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**Trastuzumab uptake in HER2-positive breast cancer patients: a systematic review and meta-analysis of observational studies**

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**OBJECTIVES:** Overexpression of the HER2 gene is predictive of treatment benefit with trastuzumab therapy for breast cancer (BC) patients. The study objective was to investigate whether all eligible patients with HER2-positive BC initiated trastuzumab therapy.

**METHODS:** A systematic search was conducted through PubMed, Web of Science and Cochrane Library. From 2651 studies identified, 107 observational studies were included for full text review, of which 26 met the inclusion criteria and an additional 7 studies were identified through citation searching. Two independent reviewers extracted data for accuracy and completeness.

**RESULTS:** From33 observational studies, 14,644 patients were exposed to trastuzumab therapy. across studies,Sample sizes ranged from 11 to 1928 and included patients from 10 countries. Studies were heterogenous and few studies accounted for confounders. We identified large variability in uptake of trastuzumab in HER2-positive early BC patients (9.1-100%) and metastatic BC patients (50.8-84.0%). The pooled uptake was 71.3% (95% CI 64.6-77.9), with high heterogeneity (I2=99.05%). Predictors of higher uptake included younger age OR 2.09 (95% CI 1.36-3.20) and lower Charlson Comorbidity Index of patients OR 1.62 (95% CI 1.32-1.99). In addition, tumour characteristics including positive lymph node status OR 2.45 (95% CI 1.83-3.29), higher tumor grade OR 1.73 (95% CI 1.23-2.45), larger tumor size OR 1.80 (95% CI 1.54-2.10), advanced tumor stage OR 2.07 (95% CI 1.44-2.96) and hormone receptor negative OR 1.54 (95% CI 1.35-1.77) were associated with higher uptake.

**CONCLUSIONS:** Uptake of trastuzumab therapy varied widely between studies and across subgroups. Findings should be interpreted with caution due to study heterogeneity and lack of reporting for confounding factors. Additional studies of patient level data which control for confounders are needed to understand more about inequalities in uptake.

**Registration:** Systematic review protocol was registered with PROSPERO, identification number: CRD42017073218

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