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Original Article

Diagnosis, treatment, and outcome of patients with oesophagogastric cancer during the COVID-19 pandemic: national study

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Abstract

Background: The national response to COVID-19 has had a significant impact on cancer services. This study investigated the effect of national lockdown on diagnosis, management, and outcomes of patients with oesophagogastric cancers in Scotland.

Methods: This retrospective cohort study included consecutive new patients presenting to regional oesophagogastric cancer multidisciplinary teams in National Health Service Scotland between October 2019 and September 2020. The study interval was divided into before and after lockdown, based on the first UK national lockdown. Electronic health records were reviewed and results compared.

Results: Some 958 patients with biopsy-proven oesophagogastric cancer in 3 cancer networks were included: 506 (52.8 per cent) before and 452 (47.2 per cent) after lockdown. Median age was 72 (range 25–95) years and 630 patients (65.7 per cent) were men. There were 693 oesophageal (72.3 per cent) and 265 gastric (27.7 per cent) cancers. Median time to gastroscopy was 15 (range 0–337) days before *versus* 19 (0–261) days after lockdown ($P < 0.001$). Patients were more likely to present as an emergency after lockdown (8.5 per cent before *versus* 12.4 per cent after lockdown; $P = 0.005$), had poorer Eastern Cooperative Oncology group performance status, were more symptomatic, and presented with a higher stage of disease (stage IV: 49.8 per cent before *versus* 58.8 per cent after lockdown; $P = 0.04$). There was a shift to treatment with non-curative intent (64.6 per cent before *versus* 77.4 per cent after lockdown; $P < 0.001$). Median overall survival was 9.9 (95 per cent c.i. 8.7 to 11.4) months before and 6.9 (5.9 to 8.3) months after lockdown (HR 1.26, 95 per cent c.i. 1.09 to 1.46; $P = 0.002$).

Conclusion: This national study has highlighted the adverse impact of COVID-19 on oesophagogastric cancer outcomes in Scotland. Patients presented with more advanced disease and a shift towards treatment with non-curative intent was observed, with a subsequent negative impact on overall survival.

Introduction

COVID-19 was declared a pandemic by the WHO on 11 March 2020. The UK government instigated a national lockdown on 23 March 2020 in an attempt to limit virus transmission and minimize the impact on the National Health Service (NHS)[1]. Nevertheless, the need to shift capacity and resources towards managing COVID-19 led to significant disruption in both elective and emergency healthcare provision, including cancer care, in the UK[2]. This disruption was mirrored globally; a WHO survey[3] undertaken in May 2020 demonstrated that 42 per cent of the 155 countries surveyed had experienced partial or complete disruption in health services for cancer. Additionally, more than 50 per cent of countries reported a postponement of cancer screening programmes, and there was a significant decline in pathology samples from cancer screening programmes[3]. In a large international collaborative involving 356 centres from 54 countries, 46.4 per cent of the centres reported that more than 10 per cent of their patients missed at least 1 treatment session[4]. The effect of disruption to cancer services on outcomes

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for patients with cancer as a consequence of the COVID-19 pandemic is not yet known.

There are approximately 1500 new cases of oesophageal and gastric cancers diagnosed annually in Scotland, accounting for about 5 per cent of all new cancer cases[5,6]. Patients often present at a late stage[7], in part owing to poor public awareness of symptoms, and prognosis is dependent on early presentation and referral. The 5-year survival rate for oesophageal cancer in Scotland is 12 per cent and that for gastric cancer is 14 per cent. In the advanced setting, prognosis in unselected populations is less than a year[8]. In Scotland in 2020 there was a 10 per cent decrease in the number of oesophageal and gastric cancer diagnoses compared with 2019[9].

The standard diagnostic test for oesophagogastric (OG) cancer is endoscopy, which was classified as an aerosol-generating procedure, with the potential to increase transmission of COVID-19. This led to the British Society of Gastroenterology and Joint Advisory Group[10] on 3 April 2020 to advise that all endoscopy except emergency and essential procedures should be suspended. During this period, the total number of endoscopies performed fell to 5–12 per cent of prepandemic levels, with a subsequent 58 per cent reduction in the number of cancers detected weekly[11,12]. This significantly limited endoscopic capability during the COVID-19 pandemic. This may have resulted in delays in presentation and diagnosis of OG cancers, potentially leading to upstaging of the disease and resulting in poorer outcomes for patients.

An initial analysis from the West of Scotland regional OG cancer multidisciplinary team (MDT) demonstrated fewer new cancer referrals as COVID-19 infections rose, with changes to the route of MDT referral and longer time to diagnostic endoscopy[13]. In this pilot study, metastatic disease was more frequently documented at presentation after lockdown, with an increase in treatment with non-curative rather than curative intent, and a shorter median survival after lockdown. To further investigate these findings, the study was rolled out at the national level.

The primary aim of this national study was to investigate the impact of the COVID-19 pandemic on the staging of OG cancers at presentation. The secondary aims were to determine the time delay in performing gastroscopy, and the impact on MDT treatment decisions and overall survival (OS).

Methods

This was a Scottish national retrospective cohort study of consecutive patients with newly diagnosed OG cancer who were discussed in an OG cancer MDT over a 1-year interval, from 1 October 2019 to 30 September 2020. All regions undertaking resectional OG cancer surgery in Scotland were invited to participate. Five of the six centres from three cancer networks contributed data covering 93.2 per cent of the estimated 5.5 million Scottish population.

MDT records were obtained from the OG cancer MDT coordinator in each region. Patients with new referrals to the MDT were included in the study; those with ongoing care, who had been discussed previously, were excluded. Patients found to have benign disease, gastrointestinal stromal tumours, carcinoma of unknown primary, lymphoma, neuroendocrine cancer, or low- or high-grade dysplasia were also excluded from the study. Electronic health records were reviewed for baseline characteristics, reason for and route of referral, timing of investigations, clinical TNM stage (according to the 8th edition) at presentation, MDT outcome, and date of death. For junctional tumours, Siewert types I and II were considered as oesophageal cancer, whereas Siewert III was considered as gastric cancer in accordance with the TNM eighth edition. Data were collected by each centre and analysed centrally.

The study period was divided into two intervals based on the UK first national lockdown, which was introduced on 23 March 2020. The results were compared between the two groups. Follow-up ended at death or on 10 April 2022. Patients lost to follow-up were censored at the date of last clinical contact. The mortality analysed was all-cause mortality.

Institutional review board approval was not required as this was a retrospective observational study, and the study protocols were consistent with the information governance frameworks and recommendations of NHS Scotland Regional Cancer Networks, national and international societies, and Caldicott requirements.

Statistical analysis

For the descriptive analysis, categorical data are presented as frequency and percentages, with *P* values calculated using the χ^2 test. Student's two-tailed unpaired test was used to compute *P* values for continuous variables. Two-sided *P* values were calculated and were considered significant at an overall significance level of 5 per cent.

Kaplan–Meier methods were used to estimate survivor functions for time-to-event endpoints with a censor date of 10 April 2022. OS was calculated as the interval from the date of diagnosis to the date of death or censoring. Cox proportional hazards regression was used to estimate HRs and 95 per cent

Table 1 Demographics and treatment intent for patients diagnosed with oesophagogastric cancer in Scotland before and after lockdown

	Before lockdown (*n* = 506)	After lockdown (*n* = 452)	P*
Age (years)			
Mean(s.d.)	70.1(11.6)	71.2(11.1)	<0.001†
Median (range)	71 (25–94)	72(25–95)	
Sex ratio (F : M)	183 : 323	145 : 307	0.207
Deprivation index			0.812
5th quintile (least deprived)	102 (20.2)	75 (16.6)	
4th quintile	106 (20.9)	97 (21.5)	
3rd quintile	107 (21.1)	98 (21.7)	
2nd quintile	90 (17.8)	89 (19.7)	
1st quintile (most deprived)	96 (19.0)	89 (19.7)	
Unknown	5 (1.0)	4 (0.9)	
ECOG PS score			0.033
0	150 (29.6)	110 (24.3)	
1	164 (32.4)	153 (33.8)	
2	84 (16.6)	73 (16.2)	
≥ 3	43 (8.5)	65 (14.4)	
Unknown	65 (12.8)	51 (11.3)	
Treatment intent			<0.001
Unknown	5 (1.0)	1 (0.2)	
Curative	173 (34.2)	101 (22.3)	
Palliative	327 (64.6)	350 (77.4)	
Missing	1 (0.2)	0 (0)	
Histology			0.018
Adenocarcinoma	392 (77.5)	342 (75.7)	
SCC	105 (20.8)	85 (18.8)	
Radiological diagnosis/ no biopsy	7 (1.4)	20 (4.4)	
Other	2 (0.4)	5 (1.1)	

Values are *n* (%) unless otherwise indicated. ECOG PS, Eastern Cooperative Oncology Group performance status; SCC, squamous cell carcinoma. *χ^2 test, except †unpaired *t* test.

confidence intervals. R version 1.3.1073 (R Project for Statistical Computing, Vienna, Austria) was used for analysis.

Results

Demographics

Some 958 new patients with OG cancer were identified, 411 in the West of Scotland Cancer Network (42.9 per cent), 335 (35.0 per cent) in the South-East Scotland Cancer Network, and 212 (22.1 per cent) in the North Cancer Alliance. In the cohort as a whole, there were 506 patients (52.8 per cent) in the prelockdown group and 452 (47.2 per cent) in the postlockdown group. Demographics are shown in *Table 1*. There were 630 men (65.7 per cent) and 328 women (34.3 per cent). Median age at diagnosis was 72 (range 25–95) years. There were 693 oesophageal cancers (72.3 per cent) and 265 gastric cancers (27.7 per cent); 734 (76.6 per cent) were adenocarcinomas, 190 (19.8 per cent) were squamous cell carcinomas (SCCs), 7 (0.7 per cent) were other cancer types, and 27 (2.8 per cent) were not biopsied.

On comparison of the populations treated before and after lockdown, demographics were balanced with no clinically significant shift in age profile, sex or deprivation index. However, there was a statistically significant shift toward poorer Eastern Cooperative Oncology Group (ECOG) performance status score at diagnosis, and a significant shift toward treatment with non-curative intent (64.6 per cent before *versus* 77.4 per cent after lockdown) (*Table 1*). There was a shift towards treatment with non-curative intent for both histological types of OG cancer (adenocarcinoma and SCC) (*Table S1*).

Table 2 TNM stage at diagnosis, source of referral, time from referral to diagnostic oesophagogastroduodenoscopy and referral route before and and after lockdown

	Before lockdown ($n = 506$)	After lockdown ($n = 452$)	P*
Stage at diagnosis			0.04
I	13 (2.6)	8 (1.8)	
II	52 (10.3)	34 (7.5)	
III	159 (31.4)	111 (24.6)	
IV	252 (49.8)	266 (58.8)	
Unknown/not fully staged	30 (5.9)	33 (7.3)	
Referrer			0.559
Primary care	352 (69.6)	311 (68.8)	
Secondary care	154 (30.4)	140 (31.0)	
Unknown	0 (0)	1 (0.2)	
Time from presentation to OGD (days)			
Mean(s.d.)	27.0(34.7)	30.8(38.0)	<0.001†
Median (range)	15 (0–337)	19.0 (0–261)	
Missing	31 (6.1)	30 (6.6)	
Referral route			0.005
Emergency/acute admission	43 (8.5)	56 (12.4)	
Routine OGD	50 (9.9)	36 (8.0)	
Urgent OGD	379 (74.9)	346 (76.5)	
Urgent clinic	31 (6.1)	9 (2.0)	
Unknown	3 (0.6)	5 (1.1)	

Values are *n* (%) unless otherwise indicated. OGD, oesophagogastroduodenoscopy. *χ^2 test, except †unpaired *t* test.

Stage migration

Given the shift in treatment intent, an analysis was undertaken to determine whether this was driven by stage migration. There was a significant shift to stage IV disease, from 49.8 per cent before to 58.8 per cent after lockdown ($P = 0.04$) (*Table 2*). There was also a documented increase in symptomatic disease at presentation (90.5 *versus* 95.8 per cent; $P = 0.006$). However, no difference in route of referral (primary *versus* secondary care) or in time from referral to oesophagogastroduodenoscopy (OGD) was observed (*Table 2*). There was an increase in median time from presentation to endoscopy after lockdown, from 15 to 19 days, but this was unlikely to be clinically significant. This was still the case when patients referred during an acute admission were removed (16 *versus* 20 days). There were significantly more patients diagnosed during an acute or emergency admission after lockdown (12.4 *versus* 8.5 per cent before lockdown; $P = 0.005$) (*Table 2*).

Survival before and after lockdown

Median OS for the population as a whole was significantly lower after lockdown: 6.9 (95 per cent c.i. 5.9 to 8.3) months *versus* 9.9

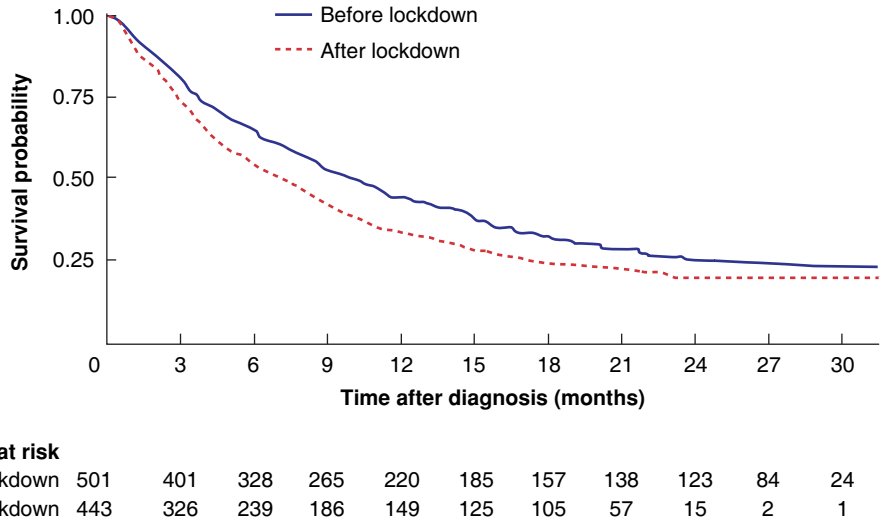

Fig. 1 Kaplan–Meier survival curves for the Scottish oesophagogastric cancer population before and after lockdown

Median OS for the population as a whole was significantly lower after lockdown: 6.9 (95 per cent c.i. 5.9 to 8.3) months versus 9.9 (8.7 to 11.4) months (HR 1.26, 95 per cent c.i. 1.09 to 1.46; P = 0.002) (log rank test).

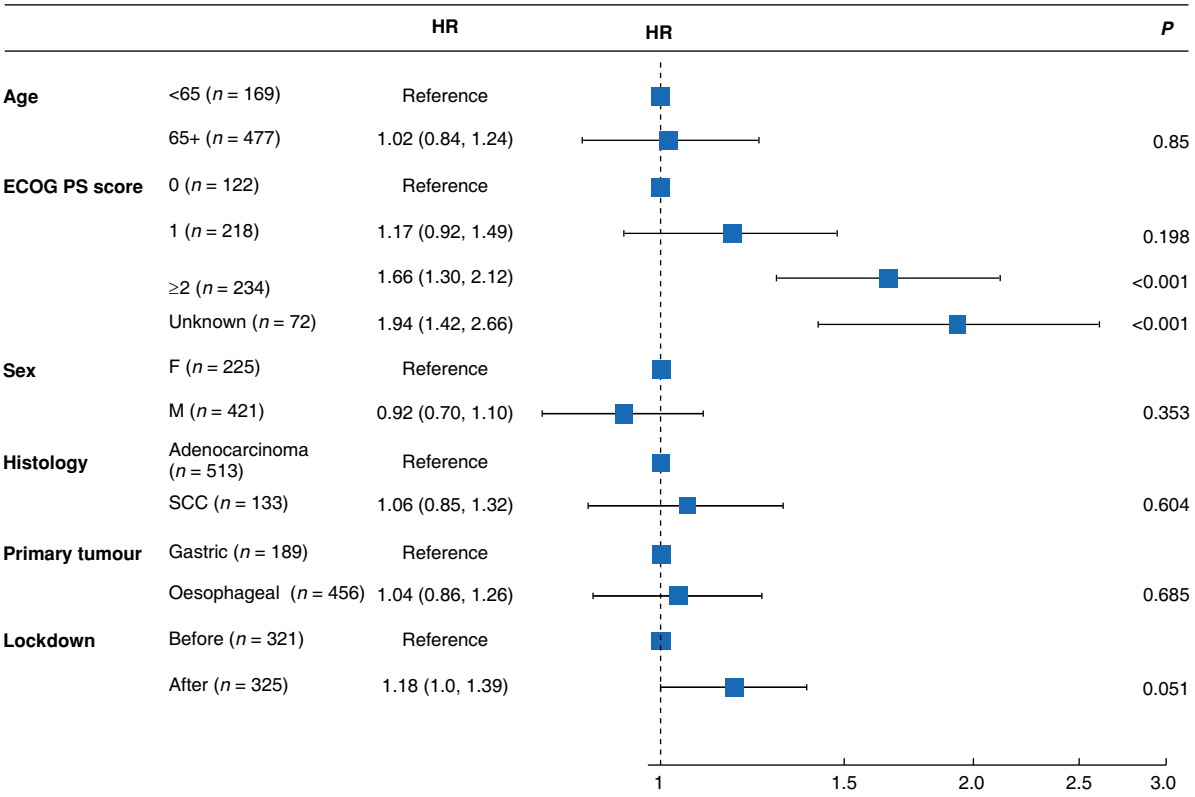

Fig. 2 Cox regression analysis for overall survival in the population treated with non-curative intent

ECOG PS, Eastern Cooperative Oncology Group performance status; SCC, squamous cell carcinoma. There were 592 events. Global $P < 0.001$ (log rank test).

(8.7 to 11.4) months (HR 1.26, 95 per cent c.i. 1.09 to 1.46; $P = 0.002$) (*Fig. 1*). Among 274 patients treated with curative intent, there was no difference in 1-year survival rates between the prelockdown and postlockdown cohorts (*Fig. S1*). Long-term survival data are immature. Among 677 patients treated with non-curative intent, there was also no difference between before and after lockdown: median OS 5.9 (95 per cent c.i. 4.6 to 6.8) *versus* 4.6 (95 per cent c.i. 4.0 to 5.8) months respectively (HR 1.15, 95 per cent c.i. 0.98 to 1.35; $P = 0.087$) (*Fig. S2*). After lockdown, more patients received non-curative chemotherapy (31.7 versus 22.0 per cent; $P = 0.030$); however, there was no difference in ECOG performance status score.

The impact of lockdown on survival almost reached significance when adjusted for other factors in Cox proportional hazards regression in the non-curative population (HR 1.18, 1.00 to 1.39; $P = 0.051$) (*Fig. 2*). This was not the case for the curative population (HR 0.76, 0.49 to 1.12; $P = 0.214$).

Survival according to tumour site (oesophagus and stomach) and histology are reported in *supplementary material* and *Fig. S3*.

Discussion

Compared with those presenting before lockdown, patients presenting after lockdown had more advanced disease (that is stage migration) and poorer performance status. They were also more likely to present as an emergency and to have symptoms at diagnosis. These factors are likely to have led to the observed lower proportion of patients treated with curative intent after lockdown and the poorer survival in the cohort as a whole.

The present data relating to more advanced stage are comparable to the findings of a study[14] from the Netherlands, which reported decreased diagnosis of oesophageal cancer, stage migration, and fewer resections being performed after the lockdown compared with historical data. In this data set, the number of patients being treated with incurable disease (that is stage IV) increased from 52.5 to 67.7 per cent for gastric cancer and 33.0 to 40.8 per cent for oesophageal cancer. In the present cohort, which combined gastric and oesophageal cancers, the rate of stage IV disease increased from 49.8 to 58.8 per cent.

In Scotland, stage migration during the COVID-19 pandemic was likely the main factor driving a shift towards more treatment with non-curative intent, from 64.6 per cent before to 77.4 per cent after lockdown in the present cohort. The change in treatment intent may explain the inferior OS in the cohort as a whole, and a more selective approach to curative treatment during the pandemic that may explain the lack of difference in 1-year survival for those treated curatively. Longer follow-up is needed to confirm this.

In the non-curative setting, even though a greater proportion patients received non-curative chemotherapy, survival after lockdown was inferior. This suggests that other factors, including poorer patient fitness because of higher tumour burden within stage groups, and limited access to supportive healthcare resources, may have played a role.

Although it is clear that patients diagnosed after lockdown had poorer outcomes owing to stage migration, the underlying reasons for this are not clear from the present analysis. There did not appear to be a clinically meaningful delay in referral time (either from primary or secondary care) to diagnostic OGD. This suggests that the delay in diagnosis may have been driven by delayed presentation. In support of this, the number of new cancer referrals to each of the local regional OG cancer MDTs fell

as the number of confirmed COVID-19 cases rose[15]. Nationally, there was a 10.7 per cent decrease in new cases discussed. Such a decrease was also observed in another UK tertiary OG cancer centre[16]. A similar study[17] using data from the Northern Ireland Cancer Registry demonstrated that, during the first 6 months of the pandemic, the proportion of OG cancer diagnoses declined by 26.6 per cent compared with the preceding 2-year period. Furthermore, an observational study[18] in England revealed that primary care consultations for cancer clinical features decreased by 24 per cent between 2019 and 2020, particularly in the 6–12 weeks after the first UK national lockdown. This included symptoms associated with OG cancer, such as weight loss, anaemia, or upper abdominal pain, but interestingly there was no change in consultations for dysphagia[18]. Consistent with the present findings that cancer referral pathways remained operational, it was also demonstrated that, once patients had consulted with primary care, they were referred urgently in a similar or greater proportion than in previous years.

The strict UK government message to stay at home, combined with a degree of public fear of contracting COVID-19, may explain the reduction in new presentations reviewed by the MDT. In an attempt to curb the spread of COVID-19, it was necessary to make changes to general practice service delivery along with reduced access to secondary specialist care, with limited face-to-face encounters and reduced availability of endoscopy[10]. There was additionally a public perception among some that healthcare staff were busy caring for patients with COVID-19, and that their worsening heartburn or new dysphagia was of lower priority, leading to their delay in presenting[19]. In light of these findings, concern remains regarding patients who have yet to present with symptoms of OG cancer, and that there may still be a late surge of cancer presentations at an advanced stage[10].

Understanding the impact of the pandemic nationally also helps with future cancer treatment planning. National Public Health Scotland data[10] demonstrated that the numbers of new OG cancers diagnosed throughout 2020, after the first UK lockdown, were below levels reported during the same interval in 2019. However, in 2021 there was a rebound increase in the number of oesophageal cancers being diagnosed to account for the missing cases. Perhaps more concerning is the fact that gastric cancer numbers for 2021 have not yet caught up with 2019 levels, and so there could be a further cohort of patients with undiagnosed gastric cancer in the community who have yet to present. This anticipated delay in presentation and detection may have a further impact on the oncology, palliative care, surgical, and endoscopic services nationally.

The strengths of this study include that it is the first OG cancer study at a national level to quantify the effect of COVID-19 on OG cancer diagnosis, treatment intent, and outcomes. The population appears representative of the UK OG population in terms of age, sex distribution, and proportion of patients presenting with advanced disease before lockdown[7]. Other studies[20,21] have suggested that the impact of the pandemic on cancer care is not limited to OG cancer, with modelling studies predicting a substantial rise in avoidable cancer deaths resulting from delays in diagnosis.

Limitations include that, as this was a retrospective study, there were limited data on demographics, and only medium-term follow-up data were available. Long-term outcome data are not yet available, and the analysis of such data will be required to fully understand the impacts of the pandemic.

This study has highlighted the importance of maintaining patient awareness of cancer symptoms, and access to primary care and specialist cancer services during any future waves of the COVID-19 pandemic. These findings have important broader relevance beyond the impact of the COVID-19 pandemic, by evidencing the impact on treatment profiles and outcomes of patients with OG cancer as a result of even short delays owing to limited access to healthcare, and indicate the very narrow curative window for OG cancers based on current diagnostic pathways. Hopefully, this study will accelerate the investigation and development of optimized interventions to mitigate the survival impact of OG cancer diagnostic delays. The data have also highlighted an urgent increased need for non-curative treatments (oncological and supportive care) for patients with OG cancer at the present time, and suggest it is imperative that clinical service delivery and clinical trial planning take this into account.

Author contributions

Mark Baxter (data curation, formal analysis, software, writing—original draft, writing—review and editing), Khurram Khan (CRediT contribution not specified), Khurram Khan (conceptualization, data curation, methodology, project administration, writing—original draft, writing—review and editing), Lewis Gall (data curation, formal analysis, writing—original draft, writing—review and editing), Catherine Samuelson (data curation, writing—review and editing), Catherine McCollum (data curation, writing—review and editing), Rongkagorn Chuntamongkol (data curation, writing—review and editing), Lakshmi Narramneni (data curation, writing—review and editing), Manaf Al-Zuabi (data curation, writing—review and editing), Gavin Bryce (data curation, writing—review and editing), Hala Shareef (data curation, writing—review and editing), Matthew Forshaw (conceptualization, methodology, supervision, writing—original draft, writing—review and editing), Russell Petty (conceptualization, methodology, supervision, writing—original draft, writing—review and editing).

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M.A.B. has undertaken speaking roles for Ipsen and BMS; and has received expenses from Ipsen and Servier. R.D.P. has undertaken speaking, consulting, and advisory roles for Eli Lilly, BMS, Pfizer, Sanofi, and Servier; and received research funding (not related to the work in this manuscript) from Astra Zeneca, Roche, MSD, Merck serrano, Eli Lilly, Five Prime Therapeutics, Clovis, Boston Biomedical, and Janssen. The authors declare no other conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Anonymized data and code for the analysis can be requested from the corresponding author.

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