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Targeted Literature Review and Qualitative Synthesis of Oral Corticosteroid-Related Adverse Event Burden in Autoimmune Conditions

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BACKGROUND

Exploring the Adverse Event Burden Associated with Treatment of Autoimmune Conditions

- Patients with autoimmune conditions are often managed with oral corticosteroids (OCS) for long durations, which can be prescribed at relatively high doses.
- Despite common use of OCS, there is limited information on the general clinical and economic burden of OCS across disease areas.
- A targeted literature review was conducted with the following key objectives: **(1) understand the types and rates of adverse events (AEs), and (2) understand economic impacts, associated with OCS-related AEs.**

METHODS

Targeted Literature Review (TLR)

- Studies published in January 2017-October 2024 were identified using Embase®, MEDLINE®, Cochrane Database of Systematic Reviews, NHS Economic Evaluation Database, and Health Technology Assessment Databases via OvidSP.
- Search strategy was informed by clinical input and included terms for corticosteroids, autoimmune conditions, and AEs.
- To supplement the search strategy, a hand search was also conducted via Google Scholar and PubMed between 2009-2024.

	PICOS Elements	
	Inclusion Criteria	**Exclusion Criteria**
Population	Patients with autoimmune diseases*	Patients with non-autoimmune diseases
Interventions	Oral corticosteroids	Non-corticosteroids Non-oral
Comparators	Any or none	—
Outcomes	Steroid-related AE incidence/rates/frequency	—
Study Design	Registries Administrative claims data Chart reviews and electronic medical records SLR/MA Economic models	Case reports, case series, surveys, non-systematic literature reviews, narrative reviews, editorials, letters, opinions, animal/preclinical studies, individual clinical trials
Language	English only	Non-English
Publication Year	Published 2017-2024	Published 2016 or earlier

* Patients with autoimmune diseases, including but not limited to: rheumatoid arthritis, lupus, dermatomyositis, polymyositis, sarcoidosis, psoriasis, psoriatic arthritis, neuromyelitis, multiple sclerosis, myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, thyroid eye disease, multifocal motor neuropathy, congenital myasthenic syndrome, amyotrophic lateral sclerosis, primary immune thrombocytopenia, bullous pemphigoid, dermatomyositis, membranous nephropathy, lupus nephropathy, antibody mediated rejection, delayed graft function.

RESULTS

Studies Identified in TLR

- From the TLR, 145 total studies were identified, with 18 additional studies identified via hand-search techniques such as snowballing. 26 studies met final inclusion criteria (Figure 1, Table 1).[1-26]

AEs Commonly Associated with OCS Use

- OCS treatment-associated AEs reported in at least two studies included: Bone (osteoporosis, fracture, osteonecrosis), infection (pneumonia, sepsis), renal (impairment), cardiovascular, metabolic (diabetes, weight gain, lipodystrophy), ocular (cataracts, glaucoma), gastric (peptic ulcer, nausea, vomiting), psychiatric (mood disorders, psychosis, suicidal behavior, sleep disturbance), and induced hormone dysfunction (cushingoid, adrenal insufficiency).

Clinical Burdens of Long-term OCS Use

- For most AEs, long-term OCS use was associated with significant risks of increased incidence.[1]
- Some studies reported on the correlation between OCS dose and AEs (generally, higher dose correlated with higher incidence),[1-19] while other studies reported on the association between longer OCS duration and higher risk of AEs[1,7,11,13,20] (Figure 2).
- Higher mortality rates for patients taking OCS were reported in 6 studies[2,10,17,19,21,22] with significant associations reported in 3 studies.[2,17,19] Across these studies, mortality was attributed to several causes such as infections, pulmonary embolism, and myocardial infarction, with one study reporting a 5- to 7-fold increase in suicide attempts for patients who were taking OCS compared to those who were not.[2]

Economic Burdens of Long-term OCS Use

- The economic burden of treatment-related AEs was sensitive to the specific details of the study such as disease and severity, with average annual per patient estimates ranging from $340 (2010 USD) among an asthmatic population[11] to $25,504 (2020 USD) in patients with polymyalgia rheumatica.[6]
- Both healthcare resource utilization and costs were found to increase with OCS dose.[6,8,11,13-15]
- Costs of treatment-associated AEs can be burdensome for patients and payers (Table 2),[8,13] with higher costs incurred at higher cumulative dose levels (above 1800mg per year).[15]
- Use of OCS was significantly associated with an increase in infection-related hospitalization.[3]
- In one model, 50% sparing at the 15mg maintenance dose level yielded lifetime gains of 0.36 quality-adjusted life years (QALY).[21]

FIGURE 1 PRISMA Diagram

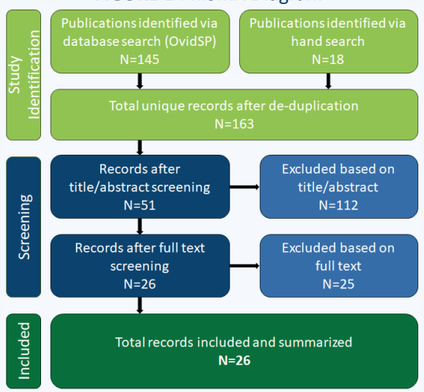
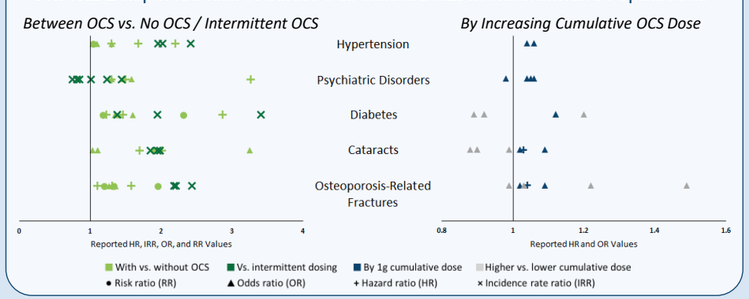


TABLE 1 Studies Identified

Data Reported	Number of Studies
Disease-agnostic/broad	8
Clinical burden	
Types of AEs	26
Rates of AEs	26
Mortality	6
Economic Burden	
Costs	7
Hospitalizations	2
QALY impact	1

FIGURE 2 Reported Risk of Select OCS-Related AEs in Autoimmune Populations



LIMITATIONS

The review was subject to standard search and selection biases and there was a high level of study heterogeneity. Follow-up periods for cost and AE reporting differed between studies. Data are summarized qualitatively rather than via meta-analysis and should be interpreted with these limitations in mind.

TABLE 2 Reported Annual Costs of OCS-Related AEs in Autoimmune Populations

			Reported Annual Costs					
	Cost Unit (Currency Year)	**Country**	**Fractures**	**Diabetes**	**Psychiatric Disorders**	**Hypertension**	**Cataracts**	**Overall**
Manson (2009)[13]	Per episode per year (2007 GBP)	UK	£6,541	£2,520	–	–	£891	–
Sarnes (2011)[8]	Per episode per year (2009 USD)	International	$1,743-$18,358	$3,370-$5,411	$1,914-$6,012	$1,511	$1,913-$4,416	–
Shah (2013)[14]	Mean annual cost of AE management (2010 USD)	US	–	–	–	–	–	$4,607
Best (2018)[15]	Adjusted* cost per patient over a year (2013 USD)	US	$6,360-$11,768	$5,606-$11,480	–	–	$908-$1,329	–
Curtis (2024)[6]	Total all-cause costs per patient 6-18 months post-index (2020 USD)	US	–	–	–	–	–	Median: $6,821 Mean: $25,504

* Adjusted via regression for patient demographics and additional metrics related to autoimmune disease severity, comorbidities, and treatment.

KEY TAKEAWAYS

Across disease areas, OCS use is linked to a range of AEs, including severe and life-threatening conditions, and imposes substantial clinical and economic burden.

Further research is needed to quantify the cost and quality-of-life burden of long-term OCS-related AEs among patients with autoimmune conditions.

CONCLUSIONS

- **Patients taking OCS for an autoimmune condition can experience a wide range of burdensome AEs, some of which can be life-threatening.**
- **The risk of AE incidence among autoimmune populations generally increases with OCS exposure at higher daily or cumulative doses.**
- **Patients using OCS for long-term disease management experience dose-related increases in health resource utilization and in healthcare costs.**
- **Although autoimmune conditions are commonly managed with OCS, real-world evidence characterizing the long-term burden of OCS use across relevant autoimmune diseases remains limited.**
- **As novel treatments arise to provide alternative management strategies for autoimmune diseases, it is important to explore the costs of long-term OCS use and the potential impact of steroid-sparing practices and therapies.**

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