BMJ Open Respiratory Research

Retrospective cohort study of survival length in malignant pleural effusion between 2015 and 2023

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To cite: Mounsey C, Kanellakis N, Addala D, *et al*. Retrospective cohort study of survival length in malignant pleural effusion between 2015 and 2023. *BMJ Open Respir Res* 2025;**12**:e003609. doi:10.1136/bmjresp-2025-003609

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjresp-2025-003609).

Received 4 July 2025
Accepted 19 October 2025

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ABSTRACT

Background Malignant pleural effusion (MPE) is common, affecting approximately 15% of patients with cancer. Over recent years, there have been significant changes in both the diagnostic and therapeutic strategies for the condition, and recent epidemiological studies have shown improvements in survival across most major cancer types. However, it is currently unclear whether there has been an increase in survival in patients with MPE.

Methods Medical records of patients diagnosed with MPE between 2015 and 2023 at Oxford University Hospitals were retrospectively reviewed. Patients were split into groups of equal size based on the date of MPE diagnosis and Kaplan-Meier survival analyses were performed. Subgroup analyses were conducted in patients with MPE by causative cancer type, performance status at diagnosis and treatment with systemic anti-cancer therapy. Cox regression analyses were carried out using the individual year of MPE diagnosis as an included variable.

Results 742 patients with MPE were included. There was no improvement in survival length in patients managed in more recent years. This was consistent across effusions secondary to any primary malignancy; effusion secondary to lung cancer, mesothelioma or breast cancer; in patients with better performance status; and in patients who received systemic anti-cancer therapy.

Conclusions Despite recent changes in the management of MPE and improving survival trends in cancer overall, survival time following the development of MPE appears to have remained stagnant over the 8-year time period under study. This suggests that MPE should potentially be considered as a discrete clinical entity, necessitating investigation of oncological therapies specifically targeted to the pleural space.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Improvements in survival have been seen in most major cancer types over recent years. However, whether there has been an increase in survival time following the development of malignant pleural effusion is unclear.

WHAT THIS STUDY ADDS

⇒ Our results indicate that while the incidence of malignant pleural effusion is increasing, survival time following the development of this condition has not improved.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Malignant pleural effusion should be considered as a discrete clinical entity to the underlying causative cancer type, and therapies specifically targeting the pleural space should receive further investigation.

INTRODUCTION

Malignant pleural effusion (MPE) describes excess fluid in the pleural space accompanied by cancer cells and can result from either primary pleural malignancy or extrapleural malignancy with pleural metastases.[1] As almost any advanced malignancy can invade the pleura and cause effusion,[2] MPE is a common clinical condition with an estimated incidence of one million individuals per year globally,[3] and, given the growing rate of new cancer diagnoses, it is anticipated that this will continue to increase.[4 5]

The presence of MPE indicates poor prognosis, with median survival time typically quoted as 3–12 months.[6] However, while the focus of treatment in MPE remains primarily palliative, over recent years there have been significant changes in its management, with moves to streamline diagnostic pathways and several well-designed randomised clinical trials altering recommended therapeutic strategies.[7 8] Furthermore, a number of recent epidemiological studies have shown improvements in mortality rates across most major cancer types[4 9 10]; this has included the common causative malignancies of MPE, such as lung cancer, mesothelioma and breast cancer.[4] These improvements reflect success in cancer prevention strategies, improved diagnostic tests and more effective treatment options,[4 9] an important example of which has been the implementation of immunotherapeutic agents across a range

of malignancies.[11 12] In non-small cell lung cancer, for instance, immune checkpoint inhibitors have become widely integrated into standard treatment pathways, following numerous clinical trials demonstrating benefit in terms of patient quality of life, progression-free survival and overall survival.[13 14]

However, it is currently unclear whether these advances in the management of MPE and its underlying causative malignancies have led to improvement in the survival time of MPE patients. We hypothesised that MPE survival would have improved. Therefore, we retrospectively investigated the survival length of patients diagnosed with MPE at Oxford University Hospitals NHS Foundation Trust (OUH) between 2015 and 2023, to assess for changes in survival over this time period. In addition, we calculated the number of new MPE diagnoses per year, to review for local changes in disease incidence.

METHODS

Participants and eligibility

Identification of patients with MPE was undertaken through retrospective analysis of the Oxford Pleural Database. This represents a comprehensive record of all patients discussed at the OUH pleural multidisciplinary team (MDT) meeting since July 2015 (n=2568). The OUH pleural MDT is a weekly meeting in which all patients managed by the pleural team at OUH are discussed on a case-by-case basis. Established referral pathways to the OUH pleural team have been in place since 2015 for patients with pleural diseases presenting locally to: primary care, medical/surgical specialties, radiology and oncology teams. All patients with symptomatic pleural effusions or pleural effusions requiring intervention for diagnosis are referred to the OUH pleural team and will therefore be recorded on the Oxford Pleural Database.

For the current study, patients reviewed at the OUH pleural MDT between July 2015 and October 2023 with a final diagnosis of MPE had their electronic medical records screened. Patients were only excluded in the presence of key missing data, specifically insufficient baseline information to determine date of MPE diagnosis or insufficient follow-up information regarding length of survival. Patients were included in the absence of confirmatory pleural fluid cytology or pleural histopathology if a diagnosis of MPE was made following discussion with expert pleural clinicians at the MDT. In these cases, the diagnosis was based on radiological and clinical features, such as a large effusion with radiological characteristics suggestive of malignancy in the presence of known metastatic cancer.

Data collection

Data were collected from the electronic patient records of identified individuals at least 6 months after their MPE diagnosis date, to allow meaningful data on survival to be assessed. Data collected included age, gender, date of MPE diagnosis, date of underlying primary malignancy diagnosis, date of death (if applicable), type of systemic anti-cancer therapy (SACT) received, and parameters required for calculation of the LENT[15] and clinical PROMISE[16] prognostic scores. Survival was calculated as time from MPE diagnosis to date of death. Patients were censored at the time of data collection or loss to follow-up.

Statistical analysis

Descriptive statistics were expressed as frequency (percentages) for categorical variables, and median (IQR) for continuous variables. To investigate changes in survival length over time, patients were split into three time period groups of equal size based on the date of MPE diagnosis (group 1: July 2015–October 2018; group 2: October 2018–April 2021; group 3: April 2021–October 2023) and Kaplan-Meier analyses with log-rank (Mantel-Cox) tests performed. Cox regression analyses using the individual year of MPE diagnosis as an included variable were conducted. Cox models were performed with diagnosis year treated as both a fixed effect and a random effect, to adjust for random bias from the year of diagnosis. As a sensitivity analysis, Cox models were conducted including only patients with confirmatory cytology or histopathology. Subgroup analyses were performed in patients with MPE by causative cancer subtype (ie, lung cancer, mesothelioma or breast cancer, as the most common underlying malignancies), by performance status (ie, Eastern Cooperative Oncology Group Performance Status 0–2 vs 3–4) at MPE diagnosis, and by treatment with SACT. The time from primary cancer diagnosis to MPE development was assessed to review for evidence of change over time. For this analysis, mesothelioma patients were excluded, based on the expectation that the majority of these patients would have received their oncological diagnosis through investigation for pleural abnormality. All statistical tests were two-sided, and a $p<0.05$ was considered statistically significant. Missing data were handled through complete-case analysis only for all tests. Statistical analyses were performed using IBM SPSS Statistics (V.29.0.1.0) and R (V.4.5.1).[17]

Patient and public involvement

Patients and members of the public were not involved in the design or conduct of the study.

RESULTS

Cohort demographics and clinical characteristics

From the 2568 patients in the Oxford Pleural Database, a total of 781 patients with MPE were identified. Of these, 39 (5.0%) had either inadequate baseline or follow-up information and were excluded. In the remaining 742 patients, the median age at MPE diagnosis was 72 years (IQR 64–80) and median overall survival from MPE diagnosis was 150 days (IQR 55–473) (table 1). Lung cancer

Table 1 Patient demographics and clinical characteristics

Characteristic	N (%) or Median (IQR)
Age	72 (64–80)
Sex	
Female	371 (50.0)
Male	371 (50.0)
Survival from MPE diagnosis (days)	150 (55–473)
Primary cancer	
Lung	214 (28.8)
Adenocarcinoma	170
Small cell	21
Squamous cell	15
Unspecified	8
Mesothelioma	152 (20.5)
Epithelioid	105
Biphasic	25
Sarcomatoid	17
Unspecified	5
Breast	123 (16.6)
Gynaecological	71 (9.6)
Upper GI	67 (9.0)
Haematological	33 (4.4)
Lower GI	15 (2.0)
Renal	14 (1.9)
Sarcoma	14 (1.9)
ECOG PS	
0	121 (16.3)
1	289 (38.9)
2	172 (23.2)
3–4	149 (20.1)
Not recorded	11 (1.5)
LENT Category	
Low	114 (15.4)
Moderate	429 (57.8)
High	133 (17.9)
Unable to calculate	66 (8.9)
PROMISE category	
A	256 (34.5)
B	186 (25.1)
C	151 (20.4)
D	21 (2.8)
Unable to calculate	128 (17.3)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; GI, gastrointestinal; MPE, malignant pleural effusion.

was the most common underlying malignancy (28.8%), followed by mesothelioma (20.5%) and breast cancer (16.6%). In the majority of included patients the diagnosis was confirmed through cytology and/or histopathology (n=661, 89.1%). The remaining patients were diagnosed with MPE based on radiological and clinical features following discussion at MDT. At the time of analysis, 650 (87.6%) of the included patients had died.

Local incidence of MPE

Changes in the local incidence of MPE over time were estimated through the number of patients on the Oxford Pleural Database diagnosed with MPE per year. This demonstrated a steady rise over the period of time assessed (online supplemental figure 1), with a 53.6% increase in the number diagnosed in 2022 (n=106) compared with 2016 (n=69). For comparison, the number of patients on the Oxford Pleural Database with a diagnosis of heart failure-related effusion or pleural infection was calculated, which showed no such increase (44 in 2016 compared with 39 in 2022).

Changes in MPE survival length over time

To investigate for changes in survival length over time, patients were divided into three groups of equal size based on date of MPE diagnosis (group 1: July 2015–October 2018; group 2: October 2018–April 2021; group 3: April 2021–October 2023). Kaplan-Meier analysis demonstrated similar median survival times between the three groups (157, 138 and 151 days for groups 1–3, respectively), and log-rank (Mantel-Cox) tests showed no significant differences. Kaplan-Meier survival curves are shown in figure 1.

Univariable Cox regression analyses showed that year of MPE diagnosis was not significantly associated with survival time (p=0.71) (table 2). LENT score, PROMISE score, age and sex were significantly associated with survival in univariable Cox models. In a multivariable model adjusted for age, sex and LENT score, year of diagnosis was not significantly associated with survival (p=0.56) (table 2). Sex and LENT score maintained significant associations with survival. The PROMISE score was excluded from the final multivariable model due to collinearity with the LENT score and the greater amount of missing data. A sensitivity analysis was performed with the PROMISE score included rather than LENT, in which year of diagnosis again showed no significant association with survival. Excluding patients without confirmatory pleural fluid cytology or pleural histopathology for diagnosis did not impact the association between year of diagnosis and survival in univariable (HR 1.01, p=0.57) or multivariable (HR 1.03, p=0.16) Cox analysis.

A mixed-effects Cox model was performed including year of diagnosis as a random effect. The estimated variance of the random effect was negligible (1.56×10^{-5}), suggesting minimal variability in survival attributable to year of diagnosis after adjusting for LENT score, age and sex. In this model, both LENT score (HR 1.70, p<0.0001) and sex (HR 1.34, p=0.0005) remained significantly associated

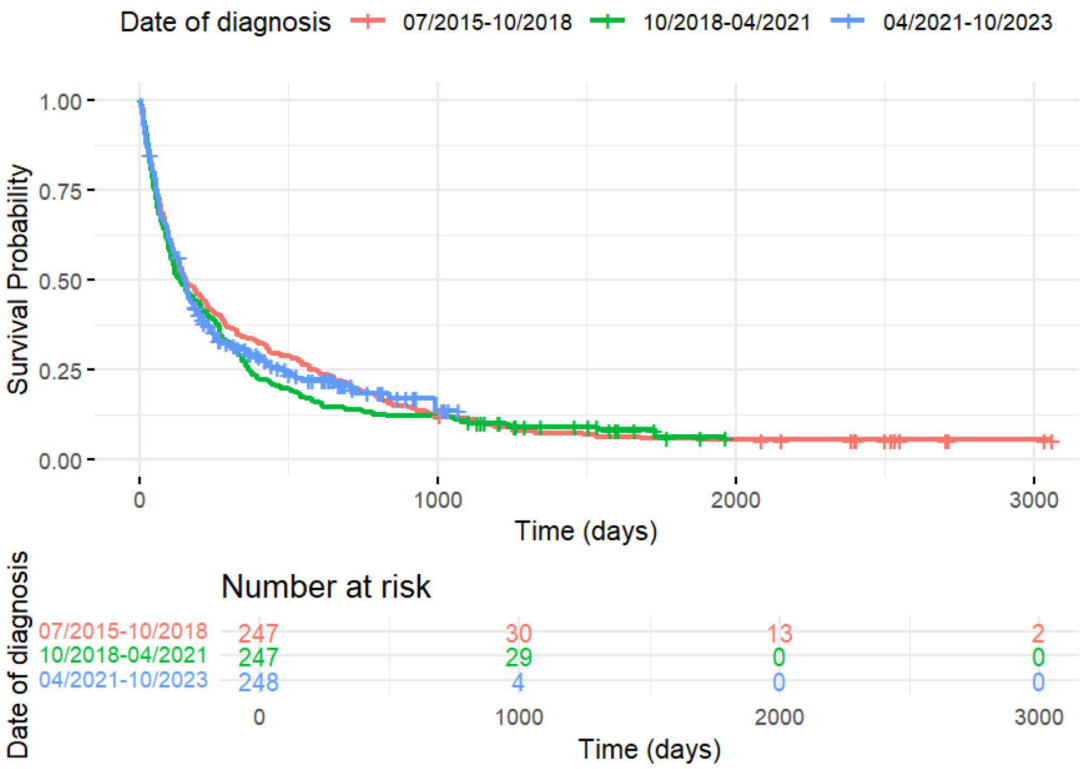

Figure 1 Survival probability over time stratified by date of MPE diagnosis. MPE, malignant pleural effusion.

with survival, while age was not significantly associated (HR 1.00, p=0.36).

Proportion of patients treated with SACT

Across groups stratified by date of MPE diagnosis, the proportion of patients receiving SACT increased in those managed in more recent years (figure 2). Furthermore, the SACT provided to patients with a later date of MPE diagnosis was more likely to include immunotherapy or targeted therapies. χ^2 tests confirmed that differences in SACT provision across diagnosis periods were statistically significant (any SACT: χ^2=12.5, df=2, p=0.002; immunotherapy or targeted therapy: χ^2=42.1, df=2, p<0.001; immunotherapy: χ^2=30.7, df=2, p<0.001).

Subgroup analyses

We hypothesised that improvements in survival over time may be masked by inclusion of patients with poor performance status, who would be less likely to have benefitted from advances in diagnostic pathways and treatment options. To investigate this, subgroup analyses were performed with patients with a performance status of 3 or 4 at MPE diagnosis excluded, and in only patients who received SACT following their cancer diagnosis. Log-rank tests showed no significant difference in survival between groups in either analysis (figure 3).

In subgroup analyses by causative cancer type, Kaplan-Meier analysis showed no significant difference in survival for those with a later date of diagnosis in any

Table 2 Cox regression analysis with the individual year of MPE diagnosis in a univariable model, and a multivariable model adjusted for age, sex and LENT score

	Univariable analysis		Multivariable analysis (n=676)	
Variable (ref)	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Year of MPE diagnosis	1.01 (0.97 to 1.04)	0.71	1.01 (0.98 to 1.05)	0.56
LENT Score	1.70 (1.60 to 1.80)	<0.0001	1.70 (1.60 to 1.81)	<0.0001
PROMISE score	1.10 (1.09 to 1.11)	<0.0001		
Sex (female)	1.28 (1.10 to 1.50)	0.0017	1.34 (1.14 to 1.58)	0.0005
Age	1.01 (1.00 to 1.01)	0.031	1.00 (0.99 to 1.00)	0.35

Numbers included in univariable analyses: year of MPE diagnosis, sex and age n=742; LENT score n=676; PROMISE score n=614.
MPE, malignant pleural effusion; ref, reference.

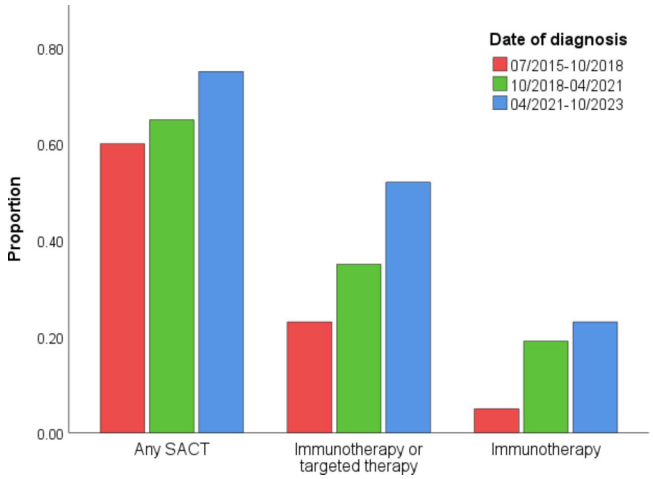

Figure 2 The proportion of patients, stratified by date of MPE diagnosis, receiving: (1) any SACT, (2) immunotherapy or targeted therapy and (3) immunotherapy. MPE, malignant pleural effusion; SACT, systemic anti-cancer therapy.

of the underlying malignancies assessed (lung cancer, breast cancer and mesothelioma) (figure 3).

Time from primary cancer diagnosis to MPE development

Excluding patients with mesothelioma, all of whom were diagnosed through investigations for pleural effusion and/or pleural abnormality, 281 (47.6%) of the remaining patients either had the diagnosis of their primary malignancy identified through pleural fluid investigations, or had pleural effusion present at the time of their diagnosis that was subsequently confirmed to be malignant. This was particularly common for lung cancers, with 168 (78.5%) diagnosed through pleural investigations, while only 10 (8.1%) breast cancer patients had effusion present at the time of initial cancer diagnosis. In the remaining patients who developed MPE following a previous diagnosis of malignancy, the time from primary cancer diagnosis to the development of MPE was particularly long for patients with breast cancer, with a median time of 3204 days (IQR: 1901–5727 days). There was no evidence that time from primary cancer diagnosis to MPE development had lengthened over the time of our analysis; however, there was marked variability between cancer types and limited patient numbers for this assessment.

DISCUSSION

In this single-centre, large retrospective cohort study, we have demonstrated that survival time in patients with MPE has not increased over an 8-year time period. Rather, it appears that survival has remained relatively stagnant, with an overall median survival in our cohort of 150 days. This finding was consistent across MPE secondary to any primary malignancy, MPE secondary to lung cancer, mesothelioma or breast cancer, in patients with better performance status (0–2) at MPE diagnosis and in patients who received SACT.

Our findings diverge from recent encouraging trends in cancer survival overall, where improvements in mortality rates have been shown across most major cancer types.[4 10] Specifically in mesothelioma, a recent large-scale epidemiological study by Shelton *et al* demonstrated a 4.2% reduction in mortality rate in men and a 2.0% reduction in mortality rate in women between 2001–2003 and 2016–2018.[4] However, in contrast, a retrospective cohort study by Ossowski *et al* in the USA, which included 368 adult patients with malignant pleural mesothelioma, showed no difference in survival between patients diagnosed from 2009 to 2014 and those diagnosed between 2015 and 2020.[18] In combination with our results, this may suggest that previous survival improvements in mesothelioma have plateaued.

While the year of diagnosis was not associated with survival in Cox regression analyses, increasing LENT or PROMISE score, and male sex, were demonstrated to be factors associated with poor prognosis. The LENT and PROMISE scores have been repeatedly shown to be predictive of survival in patients with MPE[15 16 19]; however, their uptake in clinical practice has been limited to date. This is likely explained by the lack of requirement to stratify patients to different treatment options based on prognosis, as currently decisions regarding management are predominantly led by patient preference rather than any potential options to alter survival.[19] Furthermore, a concern with prognostic scores is that their performance may diminish over time with changing healthcare practices, and notably both scores predate the modern immunotherapy era. Nonetheless, in this study, the cohort spans the introduction of many agents targeted to causative underlying malignancies of MPE, yet the scores remain strongly associated with survival.

Multiple studies have shown an overall increasing uptake of SACT over recent years, with a shift from traditional chemotherapy towards immunotherapy and targeted therapies.[20–22] This was also demonstrated in our cohort (figure 2). Furthermore, over the time course of this study, there have been particular landmark National Institute for Health and Care Excellence (NICE) approvals for therapies against many common causative malignancies of MPE, such as pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer in 2018,[23] and nivolumab with ipilimumab for untreated unresectable malignant pleural mesothelioma in 2022.[24] In our analyses, we split patients into groups of equal size, rather than groups of before and after individual NICE approvals, to account for multiple intervention changes across the time course of the study, and to avoid small sample sizes after more recent changes. Given the increased use of targeted cancer therapies in those with a later date of MPE diagnosis, one would have expected some survival differences over the time course of our analysis. Potential reasons for the lack of improvement in survival time following the development

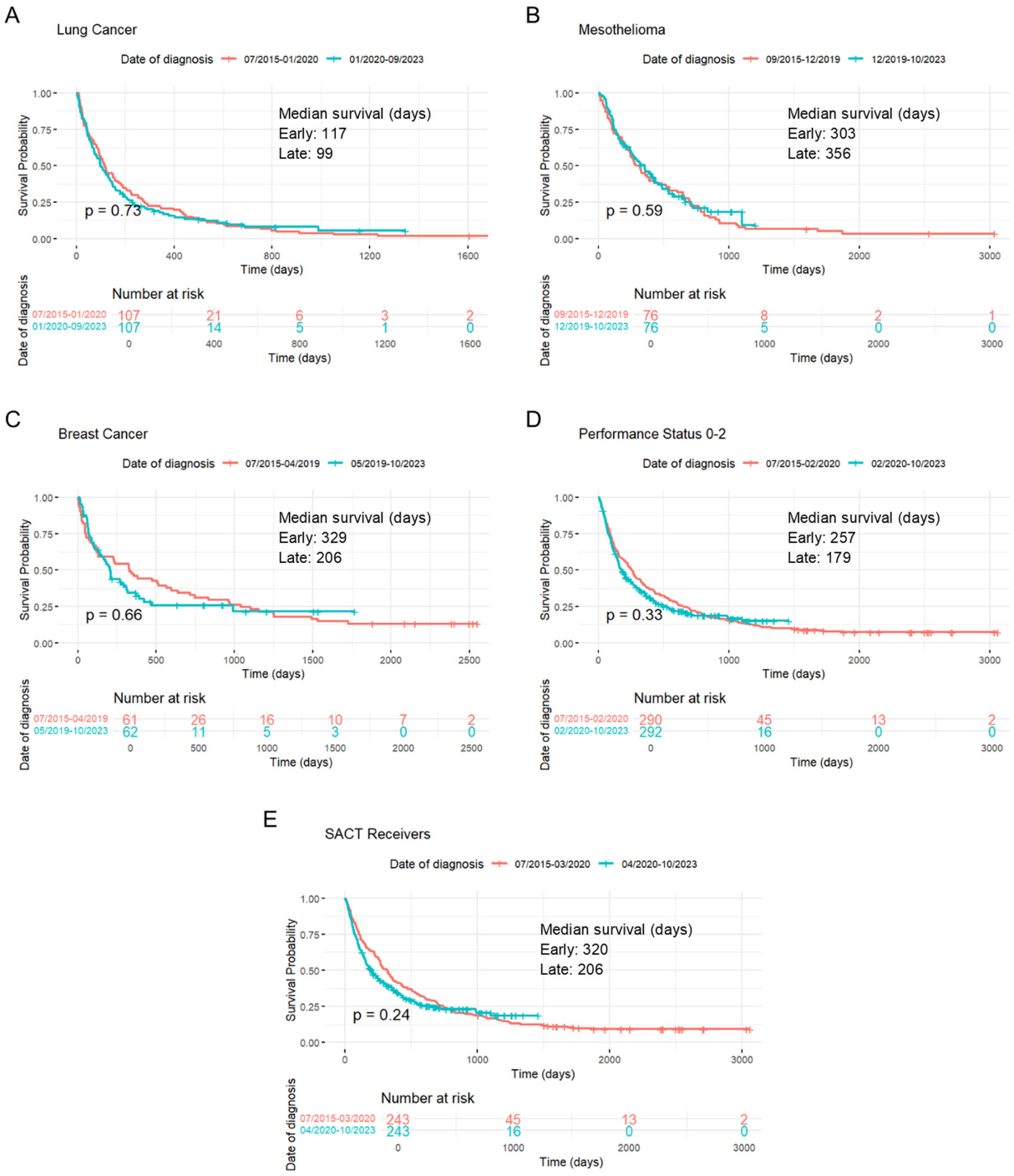

Figure 3 Survival probability over time in patients with lung cancer (A), mesothelioma (B), breast cancer (C), performance status 0–2 with any malignancy (D), receiving SACT with any malignancy (E). P values indicate the significance level from the comparison of curves using the log-rank (Mantel-Cox) test. Median survival times are shown for cohorts with an earlier date of diagnosis ('early') and those with a later date of diagnosis ('late'). SACT, systemic anti-cancer therapy.

of MPE are therefore important to consider. Over recent years, there has been increasing evidence that malignant pleural fluid is a biologically active contributor to tumour progression, and that the local tumour microenvironment within the pleural space promotes an aggressive and invasive tumour phenotype that can effectively evade the immune system.[25–28] Furthermore, as the pleural space represents a sequestered local environment bounded by tight junction-connected mesothelial cells, protein biologics administered systemically pass relatively poorly into this space.[28 29] This suggests that MPE should potentially be thought of as a separate entity to the underlying malignancy, and that MPE-specific therapeutics should be considered. One such example may come through the intrapleural administration of protein biologics which, given the aforementioned mesothelial cell tight

junctions, will remain highly concentrated in the pleural space.[30] The initial results from investigations in this field have been promising, with evidence from mouse models of MPE that intrapleural injection of antibodies targeting the PD-1/PD-L1 pathway prolongs survival,[31 32] and clinical trials of intrapleurally administered anti-angiogenic agents showing improved prognosis in patients with MPE.[33] It is also possible that while survival time following the development of MPE has remained consistent, the lead time from the diagnosis of primary malignancy to pleural spread and effusion formation may have lengthened. However, in our cohort, a significant number of patients had MPE present at the time of primary malignancy diagnosis (47.6% after mesothelioma excluded). In the remaining patients we were still unable to demonstrate an increase in the time from primary malignancy diagnosis to MPE development, although this was limited by small patient numbers and a large spread of results.

Despite the overall disappointing findings of this study, there are some reasons for cautious optimism that survival improvements for subsets of patients with MPE may be forthcoming. In mesothelioma, for instance, clinical trials demonstrating improved overall survival with immunotherapy have led to recent approval for use in this disease, and the benefits of this may not have yet been detected in our cohort.[24 34 35] Furthermore, the roll-out of lung cancer screening in the UK offers hope of detecting more lung malignancies before pleural spread.[36] Our findings support the importance of this, as large numbers of lung cancer patients in our cohort had developed MPE at their time of presentation and were diagnosed through pleural fluid investigations.

Our findings also support previous assertions that the incidence of malignant pleural disease will continue to rise.[3 5] In our centre, there was a>50% increase in the number of patients diagnosed with MPE in 2022 compared with 2016, with a steady rise in incidence year-on-year, while no such increase was seen in patients diagnosed with pleural infection or heart-failure related effusions. This finding likely reflects growth in the rates of new cancer diagnoses and the increasing length that patients are surviving with cancer (prior to the development of MPE).[5]

Limitations of the current study include the single-centre design, which may limit the generalisability of these findings to other healthcare settings. Additionally, not all potential confounders were included in Cox analyses, for instance, the sensitising mutation status of the underlying primary malignancy and pleurodesis success.[19 37] Nonetheless, our findings were consistent after adjustment with either the LENT or PROMISE scores, the two most well-validated prognostic models in MPE, increasing confidence in the robustness of the results. Finally, as individuals with MPE were identified from the OUH pleural MDT, it is possible that not all local cases of MPE were included in the present study. Local referral pathways direct that all patients with symptomatic pleural effusion or pleural effusion requiring intervention for diagnosis are referred to the OUH pleural team and should therefore be included in the study population. However, patients with known cancer and small, asymptomatic effusions are often not referred, as are palliative patients ineligible for intervention due to poor performance status. Nonetheless, the criteria for patient discussion at the MDT have remained consistent over the period assessed, and only a relatively small number of local MPE cases will be missed; hence, it is unlikely that this has introduced any significant bias into our analyses.

CONCLUSIONS

Despite recent evidence demonstrating improving survival trends in cancer overall, and the increasing use of targeted treatments in metastatic cancer, our results suggest that survival time following the development of symptomatic MPE has remained stagnant, while the incidence of MPE is increasing. This concerning finding suggests the development of MPE is a potentially clinically distinct entity and supports the need for a step change in our consideration of MPE, including investigation into specific oncological treatment of the MPE space.

Contributors Study concept and design: CM, NIK, DA, RH and NR. Acquisition of data: CM, IRM and DA. Statistical analysis and interpretation of data: CM, NIK, DA, WMC, BI, AE, AS, RH and NR. Drafting and revision of the manuscript: CM, NIK, DA, WMC, IRM, BI, AE, AS, RH and NR. Guarantor: CM.

Funding NIK, AS, RH and NR are supported by the NIHR Oxford Biomedical Research Centre. NIK is supported by the Chinese Academy of Medical Sciences, Oxford.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethical and regulatory approval for the study was obtained through Health Research Authority (HRA) and Health and Care Research Wales (HCRW) Approval (REC reference number 24/HRA/1980).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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REFERENCES

1 Psallidas I, Kalomenidis I, Porcel JM, *et al*. Malignant pleural effusion: from bench to bedside. *Eur Respir Rev* 2016;25:189–98.
2 Yang L, Wang Y. Malignant pleural effusion diagnosis and therapy. *Open Life Sci* 2023;18:20220575.
3 Piggott LM, Hayes C, Greene J, *et al*. Malignant pleural disease. *Breathe (Sheff)* 2023;19:230145.
4 Shelton J, Zotow E, Smith L, *et al*. 25 year trends in cancer incidence and mortality among adults aged 35-69 years in the UK, 1993-2018: retrospective secondary analysis. *BMJ* 2024;384:e076962.
5 Bodtger U, Hallifax RJ. Epidemiology: why is pleural disease becoming more common? In: *Pleural disease*. European Respiratory Society, 2025: 1–12.
6 Bibby AC, Dorn P, Psallidas I, *et al*. ERS/EACTS statement on the management of malignant pleural effusions. *Eur Respir J* 2018;52:1800349.
7 Roberts ME, Rahman NM, Maskell NA, *et al*. British Thoracic Society Guideline for pleural disease. *Thorax* 2023;78:s1–42.
8 Feller-Kopman DJ, Reddy CB, DeCamp MM, *et al*. Management of Malignant Pleural Effusions. An Official ATS/STS/STR Clinical Practice Guideline. *Am J Respir Crit Care Med* 2018;198:839–49.
9 Cui J, Ding R, Liu H, *et al*. Trends in the incidence and survival of cancer in individuals aged 55 years and older in the United States, 1975-2019. *BMC Public Health* 2024;24:72.
10 Mariotto AB, Zhang F, Buckman DW, *et al*. Characterizing Trends in Cancer Patients' Survival Using the JPSurv Software. *Cancer Epidemiol Biomarkers Prev* 2021;30:2001–9.
11 Ling SP, Ming LC, Dhaliwal JS, *et al*. Role of Immunotherapy in the Treatment of Cancer: A Systematic Review. *Cancers (Basel)* 2022;14:5205.
12 Waldman AD, Fritz JM, Lenardo MJ. A guide to cancer immunotherapy: from T cell basic science to clinical practice. *Nat Rev Immunol* 2020;20:651–68.
13 Overview | lung cancer: diagnosis and management | guidance. NICE; 2019. Available: https://www.nice.org.uk/guidance/ng122
14 Lahiri A, Maji A, Potdar PD, *et al*. Lung cancer immunotherapy: progress, pitfalls, and promises. *Mol Cancer* 2023;22:40.
15 Clive AO, Kahan BC, Hooper CE, *et al*. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. *Thorax* 2014;69:1098–104.
16 Psallidas I, Kanellakis NI, Gerry S, *et al*. Development and validation of response markers to predict survival and pleurodesis success in patients with malignant pleural effusion (PROMISE): a multicohort analysis. *Lancet Oncol* 2018;19:930–9.
17 R: the r project for statistical computing. 2025. Available: https://www.r-project.org
18 Ossowski S, Hung Y-Y, Banks K, *et al*. Improving outcomes in malignant pleural mesothelioma in an integrated health care system. *J Thorac Dis* 2022;14:3352–63.
19 Mounsey CA, Kanellakis NI, Addala DN, *et al*. External validation of the LENT and PROMISE prognostic scores for malignant pleural effusion. *ERJ Open Res* 2025;11:01019-2024.
20 Carroll NM, Eisenstein J, Burnett-Hartman AN, *et al*. Uptake of novel systemic therapy: Real world patterns among adults with advanced non-small cell lung cancer. *Cancer Treat Res Commun* 2023;36:100730.
21 Snee M, Cheeseman S, Thompson M, *et al*. Trends in the prescription of systemic anticancer therapy and mortality among patients with advanced non-small cell lung cancer: a real-world retrospective observational cohort study from the I-O optimise initiative. *BMJ Open* 2021;11:e043442.
22 Young A, Marshall E, Krzyzanowska M, *et al*. Responding to Acute Care Needs of Patients With Cancer: Recent Trends Across Continents. *Oncologist* 2016;21:301–7.
23 Overview | Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer | Guidance. NICE; 2018. Available: https://www.nice.org.uk/guidance/ta531
24 Overview | nivolumab with ipilimumab for untreated unresectable malignant pleural mesothelioma | guidance. NICE; 2022. Available: https://www.nice.org.uk/guidance/ta818
25 Asciak R, Kanellakis NI, Yao X, *et al*. Pleural Fluid Has Pro-Growth Biological Properties Which Enable Cancer Cell Proliferation. *Front Oncol* 2021;11:658395.
26 Cheah HM, Lansley SM, Varano della Vergiliana JF, *et al*. Malignant pleural fluid from mesothelioma has potent biological activities. *Respirology* 2017;22:192–9.
27 Ge S, Zhao Y, Liang J, *et al*. Immune modulation in malignant pleural effusion: from microenvironment to therapeutic implications. *Cancer Cell Int* 2024;24:105.
28 Donnenberg AD, Luketich JD, Dhupar R, *et al*. Treatment of malignant pleural effusions: the case for localized immunotherapy. *J Immunother Cancer* 2019;7:110.
29 Markov AG, Amasheh S. Tight junction physiology of pleural mesothelium. *Front Physiol* 2014;5:221.
30 Goey S, Eggermont A, Punt C, *et al*. Intrapleural administration of interleukin 2 in pleural mesothelioma: a phase I-II study. *Br J Cancer* 1995;72:1283–8.
31 Liu Y, Wang L, Song Q, *et al*. Intrapleural nano-immunotherapy promotes innate and adaptive immune responses to enhance anti-PD-L1 therapy for malignant pleural effusion. *Nat Nanotechnol* 2022;17:206–16.
32 Li X, Wu G, Chen C, *et al*. Intrapleural Injection of Anti-PD1 Antibody: A Novel Management of Malignant Pleural Effusion. *Front Immunol* 2021;12:760683.
33 Zeng H, Zhang Y, Tan S, *et al*. Efficacy of bevacizumab through an indwelling pleural catheter in non-small cell lung cancer patients with symptomatic malignant pleural effusion. *BMC Pulm Med* 2024;24:89.
34 Fennell DA, Ewings S, Ottensmeier C, *et al*. Nivolumab versus placebo in patients with relapsed malignant mesothelioma (CONFIRM): a multicentre, double-blind, randomised, phase 3 trial. *Lancet Oncol* 2021;22:1530–40.
35 Baas P, Scherpereel A, Nowak AK, *et al*. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial. *Lancet* 2021;397:375–86.
36 New lung cancer screening roll out to detect cancer sooner. GOV.UK; 2023. Available: https://www.gov.uk/government/news/new-lung-cancer-screening-roll-out-to-detect-cancer-sooner
37 Hassan M, Harriss E, Mercer RM, *et al*. Survival and pleurodesis outcome in patients with malignant pleural effusion - a systematic review. *Pleura Peritoneum* 2021;6:1–5.