

# Lymphoepithelial Carcinoma of the Parotid Gland: A Rare Malignant Tumour

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## Abstract

Primary lymphoepithelial carcinoma of the parotid gland is a rare salivary gland tumour which is more common in women with an ethnic predilection. Association of Epstein-Barr Virus with the tumour in endemic areas suggested a role of tumorigenesis in susceptible population. We report a case of 67-year-old woman who presented with a long standing, painless right parotid region swelling. The diagnosis of lymphoepithelial carcinoma of the parotid gland was made based on histopathological examination after parotidectomy and neck dissection. Metastatic nasopharyngeal carcinoma was ruled out by targeted biopsies of bilateral fossa of Rosenmuller. Surgical resection followed by postoperative radiotherapy was essential to achieve local control of disease.

**Keywords:** Parotid Gland, Parotid Neoplasms, Head And Neck Neoplasms, Neck

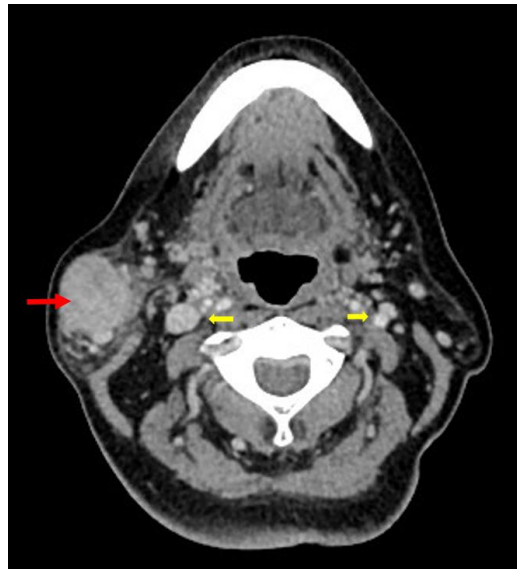
## Introduction

Lymphoepithelial carcinoma (LEC) is a subtype of undifferentiated carcinoma which commonly arises from the nasopharynx. Primary LEC of the salivary gland is a rare and clinic-pathologically distinctive neoplasm. It accounts for 0.4% of malignant salivary gland tumours, affecting the parotid gland in approximately 80% of the cases.<sup>1</sup> Epidemiologically, LEC has an ethnic predilection for Inuits (Eskimos), Chinese and Japanese with female predominance.<sup>1,2</sup> Patients typically present with an enlarging parotid lump with or without facial nerve involvement and cervical lymphadenopathy. We present a case of primary LEC of the right parotid gland and discuss the clinicopathological pattern and management of this rare tumour.

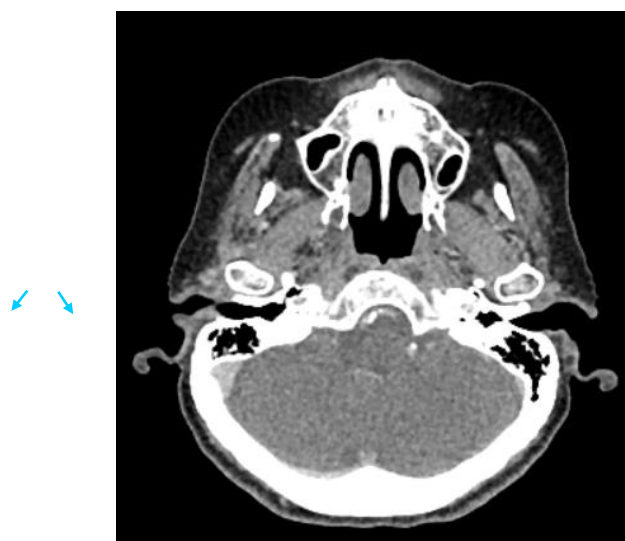
## Case Report

A 67-year-old Chinese lady presented to the Otorhinolaryngology clinic with a complaint of painless right parotid region swelling. The swelling has been progressively increasing in size over the last 2 years. She denied any history of facial weakness, odynophagia, dysphagia or difficulty in breathing. There was no other ear, nose and throat or constitutional symptoms. She had underlying Type II Diabetes Mellitus which was well-controlled with oral hypoglycaemic agents. Her family history was unremarkable.

Physical examination revealed a 3cm x 3cm well-defined mass over the right parotid region. It was firm, mobile and non-tender. Surface was smooth. Overlying skin was normal. The swelling was not fixed to overlying skin. Facial nerve function was intact. No other cervical lymph node or mass were palpated. Endoscopic examination of the nasopharynx and laryngopharynx were normal. Fine needle aspiration (FNA) of the right parotid swelling was performed and revealed cohesive clusters of atypical cells displaying enlarged, pleomorphic nuclei with inconspicuous nucleoli in background of abundant inflammatory cells. Computed tomography (CT) imaging of the neck revealed two fairly well circumscribed heterogeneously enhancing lesions in the superficial lobe of right parotid gland, measuring 2.5cm x 2.6cm and 2.1cm x 1.9cm each with subcentimeter cervical lymph nodes bilaterally (Figure 1). CT imaging of the neck also showed normal fossa of Rosenmuller bilaterally, excluding metastatic nasopharyngeal carcinoma (NPC) (Figure 2). Right total parotidectomy with ipsilateral level II selective neck dissection was performed.

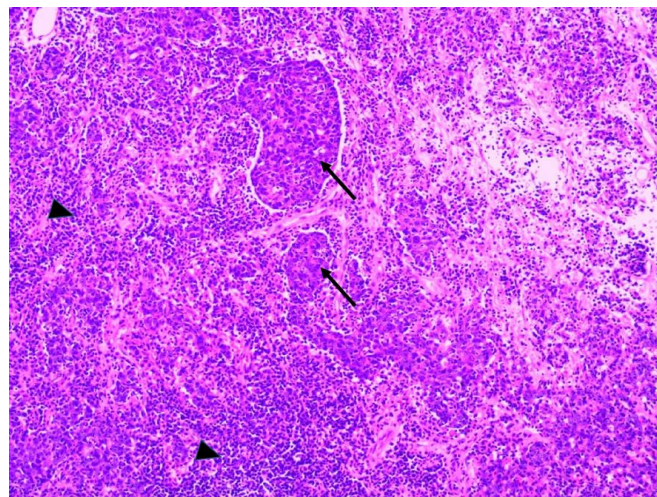


**Figure 1. Computed tomography scan revealed right parotid mass (red arrow) with subcentimeter lymph nodes (yellow arrows) in axial plane.**

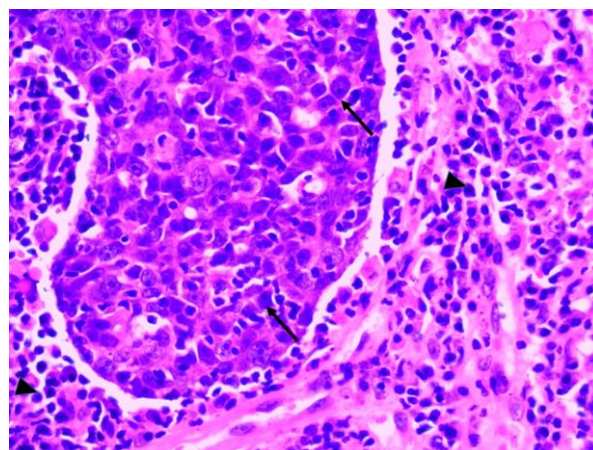


**Figure 2. Computed tomography scan showed normal fossa of Rosenmuller bilaterally (blue arrows) in axial plane.**

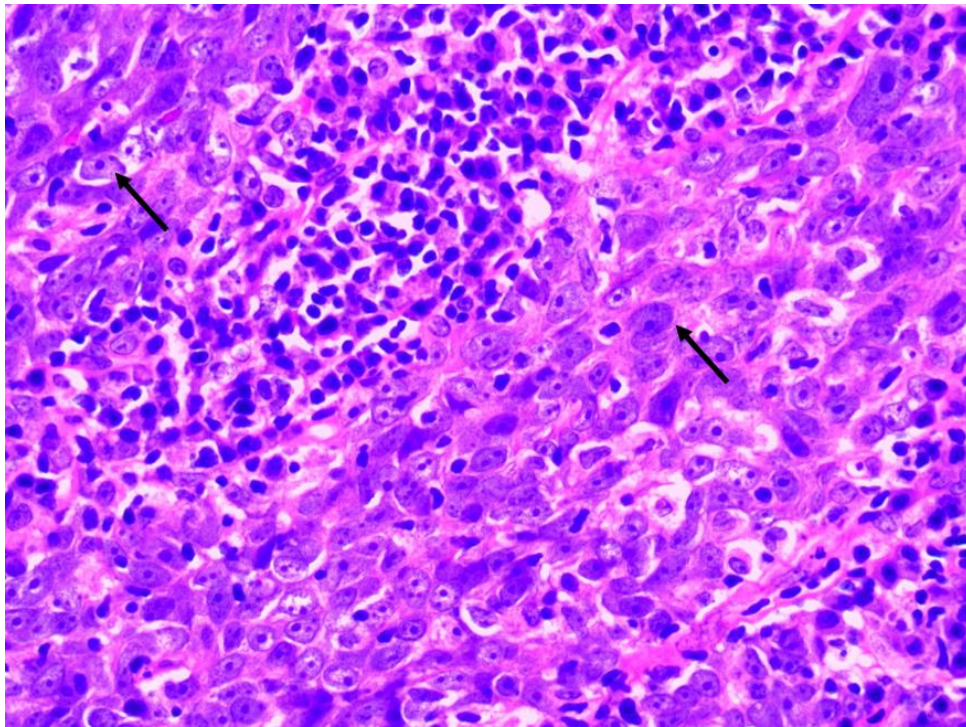
The resected gland showed a circumscribed greyish tissue with lobulated cut surfaces, which measured 5 cm x 3 cm x 2.5 cm. Macroscopically, the tumour showed continuity with adjacent parotid gland parenchyma, indicating extra-parenchymal involvement. Histopathological examination (HPE) suggested LEC, microscopically evidenced by infiltration of malignant tumour arranged in islands, trabeculae, nests, cords and sheets in a lymphoid-rich stroma. (Figure 3 and 4) The tumour was composed of large polygonal-spindled malignant epithelial cells displaying round to ovoid vesicular nuclei with one or more prominent nucleoli and eosinophilic cytoplasm (Figure 5). Focal area of cystic degenerative changes and haemorrhage was present. The immunohistochemical (IHC) stains for CKAE1/AE3 (Figure 6), p63 (Figure 7) and p16 were positive in tumour cells. They showed positive reactivity for EBV IHC stain, suggesting EBV infection (Figure 8). CD3 highlighted the predominant benign T-cells within the lymphoid stroma with some CD20 positive B-cells noted. HMB45 stain is negative. Metastatic NPC was ruled out by targeted biopsy of bilateral fossa of Rossenmuller, in which no malignancy was seen. A diagnosis of the right parotid LEC, stage IVA (pT<sub>3</sub>N<sub>2b</sub>M<sub>0</sub>) was made. Postoperative period was uneventful. The patient was referred for postoperative radiotherapy. However, the patient defaulted her appointment for radiotherapy and subsequent follow-up.



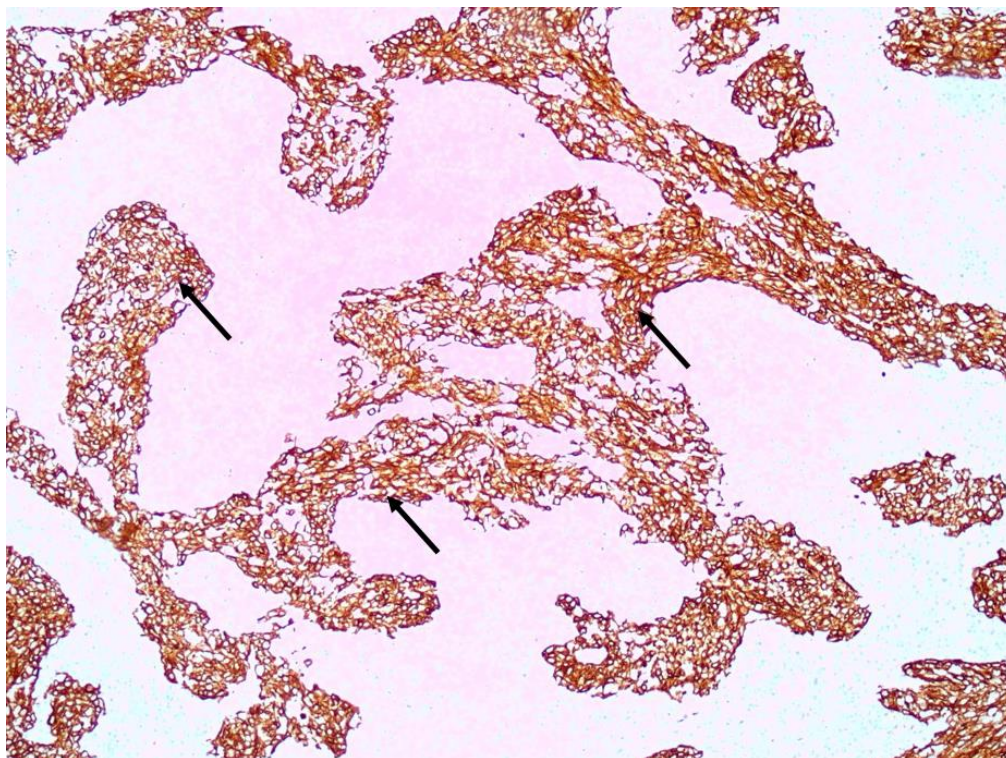
**Figure 3. Microscopic findings revealed sheets of cohesive tumor nests (arrows) with admixed dense non-neoplastic lymphoid cells (arrowhead). (x100)**



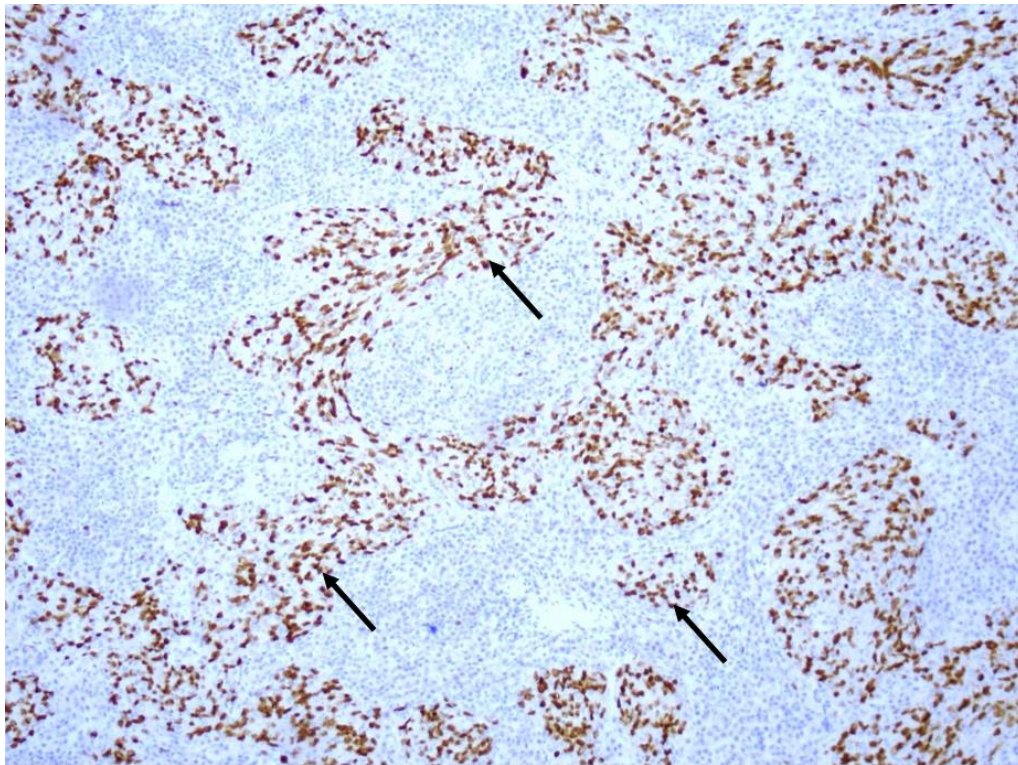
**Figure 4. Sheets of cohesive tumor nests (arrows) with admixed dense non-neoplastic lymphoid cells (arrowhead). (x400)**



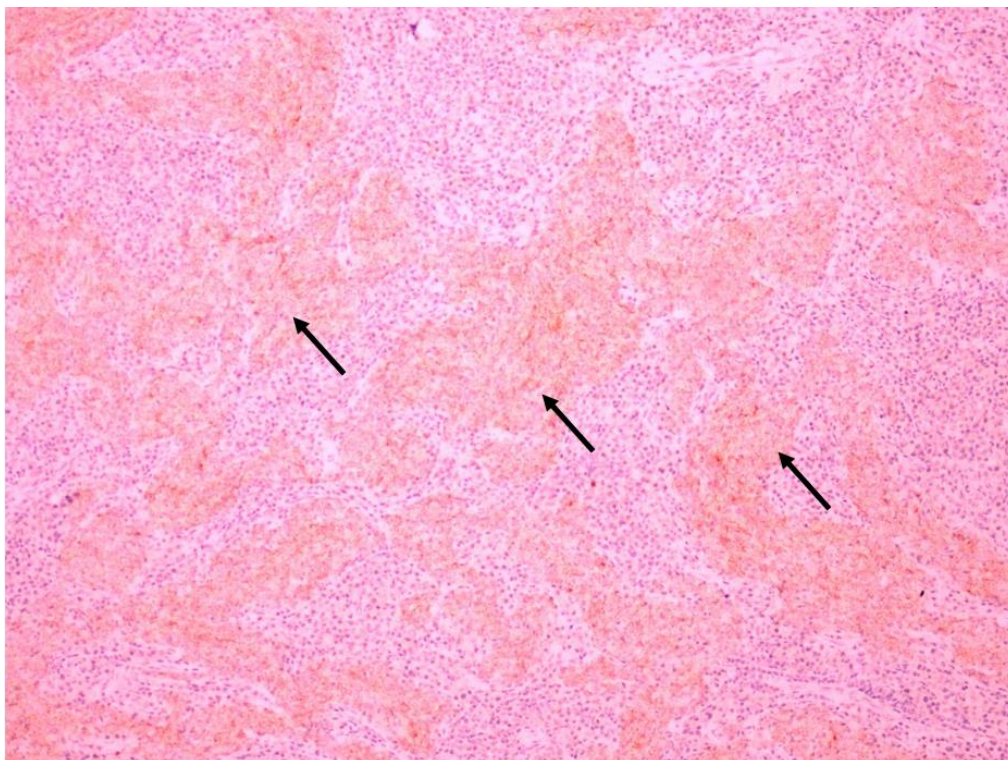
**Figure 5. The tumor cells had enlarged pleomorphic vesicular nuclei with prominent nucleoli and indistinct cell borders (arrows) (H&E x 400).**



**Figure 6. IHC stained positive for CKAE1/AE3(arrows) (x100).**



**Figure 7. IHC expression of p63 (x100).**



**Figure 8. Tumour cells were positive for EBV IHC stain (black arrows). (x100)**

**Table 1. Clinicopathological features of index patient and patients with LEC of the parotid gland described in previous literatures.**

Author	Age/ Gender/ Ethnic	Clinical presentation	Histopathological description	Immunohistochemical stains	
Index patient	67/ Female/Chinese	Right parotid swelling for 2 years	Infiltration of malignant tumour arranged in islands, trabeculae, nests, cords and sheets in a lymphoid-rich stroma.	CKAE1/AE3 p63 p16 HMB45 CD3 (T cells) CD20 (B cells) EBV IHC	+ + + - + + +
Tang C, 2012	29/ Female/ Chinese	Right parotid swelling for 10 months	Lymphoplasmacytic cell infiltration between and around tumour nests. Abundant histiocytes demonstrating starry-sky appearance.	CK7 CK20 EMA CD3 (T cells) CD20 (B cells) EBER	+ - + + + +
Kim YJ, 2017	44/ Male/ Korean	Left parotid swelling for 1 year	Sheets of cohesive tumour nests with dense lymphoid proliferation.	EBER	+
Ambrosio, 2013	45/ Female	Right parotid swelling for 2 years	Solid carcinomatous sheets, trabeculae, isolated small groups of neoplastic epithelial cells, intermingled with lymphoid tissue.	CK7 CK20 Fascin Vimentin CD3 (T cells) CD20 (B cells) LMP1 EBER	+ - + + + + + +
Abdelkrim SB, 2009	70/ Female/ North African	Left parotid swelling for few months	Irregular sheets, islands, and strands of poor differentiated carcinoma, richly infiltrated by lymphocytes and plasma cells, accompanied by large lymphoid follicles	CD3 (T cells) CD20 (B cells) LMP1 EBER	+ + - -

### Discussion

Histologically, LEC is defined as an undifferentiated carcinoma featuring atypical epithelial cells with interstitial infiltrations by lymphocytes and plasma cells, most common primary being the nasopharynx.<sup>3</sup> It was reported that LEC has nearly 100% association with Epstein-Barr virus (EBV) in endemic areas.<sup>1,4</sup> Primary tumour of salivary gland is histologically indistinguishable from nasopharyngeal lymphoepithelial carcinoma, therefore the major differential diagnosis for LEC of the salivary glands is metastatic NPC. A full endoscopic examination with targeted biopsies of nasopharynx is thus necessary to exclude the possibility of nasopharyngeal tumour.<sup>5</sup>

As reaffirmed in our case, LEC is more common in women with an ethnic predilection for Chinese and occurs primarily in the parotid gland. IHC staining confirmed EBV infection in the index case. We excluded the possibility of a NPC by performing an endoscopic examination with targeted biopsies of the nasopharynx in our clinic despite unremarkable findings from CT because NPC is very common in Malaysia especially amongst middle aged people of Chinese descent. Post-operative HPE revealed 3 lymph node involvements out of 10 lymph nodes sent from the neck dissection sample. The tumour was classified as right parotid LEC, stage IVA, pT<sub>3</sub>N<sub>2b</sub>M<sub>0</sub>, according to the American Joint Committee on Cancer staging system because the tumour was greater than 4 cm with extra parenchymal extension. Multiple ipsilateral lymph nodes were involved, none more than 6 cm in greatest dimensions.<sup>6</sup>

The diagnosis of LEC depends mainly on HPE findings. Histologically, specimens of LEC are characterized by nests, sheets and cords of syncytial-like growth pattern of anaplastic cells with prominent eosinophilic nucleoli surrounded by moderate to heavy lymphocyte infiltrates.<sup>1,2</sup> Primary LEC is histologically indistinguishable from nasopharyngeal lymphoepithelial carcinoma, thus the possibility of metastatic NPC needs to be excluded.<sup>2</sup> In our patient, IHC staining of tumour cells showed positivity for CKAE1/AE3 and p63. Tumour cells also had positive results from in situ hybridization for EBV, indicating latent EBV infection in the tumour cells. These IHC stain patterns are similar to that reported for NPC, indicating that LEC of salivary gland originates from epithelial tissue and belong to the category of squamous carcinoma.<sup>2</sup> Comparison of the patient's clinical and histopathological data with previous studies is shown in Table 1. Molecular testing is increasingly important in diagnosing and monitoring of EBV-related diseases.<sup>7</sup> In biopsy tissues, molecular detection of EBV-encoded RNA transcripts by in situ hybridization remains the gold standard for proving that a histopathological lesion is EBV-related.<sup>7</sup> EBV-encoded RNA hybridization and EBV LMP1 immunostains are used to detect latent EBV infection.<sup>7</sup> Further research is needed to determine the feasibility of viral load tests in the full spectrum of EBV-associated diseases. EBV infection is a critical oncogenic event that correlates with a rapid tumour progression and metastatic phenotype.<sup>8</sup> A considerable portion of tumours exhibited C-terminal deletions/mutations, which are thought to promote cellular proliferation and may enhance the oncogenic effects of EBV in salivary gland epithelioma.<sup>8</sup>

LEC of the parotid gland are radiosensitive. Current treatment recommendations involve combination therapy with surgery and radiation therapy.<sup>1,2,5</sup> Our patient received a total parotidectomy on the affected side with selective neck dissection. She was referred for postoperative radiation therapy to the primary site to achieve local control of disease.

## Conclusion

LEC is a rare parotid tumour with unique pathological features. It is worth highlighting the diagnostic difficulty in this case, mainly due to the rare occurrence of primary LEC in parotid gland. Besides, primary parotid LEC shares similar histopathological characteristic with NPC, thus the need to exclude metastatic NPC especially amongst Chinese patients. Management of primary LEC involves a multidisciplinary approach including surgical excision and postoperative radiotherapy.

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## Declaration of conflicting interest

The author(s) declared no potential conflicts of interest.