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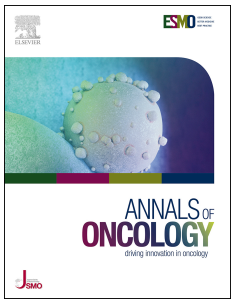

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Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic

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ABSTRACT

Background: Cancer diagnostics and surgery have been disrupted by the response of healthcare services to the COVID-19 pandemic. Progression of cancers during delay will impact on patient long-term survival.

Methods: We generated per-day hazard ratios of cancer progression from observational studies and applied these to age-specific, stage-specific cancer survival for England 2013-2017. We modelled per-patient delay of three months and six months and periods of disruption of one year and two years. Using healthcare resource costing, we contextualise attributable lives saved and life-years gained from cancer surgery to equivalent volumes of COVID-19 hospitalisations.

Findings: Per year, 94,912 resections for major cancers result in 80,406 long-term survivors and 1,717,051 life years gained. Per-patient delay of three/six months would cause attributable death of 4,755/10,760 of these individuals with loss of 92,214/208,275 life-years. For cancer surgery, average life-years gained (LYGs) per patient are 18.1 under standard conditions and 17.1/15.9 with a delay of three/six months (an average loss of 0.97/2.19 LYG per patient). Taking into account units of healthcare resource (HCRU), surgery results on average per patient in 2.25 resource-adjusted life-years gained (RALYGs) under standard conditions and 2.12/1.97 RALYGs following delay of three/six months. For 94,912 hospital COVID-19 admissions, there are 482,022 LYGs requiring of 1,052,949 HCRUs. Hospitalisation of community-acquired COVID-19 patients yields on average per patient 5.08 LYG and 0.46 RALYGs.

Interpretation: Modest delays in surgery for cancer incur significant impact on survival. Delay of three/six months in surgery for incident cancers would mitigate 19%/43% of life-years gained by hospitalisation of an equivalent volume of admissions for community-acquired COVID-19. This rises to 26%/59% when considering resource-adjusted life-years gained. To avoid a downstream public health crisis of avoidable cancer deaths, cancer diagnostic and surgical pathways must be maintained at normal throughput, with rapid attention to any backlog already accrued.

KEY WORDS

Oncology, Survival, Delay, COVID-19, Diagnostics

INTRODUCTION

Following the first case reports in Hubei province, China in late 2019, a pandemic of COVID-19 coronavirus was declared by the World Health Organisation in March 2020. Whilst COVID-19 causes minimal or mild illness in most, a small but appreciable proportion of individuals require oxygen therapy and often admission to an Intensive Care Unit (ICU). The ensuing unprecedented pressure on hospital wards and ICUs has necessitated rapid redeployment of staff and capacity towards the management of COVID-19 cases with deprioritisation of non-emergency clinical services, including diagnostics and elective specialist surgery. Concurrently, lockdown of the population has impacted dramatically on presentation and referral of symptomatic patients from primary into secondary care[1].

For patients with cancer, delay of surgery has the real potential to increase the likelihood of metastatic disease, with some patients' tumours progressing from being curable (with near normal life expectancy) to non-curable (with limited life expectancy)[2]. The situation has been further exacerbated by recent safety concerns regarding aerosol generation from endoscopy, cystoscopy and surgery[3, 4].

Current projections indicate that COVID-19-related disruption may well last for 18 months or more, until there is either long term effective containment in the population or large-scale vaccination. To inform healthcare prioritisation and resource allocation, we have examined the impact on cancer outcomes of different periods of delay of cancer surgery with disruption extending over variable time periods, comparing resource-weighted outcomes to hospital management of COVID-19 patients.

METHODS

Data sources

Number and age-specific five-year net survival of cancer patients that had potentially curative surgical resections for non-haematological malignancies between 2013 and 2017 were obtained from Public Health England National Cancer Registration Service (NCRAS)[5]. As well as cancer stage at diagnosis for each cancer type, breast tumour receptor data allowed subtyping of these cancers as ER+ HER2-, HER+ (any), ER- HER2-, and other. Estimates for nosocomial infection rates, median duration of hospital stay for each cancer type, staffing of theatres, ICU and surgical wards were based on information from three large UK surgical oncology centres. Patterns of administration of adjuvant systemic anti-cancer therapy (SACT) were based on oncologist-reviewed standard practice guidance[6]. ICU COVID-19 mortality, distribution by age, and duration of stay and proportion referred into ICU were obtained from ICNARC and data from hospitalised UK cases[7, 8]. Due to lack of UK data, data from Wuhan was used as the basis for the age distribution of community infection, age-specific likelihoods of admission from community to hospital, and mortality rates for non-ICU COVID-19 patients [9, 10] (Supplementary Table 1).

Analysis

Impact of COVID-associated delay on cancer outcomes

We used published data from studies examining the impact on overall survival from delay in cancer surgery to estimate per day hazard ratios (HRs) associated with delay for different cancers (the "Fatality HR") [11-21]. We had sufficient data to generate Fatality HRs for three tumour types and assigned these to other tumours, based on comparability of 5-year survival as low (>90%) moderate (50-90%) or high (<50%) progressiveness tumours[5]. Because we were unable to identify any suitable observational data for tumours of high progressiveness (e.g. oesophageal, gastric), we applied the Fatality HR from tumours of moderate progressiveness; this is likely to be a conservative assumption (Supplementary Table 2).

By accounting for COVID-related post-surgical mortality and changes in SACT, we adjusted five-year net survival figures for each cancer for surgical patients under ***standard*** care to estimate ***current*** five-year net survival. To model outcomes of surgery ***post-delay***, we apply to standard five-year net survival, the Fatality HR relating to the specified number of days of

delay, again including COVID-related post-surgical mortality. Based on estimates from a UK surgical oncology centre, supported by the literature, we applied a current per day rate of nosocomial infection of 5%. Assuming improvement in cold protocols, we modelled reduction in this rate over time. We estimated COVID-associated surgical mortality based on per day rate of nosocomial infection, operation-specific duration of post-surgical admission, and age-specific mortality from infection. We estimated COVID-19 associated mortality for SACT administration, based on per day rate of nosocomial infection, the frequency of SACT scheduling, increased risk associated with immunosuppression, and age-specific mortality from infection. We assumed, where standard-of-care, that SACT offers a uniform survival benefit (5% in Stage 1, 7.5% in Stage 2 and 10% in Stage 3) and administration would only continue where this benefit exceeds COVID-related mortality.

We used mean life-expectancies per 10-year age-group to calculate life years gained, averaged per patient. We examined reduction in overall survival and life years gained (LYG), comparing surgery under standard care, current conditions and post-delay, by cancer type and by age and stage. Using 2013-2017 surgical workload data, we calculated across all adult cancers examined, the total number of deaths and life years lost attributable to delay. To address possible scenarios, we considered per-patient delay of up to six-months, and 1- and 2-year periods of disruption.

COVID-19 outcome

To compare life years associated with timely cancer surgery with that afforded by hospitalisation of COVID-19 patients, we modelled a volume of community-ascertained COVID-19 infection resulting in an equivalent volume of hospital admissions to cancer surgeries (**Supplementary Table 1).**

Resource

We analysed healthcare resource units (HCRU) focused specifically on frontline medical and nursing staff, where one HCRU is one 12-hour shift of direct nursing or medical care. We up-weighted for shifts from healthcare workers of high-salary (senior doctors) and/or of current scarcity (anaesthetists, ICU nurses). We calculated HCRUs per patient using estimated staffing ratios for theatres, ICU and ward care and operation-specific data for theatre hours, ICU stay and ward days from oncology centres.

Details of assumptions and parameter estimates are detailed in **Table 1** and **Supplementary Table 1.** Analyses were performed using STATA (version 15) and transcribed to Excel, to provide a full visibility of parametrisation, model outputs, and opportunity for the reader to customise parameters (**Supplementary Materials**).

RESULTS

Impact of surgical delay on survival for different cancers

The greatest rates of deaths arise following even modest delays to surgery in aggressive cancers, with over 30% reduction in survival at six months and over 17% reduction in survival at three months for patients with stage 2 or 3 cancers of the bladder, lung, oesophagus, ovary, liver, pancreas and stomach (**Table 2, Supplementary Table 3, Supplementary Materials)**. Accounting for nosocomial COVID-19 infection, for cancers with a relatively good overall prognosis, delay of surgery by three months had a minimal impact on survival: <1% for all Stage 1 ER+ and HER2+ breast cancers, for example. In older patients (>70 years), for early stage colorectal, kidney and ER+ breast cancers, the current impact on survival of COVID-related mortality exceeded the impact of three or even six months delay (**Table 2, Supplementary Table 3**).

For a high proportion of solid cancers, survival at five years is generally considered to be equivalent to cure. Predicated on this assertion, we considered life-years gained adjusting for resource (resource adjusted life years (RALYGs)). Perhaps unsurprisingly, most benefit is afforded in younger age groups for operations that are shorter with no associated ICU requirement. For example, trans-urethral resection of stage 1 bladder cancers affords on average 23.4 RALYG per patient age 30-39, whereas cystectomy for stage 2 bladder cancer is only associated with 1.2 RALYGs in that age group (**Supplementary Table 4**). In the context of prioritisation, avoidance of a six-month delay restitutes on average 4.1 RALYGs in the former group, compared to 0.7 in the latter (**Table 3, Supplementary Table 5**). Wide local excision for breast cancer has low resource requirement and therefore confers substantial RALYGs, even in good prognosis subtypes.

Impact of surgical delay on cancer survival combined across cancer types

Each year, 94,912 surgical resections for common invasive adult cancer types are performed in England, with 80,406 of those patients surviving their cancer at five years. A surgical delay of three months across all incident solid tumours over one year would incur 4,755 excess deaths, escalating to 10,760 excess deaths for a six-month delay. This includes at six months, attributable deaths of 2,980 for colorectal cancer 1,439 for lung cancer and 804 for breast cancer **(Figure 1).**

For a high proportion of solid cancers, five-year survival is generally considered to be equivalent to cure. Predicated on this assertion, across all cancers a delay of three months in treatment would lead to a reduction of 92,214 life-years and for six months' reduction of 208,275 life years (**Table 3**). Prior to the COVID-19 crisis, each year cancer surgery was directly responsible for 1,717,051 LYGs. This represents on average 18·1 LYG per patient, which markedly reduces to 17·1 with three months' delay and to 15·9 with six months' delay. Cancer surgery per year requires 764,765 units of healthcare resource. Assuming this to be unchanged by delay, this affords on average 2.25 RALYG per patient under standard conditions, reducing to 2.12 with three months' delay and 1.97 with six months of delay, an average loss of 0.12 and 0.27 RALYGs, respectively, per patient.

Resource comparison for outcomes afforded by cancer surgery and COVID-19 management

For contextualisation, we compare the impact of cancer surgery delay to hospital care for patients with community-acquired COVID-19 infection. COVID-19 ICU admission for those aged 40-49 yielded on average 27.5 LYG and 0.8 RALYG. Those aged >80 years admitted to ICU benefit by on average 2.1 LYG and 0.06 RALYG. For non-ICU admission, average benefit is 9.3 LYG and 1.5 RALYG for those aged 40-49 and 1.4 LYG and 0.2 RALYG for those aged >80 years (**Supplementary Materials)**. These estimates are inherently conservative as they do not take into account the impact on life expectancy of the excess comorbidities associated with many hospitalised COVID-19 cases.

COVID-19 community-acquired infection of 683,083 individuals would result in 94,912 hospital admissions (*i.e*. the equivalent number to number of annual admissions for cancer surgery). For these 94,912 admissions, 16,135 will require ICU (critical cases) and 78,777 will not require ICU (severe cases). 1,052,949 units of healthcare resource are required in total and there are 15,587 deaths, 25,752 attributable lives saved, and 482,022 attributable LYGs (8,241 deaths/7,894 attributable lives saved/223,227 LYGs for ICU admissions, 7,346/ 17,858/ 258,795 for non-ICU). This represents on average 5.08 LYG and 0.46 RALYG per hospitalised COVID-19 patient.

It is therefore noteworthy, that a delay of surgery by six months results in 208,275 lost life-years for an annual quota of surgical patients: this equates to 43% of the total 482,022 life-years gained from hospitalisation of an equivalent number of community-acquired COVID-19 cases. This rises to 59% when adjusted for differences in resource (RALYGs).

Sensitivity Analysis

The outcomes from the model were mostly sensitive to changes in the Fatality HR for the per-day delay: varying this by ±8% (1SD) caused the average LYG with a six-month delay to range from 15.7-16.1, and attributable LY lost by 2.00-2.39. Sensitivity analysis for other parameters is shown in **Supplementary Table 2.**

DISCUSSION

We provide estimates derived from reported surgical outcomes to quantify the impact on survival of delay of cancer treatment, within the parameters of the assumptions of the model.

Implications for healthcare planning

For aggressive cancers, our analysis demonstrates that even short delays (three months) have a significant impact on patient survival. However, even for cancers of comparatively favourable prognosis, a delay of six months will result in significant summed attributable deaths as many of these cancers are common. Delay will also result in tumours being more advanced, meaning not only is survival poorer, but that the upstaged cancers will be more costly to treat both in terms of surgery and/or chemotherapy. Furthermore, resource requirements (for example, ICU stay) are dramatically higher for the many who will inevitably present as emergencies such as with obstruction, perforation or acute bleeding of the gastrointestinal tract[22].

Critical to mitigating cancer deaths is recognition that delay or bottleneck may arise at any point in the linear patient journey from (i) self-presentation of the symptomatic patient to primary care, (ii) primary care review and referral into secondary care (iii) diagnostic investigation, and (iv) surgery (or radiotherapy) with curative intent. Alongside any 'bulge' in accumulated cases will be the normal stream of incident cancer presentations. In the face of prolonged stress, it will be challenging to provide extra capacity to address these bulges alongside standard demands. In the short term, to avoid knock-on delays, immediate diversion of supra-normal resource volumes are required to process the backlog of cases that will have accrued in the initial months of the pandemic, in which referrals, investigations, and surgeries have been reduced by up to 80%[1]. In the medium-long term (over the next 3-24 months), avoidance of delay to cancer surgery should be of the highest priority: urgent attention is required to ensure sufficient resourcing for standard capacity of all pathway elements in primary care, cancer diagnostic, and surgical.

Delay in cancer surgery will have a highly deleterious health and economic impact. For the most part, the surgery will still be required (and may be more complex and costly) but

results in rapid diminution resultant life-years gained and resource-adjusted life-years. Comparing equivalent-sized hospital populations adjusted for resource, the health impact of delaying cancer surgery for six months will approximate 60% of health gains of hospitalizations for community acquired COVID-19 infection. We need to consider resourcing in the likely event of sizeable requirement for COVID-19 management for a sustained period of time, potentially up to two years. Although large facilities may be built/repurposed for COVID-19 management, these facilities are competing for the same fixed pool of healthcare workers that provide care for treating non-COVID-19 disease.

Currently, where the rate of nosocomial infection is high, for older groups in particular, surgery and/or SACT may in the short-term offer more risk than benefit (see Supplementary Materials). Active focus is required to establish 'cold' sections of the healthcare system, with rigorous protocols for staff screening and shielding protocols. This will serve to minimise nosocomial acquisition and mortality from COVID-19, to protect staff, and also to provide reassurance to the public regarding uptake of diagnostics and surgery for cancer.

Urgent review by professional bodies is required regarding best protection of their staffing groups, and guidance on surgical and diagnostic practice commensurate with the true risks[3].

Implications for prioritisation amongst cancer patients

Given an accrued backlog of cases and ongoing tight competition for resources, decisions regarding surgical prioritisation may be required for a number of years, with capacity varying geographically and temporally. Recognising its limitations regarding assumptions and parameters, we propose a model that provides a rational approach by which to evaluate across patients of different ages, tumour types, and stages, the benefit and resource implications of their cancer surgery. We highlight in our model those age-stage groups for which COVID-related mortality currently exceeds survival benefit for surgery and/or SACT. Whilst these and other groups for whom benefit is marginal will be the most rationale to delay, they will nevertheless require monitoring and surgery downstream. Longitudinal planning, monitoring of progression, dynamic re-prioritisation, and capacity-planning will inevitably be highly challenging.

Broader and International relevance

While we have used data for England, cancer survival is broadly similar across most economically developed countries, so the impact of delay per tumour is broadly applicable across Europe. However, variation in incidence of cancer, life expectancy and population age structure mean that predictions regarding total case numbers and life-years gained and lost are more difficult to extrapolate, even when scaling for relative size of reference population.

Whilst customised for surgical delay due to the COVID-19 pandemic, this model could readily be adapted to quantify the impact of surgical delay due to other causes.

Limitations

As with any model-based analysis, our predictions are predicated on the validity of assumptions and estimates used for parameterisation. While we have made use of observational data, our approach simplifies the complexity of cancer progression and is solely survival-focused. For healthcare planning, a more elaborate model capturing stage-shifting may offer additional utility. We base our analysis on survival data from 2013-17; for some tumour types, standard-of-care and survival has evolved since this time. Our modelling of the benefit of SACT is simplistic as the scheduling, benefits and immunosuppressive consequences vary by chemotherapy regimen. Whilst we have included in our model the impact withholding of SACT if nosocomical infection risk is high, we have not modelled additional reduction in survival from delays in administration of adjuvant therapy. Mortality from nosocomial COVID-19 infection during surgical admission or attendance for chemotherapy is based on a uniform per-day risk of infection: these may vary between institutions. While our resourcing analysis deliberately focuses on the requirement for the direct medical and nursing staff who most limit healthcare provision, we acknowledge it does not capture other 'costs' incurred in hospital care, primary care, and social care.

Our model of COVID-19 admissions is limited by availability of detailed individual-level UK data, in particular for non-CCU hospital admissions; this model is also conservative in regard of disregarding impact of co-morbidities on life expectancy.

Further research

Within our current approach, we only estimate the effects of a specified period of per-patient delay. Contemporaneous data for NHS activity offers the prospect of developing dynamic models to predict the impact of (i) differential prioritisation of patient groups, (ii) different patterns of re-presentation of 'accumulated' cases alongside incident cases, and (iii) varying release of bottlenecks in primary care, diagnostics, and surgery. Evaluation is also important for the alternative management approaches being adopted, such as radiotherapy with curative intent where surgery is gold-standard or *a priori* hormonal treatment for prostate and ER-positive breast cancers. For any strategies involving deliberate delay to surgery, models for re-staging and dynamic re-prioritisation are essential. We have focused on the impact to surgery with curative intent; analyses are also required to quantify the impact on mortality of changes to life-extending chemo- and radio-therapy for patients with Stage 4 disease.

CONCLUSION

Compared to COVID-19 management, cancer surgery is highly impactful in regard to life-years gained per resource expended. Delay in diagnosis and surgery cause exponential burden of attributable mortality. The COVID-19 pandemic has placed unprecedented strain on health care provision. It is highly plausible that surges of population infection, lock-downs, resource competition, bottlenecks, and back-logs could recur over the next two years. Supra-normal capacity is required to manage backlogs of accumulated cancer cases alongside ongoing incident cases. To avoid a deferred public health crisis of unnecessary cancer deaths, urgent ringfencing of substantial resources is required.

LEGENDS FOR FIGURES

Figure 1: Impact from 6-months delay lasting one year for all solid cancers analysed and six common cancer types in England expressed in **a:** Attributable deaths **b:** Life years Lost

Author contributions

C.T., M.E.J., A.S. and R.S.H. designed the model. M.E.J. provided cancer progression models. J.B. generated and quality-assured the NCRAS datasets applied to the model. M.E.J., J.B. C.T., R.S.H., A.S., C.A., G.L., M.W., and P.D.P.P provided epidemiological expertise in parameterisation of the model. F.G provided microbiology expertise in estimation of nosocomial infection rates. S.A.B, S.J., D.L.N, P.W., J.L., J.M.H, N.Y. and Y-E.S provided details of clinical pathways and estimates of clinical resourcing. B.T., A.G. and C.L. quality assured and user-tested the model. B.T. and C.L. assembled figures for presentation. C.T drafted the manuscript, with substantial contribution from A.S., R.S.H., M.E.J., G.L., M.W. and C.S.. All authors contributed to the final manuscript.

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Disclosure

The authors have no relevant disclosures to declare.

Highlights

- Lockdown and re-deployment due to the COVID-19 pandemic is causing significant disruption to cancer diagnosis and management.
- 3-month delay to surgery across all Stage 1-3 cancers is estimated to cause >4,700 attributable deaths per year in England.
- The impact on life years lost of 3-6 month to surgery for Stage 1-3 disease varies widely between tumour types.
- Strategic prioritisation of patients for diagnostics and surgery has potential to mitigate deaths attributable to delays.
- The resource-adjusted benefit in avoiding delay in cancer management compares favourably to admission for COVID-19 infection.

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COMPONENT OF MODEL	ELEMENTS	DATA SOURCE	COMMENT	Reference/specific values
Life years lost due to delay in surgery	Proportion of patients surviving after surgery	5 year survival rates for cancer surgery in England	Age, site, and stage-specific 5-year cancer survival in individuals in whom major resection was performed	PHE NCRAS[4]
	Decrease in survival due to delay in treatment	Observational studies of increased death rate due to delay in treatment	Hazard ratio for increase in death rate for each day delay in treatment based on estimates from literature, applied to standard survival rates. Applied to tumours depending on tumour aggressiveness	**Cancer progressiveness based on 5y survival:** Low: >90%, Moderate: 50-90% High: <50% **Per day Hazard ratio for fatality** [10-20]**:** Low: 0.0030, Mod: 0.0056 High: 0.0056
	COVID-related post-surgical mortality. SACT-related mortality	Nosocomial infection rate	Based on literature, estimate from clinical site data	5 % per day[29]
		Mortality from COVID-infection	Age-specific data from international series	**0-39 y** 0.2% **30-39 y** 0.2% **40-49 y** 0.4% **50-59 y** 1.3% **60-69 y** 3.6% **70-79 y** 8.0% **80+ y** 14.8%
		Survival benefit from SACT	Expert clinical interpretation of literature	**Stage 1:** 5% **Stage 2:** 7.5% **Stage 3:** 10% [30]
		Increase in COVID-related mortality due to SACT	Based on UK and international literature	2-fold [7, 8]
	Life-expectancy after survival	General population mean life-expectancies per 10 year age-band	Expected remaining life years in treated group based on proportion who survive after treatment (with and without delay)	ONS Life Tables[31]
Healthcare resourcing	Duration of operation, ICU and inpatient ward stay	Data from UK surgical oncology centres	Calculated as Healthcare Resource Unit (HCRUs) of direct clinical care. 1 HCRU= one 12 hour medical/nursing shift	
	Staffing ratios in theatre, wards, ICU			

Table 1: Summary of sources for parameters estimates for cancer surgical model (see Supplementary Table 1 for full description)

	Stage	30-39 y	40-49 y	50-59 y	60-69 y	70-79 y	80+ y
Bladder	1	15.8%	15.8%*	26.3%	18.4%	21.9%	23.8%
	2	36.0%	35.9%	32.7%	31.9%	29.0%	28.6%
	3	35.9%	35.8%*	34.8%	34.1%	32.4%	29.3%
Breast (ER+, HER2-)	1	1.5%	0.6%	-0.3%	-1.5%	-3.2%	-3.1%
	2	5.9%	2.8%	2.4%	0.7%	-1.3%	-5.6%
	3	13.4%	8.2%	9.2%	9.2%	9.1%	2.5%
Breast (ER-, HER2-)	1	6.2%	4.3%	5.4%	2.3%	0.5%	4.1%
	2	13%	12.2%	11.3%	10.0%	12.7%	14.0%
	3	18.2%	19.8%	19.4%	18.5%	18·2%	16.0%
Breast (HER2+)	1	0·4%	0·9%	1.0%	0.5%	-1.7%	3.5%
	2	4.2%	3.1%	3.4%	3.0%	3.3%	6.5%
	3	11.3%	7.0%	9.6%	8.8%	13.9%	15.0%
Colon and rectosigmoid junction	1	2.1%	4.9%	4.5%	3.0%	-1.5%	-2.8%
	2	16.7%	15.9%	14.0%	14.7%	15.0%	4.8%
	3	29.9%	29.1%	29.2%	28.5%	30.2%	28.8%
Kidney	1	2.1%	2.6%	6.0%	5.1%	0.5%	-2.5%
	2	13.2%	17.0%	11.5%	16.1%	13.8%	26.4%
	3	19.8%	23.5%	25.7%	24.9%	23.5%	22.2%
Larynx	1	11.5%	16.3%	19.0%	16.9%	11.2%	20.1%
	2	29.5%	29.5%*	20.5%	31.7%	32.3%	32.5%
	3	33.9%	33.8%*	35.4%	34.2%	32.8%	20.7%
Lung (non-small cell)	1	5.4%	14.3%	25.4%	27.5%	29.6%	24.0%
	2	31.6%	34.2%	34.8%	34.5%	32.3%	29.6%
	3	35.7%	35.7%	34.1%	29.6%	27.9%	19.6%
Melanoma of skin	1	1.1%	2.5%	0.4%	1.2%	0.2%	2.8%
	2	19.9%	22.5%	24%	28.2%	27.1%	34.4%
	3	29.0%	30.8%	31.4%	33.5%	31.4%	31.5%
Oesophagus	1	31.6%	31.5%	29.8%	29.4%	24.7%	29.9%
	2	35.9%	35.8%*	35.4%	34.3%	32.2%	28.3%
	3	35.8%	34.2%	30.4%	31.9%	27.0%	25.3%
Ovary	1	4.6%	7.1%	10.8%	10.4%	11.3%	-1.1%
	2	16.9%	26.2%	28.9%	29.6%	31.9%	35.3%
	3	31.5%	35.9%	33.8%	31.5%	28.6%	21.0%
Pancreas	1	1.0%*	9.6%*	12.7%	15.4%	20.2%*	28.1%
	2	23.8%	35.9%*	27%	23.6%	21.4%	25.9%
	3	24.8%	24.7%*	32.3%	33.2%*	31.4%*	24.1%
Prostate	1	1.4%*	1.4%	-0.3%	-0.7%	1.6%	15.4%
	2	0.0%*	-0.1%	-0.3%	-0.7%	-1.5%	16.9%
	3	0.0%*	-0.1%	-0.3%	-0.7%	-1.5%	17.8%
Stomach	1	12.2%	18.6%*	29.3%	21.4%	11.1%	-6.5%
	2	35.0%	27.9%*	35.2%	34.4%	32.2%	18.0%
	3	35.0%	32.3%	33.2%	32.3%	28.9%	26.8%
Uterus	1	3.3%	5.6%	6.1%	9.5%	12.6%	6.0%
	2	13.2%	18.4%	18.9%	26.5%	32.6%	33.0%
	3	10.2%	31.1%	33.4%	35.8%	33.1%	33.6%

Table 2: Reduction in five-year net survival as a consequence of six-month delay to surgery for 13 cancer types, by tumour stage and age of diagnosis.

Reduction in survival above the median is represented in red, at the median in yellow and below the median in green. Survival analysis is based on per-day hazard ratios for disease fatality. * indicates strata estimates of lower confidence whereby crude rather than net survival estimates were applied.

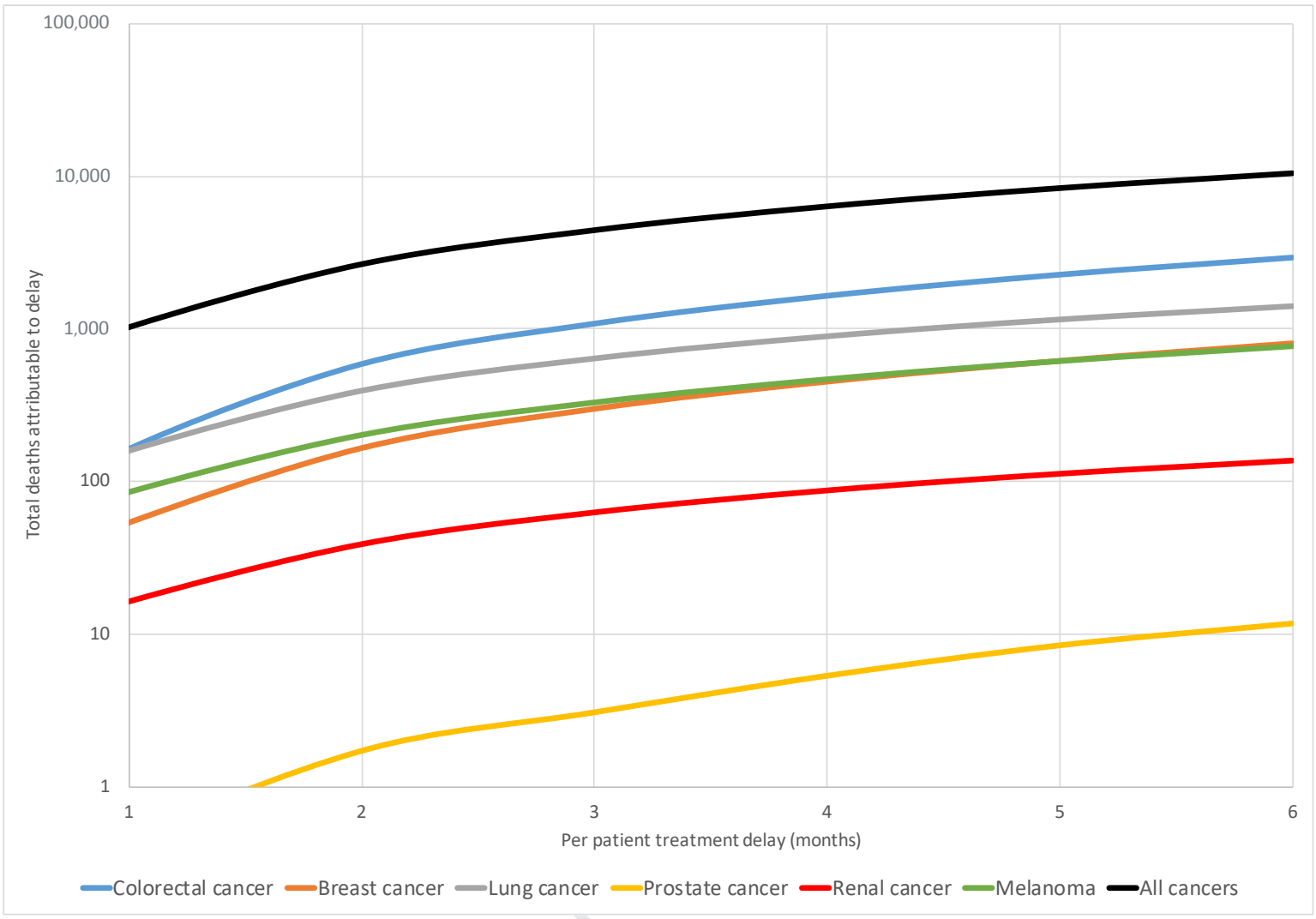
	Stage	30-39	40-49	50-59	60-69	70-79	80+
Bladder	1	4.1*	3.3*	4.1	2.0	1.5	0.8
	2	0.7*	0.6	0.4	0.3	0.1	0.1
	3	0.7*	0.6*	0.4	0.3	0.2	0.1
Breast (ER+, HER2-)	1	0.3	0.1	0.0	-0.1	-0.2	-0.1
	2	1.2	0.5	0.3	0.1	-0.1	-0.2
	3	2.8	1.4	1.2	0.8	0.5	0.1
Breast (ER-, HER2-)	1	1.3	0.7	0.7	0.2	0.0	0.1
	2	2.7	2.0	1.4	0.9	0.7	0.4
	3	3.8*	3.3	2.4	1.6	1.0	0.5*
Breast (HER2+)	1	0.1	0.2	0.1	0.0	-0.1	0.1
	2	0.9	0.5	0.4	0.3	0.2	0.2
	3	2.4	1.2	1.2	0.8	0.8	0.4
Colon and rectosigmoid junction	1	0.1	0.1	0.1	0.0	0.0	0.0
	2	0.6	0.4	0.3	0.2	0.1	0.0
	3	1.0	0.8	0.6	0.4	0.3	0.1
Kidney	1	0.1	0.1	0.2	0.1	0.0	0.0
	2	0.5*	0.5	0.2	0.2	0.1	0.1
	3	0.7*	0.7	0.6	0.4	0.2	0.1
Larynx	1	0.4*	0.4	0.4	0.2	0.1	0.1
	2	0.9*	0.7*	0.4*	0.4	0.3	0.1*
	3	1.0*	0.8*	0.6	0.4	0.3	0.1*
Lung (non-small cell)	1	0.2	0.3	0.5	0.3	0.2	0.1
	2	0.9*	0.8	0.6	0.4	0.2	0.1
	3	1.1*	0.8	0.6	0.4	0.2	0.1
Melanoma of skin	1	0.4	0.7	0.1	0.2	0.0	0.1
	2	2.1	1.9	1.5	1.2	0.7	0.5
	3	3.0	2.6	2.0	1.5	0.9	0.4
Oesophagus	1	0.6*	0.4	0.3	0.2	0.1	0.1*
	2	0.6*	0.5*	0.4	0.3	0.1	0.1*
	3	0.6*	0.5	0.3	0.2	0.1	0.1*
Ovary	1	0.5	0.6	0.7	0.5	0.3	0.0
	2	1.8*	2.2	1.8	1.3	0.9	0.5
	3	0.8	0.8	0.5	0.4	0.2	0.1
Pancreas	1	0.0*	0.1*	0.1*	0.1	0.1*	0.1*
	2	0.4*	0.5*	0.3	0.2	0.1	0.1*
	3	0.4*	0.4*	0.4*	0.3*	0.1*	0.1*
Prostate	1	0.0*	0.0	0.0	0.0	0.0	0.1
	2	0.0*	0.0	0.0	0.0	0.0	0.1*
	3	0.0*	0.0	0.0	0.0	0.0	0.1*
Stomach	1	0.3*	0.3*	0.4	0.2	0.1	0.0
	2	0.7*	0.4*	0.4	0.3	0.2	0.0
	3	0.7*	0.5	0.4	0.3	0.1	0.1
Uterus	1	0.3	0.4	0.3	0.4	0.3	0.1
	2	1.1*	1.3	1.0	1.0	0.7	0.4
	3	0.9*	2.2	1.8	1.3	0.8	0.4

Table 3: Estimated average life years gained per unit of healthcare resource for cancer surgery for 13 cancer types, by tumour stage and age of diagnosis comparing current surgery to surgery after six months delay based on 5-year net survival.

* indicates strata estimates of lower confidence whereby crude rather than net survival estimates were applied. Values for LYG per HCRU above the median are represented in blue, at the median in white and below the median in red.

CANCER SURGERY						
Reference time period (months)			12		24	
Per patient delay (months)			3	6	3	6
Per day rate of nosocomial infection (current)			5%			
STANDARD CONDITIONS	Major resections for cancer-		94,912		189,823	
	HCRUs-total		764,765		1,529,529	
	LY gained-total		1,717,051		3,434,102	
	Lives saved-total		80,406		160,812	
	LY gained from cancer		18.1			
	LY gained from cancer		2.2			
IMPACT of DELAY	Deaths attributable to delay-total		4,755	10,760	9,511	21,521
	LY lost attributable to delay-total		92,214	208,275	184,428	416,549
	LY gained from cancer treatment post-delay- average per patient		17.1	15.9	17.1	15.9
	LY lost attributable to delay-average per patient		0.97	2.19	0.97	2.19
	LY gained per HCRU from cancer treatment post-delay-average per patient		2.12	1.97	2.12	1.97
	LY lost per HCRU attributable to delay-average per patient		0.12	0.27	0.12	0.27
HOSPITALISATION OF COMMUNITY-ACQUIRED COVID INFECTION						
Reference time period (months)			12		24	
Community infections			683,083		1,366,167	
Hospital Admissions		Total admissions	94,912		189,823	
		ICU admissions	16,135		32,270	
		non-ICU admissions	78,777		157,553	
Health care resource units (HCRUs)		Total	1,052,949		2,105,899	
		ICU	556,657		1,113,313	
		non-ICU	496,293		992,586	
Deaths		Total	15,587		31,173	
		ICU	8,241		16,481	
		non-ICU	7,346		14,692	
Total lives saved -attributable to hospital admission		All	25,752		51,504	
		ICU	7,894		15,789	
		non-ICU	17,858		35,715	
Total LY gained -attributable to hospital admission		All	482,022		964,044	
		ICU	223,227		446,454	
		non-ICU	258,795		517,591	
LY gained -average per patient		All	5.08			
		ICU	13.83			
		non-ICU	3.29			
LY gained per HCRU -average per patient		All	0.46			
		ICU	0.40			
		non-ICU	0.52			
Comparison	LY lost through delay in cancer treatment as a proportion of LY gaineds from hospitalisation from COVID-19		19%	43%	19%	43%
	RALY lost through delay in cancer treatment as a proportion of RALY gaineds from hospitalisation from COVID-19		26%	59%	26%	59%

Table 4: Summary outcomes from delays in cancer surgery, with comparison to an equivalent number of admissions for community-acquired COVID-19 infection. Only major resections for common adult cancers included. Reference population: England. LY: life years. RALY: resource adjusted life years. HCRU: healthcare resource units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Total deaths attributable to delay
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Per patient treatment delay (months)
Colorectal cancer
Breast cancer
Lung cancer
Prostate cancer
Renal cancer
Melanoma
All cancers

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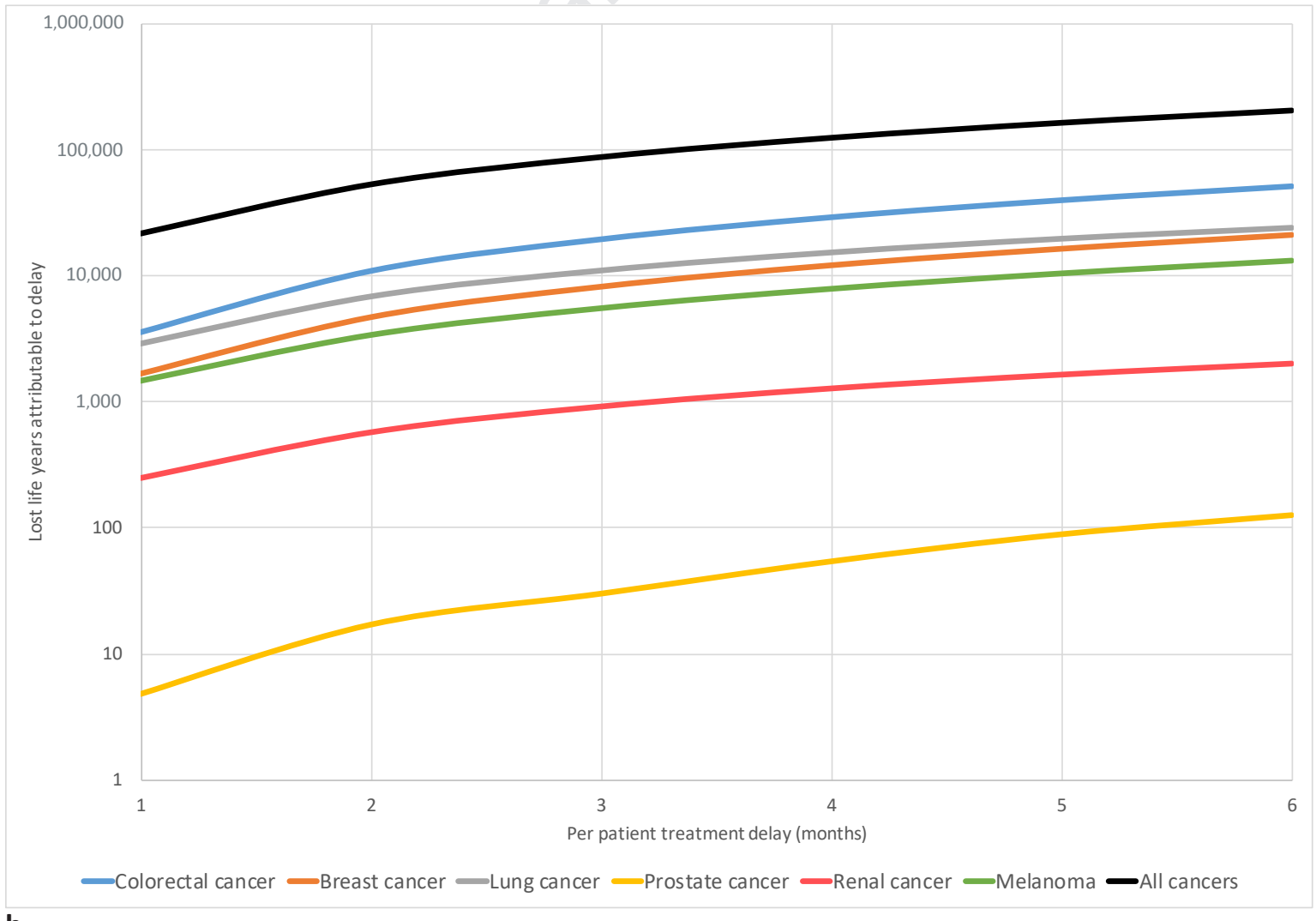
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Lost life years attributable to delay
1
2
3
4
5
6
Per patient treatment delay (months)
Colorectal cancer
Breast cancer
Lung cancer
Prostate cancer
Renal cancer
Melanoma
All cancers

b