Lupus nephritis (LN) is a serious and common complication of systemic lupus erythematosus (SLE) associated with considerable morbidity, including an increased risk of end-stage kidney disease (ESKD). Many patients do not achieve sustained remission despite treatment, leading to adverse disease outcomes. The objective of this literature review was to summarize evidence on natural history, burden of comorbidities, and real-world (RW) effectiveness of standard of care (SOC) therapy in European patients with LN.

Methods
A targeted literature review (TLR) was conducted in MEDLINE/PubMed to identify studies in adult patients diagnosed with LN. A search strategy was developed separately for the two databases to identify relevant peer-reviewed publications published in English between March 2012 and March 2022, and conference abstracts indexed in Embase since 2019. All records were screened by a single reviewer according to pre-specified inclusion and exclusion criteria.

Results
Of 4,216 records identified in the medical databases, 55 studies reported on long-term outcomes of RW and effectiveness of SOC in European adults with LN (Figure 1). The majority of studies were observational and retrospective in study design.

Background
- LN is a serious and common complication of SLE
- Associated with considerable morbidity
- Increased risk of end-stage kidney disease
- Many patients do not achieve sustained remission
- Objective: Summarize evidence on natural history, burden of comorbidities, and real-world (RW) effectiveness of standard of care (SOC) therapy in European patients with LN.

Methods
- Targeted literature review (TLR) in MEDLINE/PubMed
- Inclusion criteria: Studies in adult patients with LN, published in English between March 2012 and March 2022, and conference abstracts indexed in Embase since 2019.
- All records screened by a single reviewer.

Results
- 55 studies reported on long-term outcomes of RW and effectiveness of SOC in European adults with LN.
- Most studies were observational and retrospective.

Comorbidities & Mortality
- Among patients with SLE, over one-third developed LN, with the majority developing within 5 years of their SLE diagnosis.
- Adults with LN frequently suffered from serious infection (19-35%), chronic kidney disease (CKD) or ESKD (6-22%), and cardiovascular disease (CVD) (26%).
- Chronic immunosuppression with high-dose steroids (≥0.5mg/kg/day) further contributed to increased infections and patients on high-dose regimens had 5-times increased risk of infections compared to those on low-dose regimens (Figure 2).
- LN was associated with a higher mortality risk compared to SLE or other lupus manifestations (p<0.001), and infections (8-32%), CVD (22-58%), or malignancies (5-27%) were the most common causes of death.

Treatment Response / Remission
- Between 30-86% of patients achieved renal remission after receiving renal response/remission (CRR) within 1 year of starting SOC therapy.
- For patients with refractory LN, 29-64% of patients treated with rituximab achieved CRR after 1 year, while 23-35% of patients active LN despite SOC treated with belimumab achieved CRR after 1 year of treatment.
- Lack of response to therapy after 1 year was significantly associated with increased mortality and CKD risk.

Figure 3. Rates of CRR after starting SOC therapy
- CRR varied across patients with LN and lacked of response to treatment was significantly associated with worse long-term outcomes.

Renal Relapse / Flare after Achieving Response
- Uncontrolled LN is associated with poor long-term outcomes, such as CKD/ESKD and death, and significant comorbidities such as serious infections and CVDs.
- Long-term immunosuppression contributes to increased morbidity and mortality, especially due to infections.
- Despite initial response to treatment, a notable proportion of patients experience renal relapse, indicating a need for effective therapies that provide sustained remission.

CONCLUSIONS
- Uncontrolled LN is associated with poor long-term outcomes, such as CKD/ESKD and death, and significant comorbidities.
- Despite initial response to treatment, a notable proportion of patients experience renal relapse, indicating a need for effective therapies that provide sustained remission.

AUTHOR DISCLOSURES & ACKNOWLEDGMENTS
- Author disclosures and acknowledgments are provided in the article.

REFERENCES
- A comprehensive list of references is provided in the article.