**Systematic literature review (SLR) of disease burden related to first-line (1L) unresectable, locally advanced, or metastatic gastric cancer (GC) and gastroesophageal junction (GEJ) adenocarcinoma**

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**ABSTRACT**

**Objectives**: To conduct an SLR of disease burden, specifically health state utility values (HSUV), health-related quality of life (HRQoL), economic evaluations, and healthcare resource use (HCRU) associated with 1L treatments of unresectable locally advanced or metastatic human epidermal growth factor receptor 2 (HER2) negative GC/GEJ.

**Methods**: Embase, Ovid MEDLINE®, and Cochrane CENTRAL were searched from inception to February 2024 for relevant English-language studies. Supplementary hand searches were also conducted. Study selection was performed in duplicate. Key study, patient, and outcome details were extracted.

**Results**: Of 7963 records identified, 44 unique studies and 6 health technology assessment submissions were included. Among published US-based cost-utility analyses (CUAs) for programmed cell death protein 1 (PD-1) inhibitors, incremental cost-utility ratios (ICURs) ranged from $240,635-$944,089 (USD, year not reported) for nivolumab and $96,550-$483,742 (2021 USD) for pembrolizumab. One CUA compared pembrolizumab to nivolumab with an ICUR of $413,706 (2023 USD). Where reported, lower ICURs were observed among PD-1-positive subgroups (combined positive score [CPS] ≥5 and ≥1) versus overall patient populations. Two studies reported HSUVs for HER2-negative GC patients; baseline values ranged from 0.81-0.83, and on-treatment HSUVs ranged from 0.510-0.940. Among CUAs, HSUVs ranged from 0.793-0.897 for progression-free survival and 0.577-0.822 for progressive disease. Adding PD-1 inhibitors to chemotherapy, particularly tislelizumab and nivolumab, was typically associated with maintained or better HRQoL versus chemotherapy alone. All identified HCRU outcomes related to chemotherapy; the most common HCRU outcomes reported were proportion of patients with hospitalizations (22.2%-46.2%) and emergency room visits (25.3%-42.6%).

**Conclusions**: Adding PD-1 inhibitors to chemotherapy resulted in better HRQoL outcomes versus chemotherapy alone. Few CUAs compared PD-1 inhibitors to one another, and no HCRU outcomes were reported for these treatments, representing important data gaps. Future studies on economic burden and humanistic outcomes associated with these innovative treatments will offer insights for clinical decision-making.