1 Impact of the COVID-19 Pandemic on Lung Cancer Treatment &

2 **Research**

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8 To the Editor,

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10 Despite recent advances in immunotherapy and targeted therapy, the mortality rate seen 11 in lung cancer (LC) is the highest of all cancer forms. The recently topical coronavirus 12 disease 19 (COVID-19) and its subsequent pandemic has resulted in over 505 million 13 confirmed cases and approximately 6.2 million fatalities as of April 2022 (1), with a 14 staggering 30-50% mortality rate seen in LC patients with COVID-19 (2). Cancer 15 patients in particular are highly vulnerable to COVID-19 infection due to 16 immunosuppression, from both the tumour and treatments. Here we report the impact 17 of the pandemic to be largely negative on LC treatment and research.

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19 Impacts on Lung Cancer Treatments

20 As seen in Figure 1A, many countries saw a significant decline in observed LC cases 21 during the first peak pandemic period. Cancer care was also notably affected – a global 22 study by Jazieh et al. (3) compiled data from 356 centres across 54 countries to gauge 23 this effect. Although this study focuses on cancer care in general, rather than providing 24 a breakdown of individual cancer types, it provides insight into reasons why care may 25 have been affected. Most centres (around 64%) remained open over the pandemic but 26 at suboptimal capacity and reported various reasons for this such as precautionary 27 measures, staff shortages and overburden to the system (3). Nearly half the centres also 28 reported a shortage of personal protective equipment (PPE). Around 9% of centres were 29 either fully or partially closed and the rest remained open at full capacity. The majority 30 of centres in the study kept most services as either partially or fully available, but of 31 those that fully stopped, surgery appears to be the most disrupted across centres and 32 systemic therapy the least. This is likely due to the increased risk of infection and 33 immunosuppression that accompany surgery. However, the extent to which services 34 were partially available was not quantified and thus the magnitude of disruption cannot 35 be fully concluded. Jazieh and colleagues (3) also found the distribution of disruption 36 was relatively equal in countries across all levels of income, however only 9 of the 356 37 centres were in the low-income level, so the conclusion that low-income countries were 38 not affected disproportionately cannot be applied to all low-income countries.

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40 Impacts on Trials and Research

41 A search for the term "lung cancer" was conducted using the PubMed database, and the 42 number of papers published each year was plotted onto a graph (Figure 1B). This search 43 revealed no significant change to the overall trend in publications on lung cancer 44 following the start of the pandemic in 2020, however this does not necessarily mean 45 that research was unaffected whatsoever. Over the pandemic, the sheer volume of 46 COVID-19 related literature rapidly accumulated, with over 132,000 publications on 47 PubMed in 2021 alone -8 times as many as those on lung cancer. Whilst this is 48 understandable given the topical nature of COVID-19, it may have resulted in some 49 publications of lesser reliability and quality when compared with pre-pandemic levels 50 due to relaxation or even absence of vigorous peer-reviewing processes (4). The same 51 could extend for publications on lung cancer, meaning further assessment of literature 52 published over the pandemic must be carried out to ensure their quality and 53 trustworthiness.

Another search on PubMed for papers including both "lung cancer" and "COVID-19" yielded a total of 698 results, from 2020 to present. This number is significantly lesser than the quantity of results for "COVID-19", which may indicate the neglection of lung cancer in terms of its relevance to COVID-19 as a respiratory illness, despite the severity of lung cancer and COVID-19 comorbidity.

In terms of trials, a search on the clinical trials database (clinicaltrials.gov) for "lung cancer" studies revealed no negative impacts on the number of new trials being set up over the pandemic when compared with pre-pandemic figures (Figure 1C), although there was a global decline of 14% in clinical trial participation over the peak of the pandemic (5). However, trials can take years to complete and thus the completion and relative success of these trials cannot yet be determined at present.

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66 Conclusions

Overall, the COVID-19 pandemic has had a distinctly negative impact on the lung
cancer community, with increased morbidity and mortality, as well as a reduction in
trial participation. Many countries saw a sharp decline in LC cases and there was also

70 much public anxiety of attending in-person appointments, supplemented by conflicting 71 messages from the government and lung cancer organisations that contributed to this 72 decrease. The effectiveness of telehealth, which was outside the scope of this review, is 73 another possible aspect that may have improved or worsened delivery of care.

Further global collaborative studies need to be conducted in the near future in order to determine how different countries have been impacted based on income, magnitude of research and availability of specialist centres and relative number of COVID-19 cases. Focus should also be on if racial/ethnic disparities in the lung cancer community were further amplified due to the pandemic. Additionally, more funding and resources should be given to lung cancer trials and research, particularly for developing more early detection methods, as this is proven to significantly reduce mortality rates.

81 The volume of research paper publications may not have been outwardly affected, 82 but the reliability and quality of a small number still remains in question due to more 83 lenient peer-reviewing processes. Furthermore, the data reviewed was from a singular 84 database, *i.e.*, PubMed, and thus evaluation of data from multiple databases should be 85 considered in the future when determining the impacts on published literature. There 86 may also be a delayed effect on clinical trials, and subsequent approval of therapies, due to the lockdowns and reduction in trial participation. Whilst the pandemic 87 restrictions now appear to be lifting around the world and a majority of people are 88 immunised, there are still cases of COVID-19 present which could impact the 89 90 unvaccinated and immunocompromised, especially those with lung cancer. A slight 91 relaxation of lung screening criteria may aid in the detection of missed cases but does 92 pose a risk of increasing false-positive diagnosis. It could also expose those with a 93 slightly lower risk of lung cancer to ionising radiation, meaning the risks outweigh possible benefits. Regardless, the effects of missed cases will surely be seen in the next 94 95 5 to 10 years, with an increased number of deaths, however if novel therapies currently 96 in development are approved in time, this may change.

97 Figure legend

98 **Figure 1** – (A) Visualisation of percentage decrease in the number of lung cancer cases 99 in various countries during the approximate March – May period in 2020 when 100 compared with the baseline number of cases from previous years during the same March 101 - May period. (B) Visualisation of the trend in the number of new papers published 102 annually on lung cancer on PubMed from 2005 to 2021. The red arrow indicates the 103 start of the pandemic in 2020. Data obtained from PubMed using the search criteria 104 "lung cancer". (C) Visualisation of the trend in number of new lung cancer trials 105 registered on clinicaltrials.gov each month from August 2019 to April 2022. The red 106 line denotes the official start of the COVID-19 pandemic in March 2020.

Figure 1



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132 **Competing interests**

133 The authors declare that they have no relevant conflict of interest.