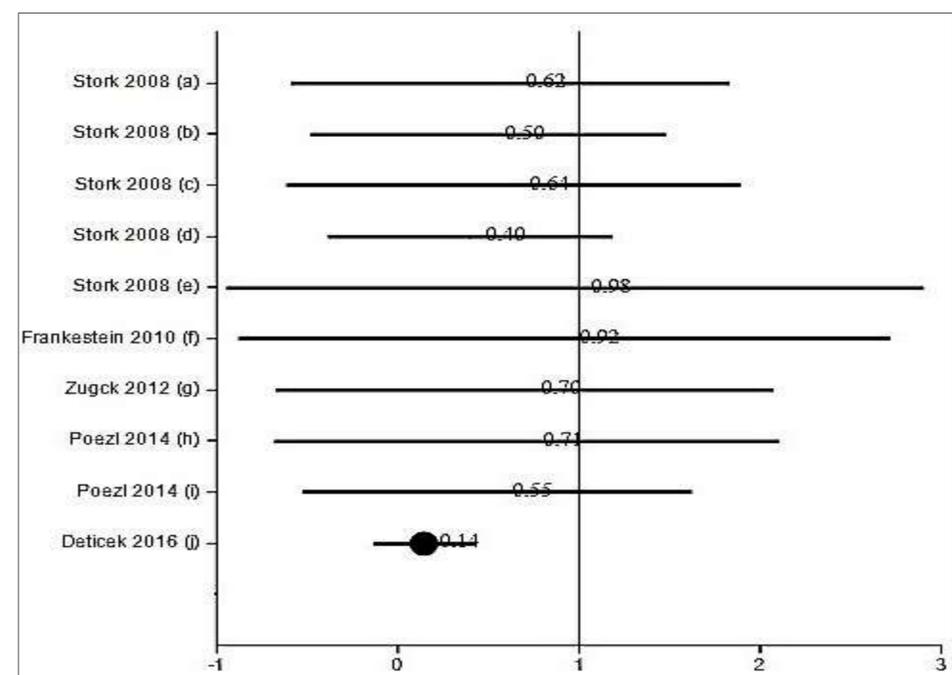
## RESULTS

- Thirteen observational studies using GAI were identified. One study was excluded from the meta-analysis due to its poor quality. A total of 14,354 HF patients (mean age 69.7 years) were enrolled. All studies included patients with HF with reduced ejection fraction (EF) while patients with HF with preserved EF were included in seven studies. GAI-3 scores varied from 14-95%. The rate of achievement of High GAI-3 rose from 38% in 2005 to 71% in 2016. **Figure 1** displays the multivariable associates of High GAI.
- One study reported rehospitalisation rates and found that patients with a High GAI score were at reduced risk of rehospitalisation over a 6-month follow-up period compared to those with Low GAI score (HR= 0.64, 95%CI 0.41-1.00). The rehospitalisation rate was reported in four studies and was lower for those with High GAI score compared to those with Low GAI scores (22.5% vs. 24.5% respectively).
- Two studies compared the estimated mortality risk between patients with High GAI compared to those with Low GAI scores and demonstrated lower mortality risk in those with High GAI score (7.7% vs. 16.5%, Log rank  $p \leq 0.005$ ). Six studies reported the association between High GAI achievement and patient mortality and overall, High GAI was associated with lower mortality (overall HR= 0.29, 95%CI 0.06-0.51, **Figure 2**).

**Figure 1. Patient factors significantly associated with High GAI in multivariable analysis.**



**Figure 2. Meta-analysis of GAI effect on mortality risk in heart failure patients.**



**Figure legends:** - a: GAI-3 Medium Vs poor; b: GAI-3 High Vs low; c: GAI-5 Medium Vs poor; d: GAI-5 High Vs low; e: High dose of ACEI/ARBs; f: GAI per 10 % increase; g: GAI-3; h: Improved GAI over 1 year; i: Improved Target dose based GAI over 1 year; j: GAI-123 Vs GAI-0.

## CONCLUSIONS

Guideline adherence in HF patients measured by GAI varies between settings however no study has reported a GAI greater than 71%. High GAI is associated with reduced mortality and rehospitalisation. Improving guideline adherence may be beneficial for HF patients outcomes.