

**PWYLLGOR STRATEGAETH A CHYNLLUNIO
STRATEGY AND PLANNING COMMITTEE**

DYDDIAD Y CYFARFOD: DATE OF MEETING:	24 April 2025
TEITL YR ADRODDIAD: TITLE OF REPORT:	Approval to progress with 5 th Linac (Radiotherapy Treatment machine) Business Case
CYFARWYDDWR ARWEINIOL: LEAD DIRECTOR:	Lee Davies – Executive Director of Strategy and Planning
SWYDDOG ADRODD: REPORTING OFFICER:	Lisa Humphrey, General Manager Anne Simpson, Head of Strategic Commissioning Eldeg Rosser, Head of Capital Planning

Pwrpas yr Adroddiad (dewiswch fel yn addas)

Purpose of the Report (select as appropriate)

Ar Gyfer Penderfyniad/For Decision

**ADRODDIAD SCAA
SBAR REPORT**

Sefyllfa / Situation

The South West Wales Cancer Centre (SWWCC) Strategic Programme Case (SPC) was developed to support regional non-surgical oncology services in South West Wales. The SPC specifically refers to radiotherapy and oncology outpatients that will require the development of regional service models and joint business cases. The SPC was signed off by both Swansea Bay University Health Board (SBUHB) and Hywel Dda University Health Board (HDdUHB) in 2023.

Two groups were established in 2024/25 under the SWWCC Regional Strategic Programme (which is covered under A Regional Collaboration for Health (ARCH) governance) to take forward the key pieces of work:

- Oncology Outpatients Modernisation Group
- Radiotherapy Modernisation Group

Membership includes key members of the SBUHB Oncology Team who provide the clinical advice to the group, i.e. Clinical Lead for Oncology, Clinical Lead for Radiotherapy, and Head of Radiotherapy Physics.

The Radiotherapy Modernisation Group priorities are:

- i. 2nd Computerised Tomography (Simulator) (CT SIM) at Singleton Hospital – Health Board joint revenue and Welsh Government (WG) Capital Case approved January 2025, to be operational from September 2025.
- ii. 5th Linear Accelerator (Linac) utilising the current empty bunker in Singleton Hospital.
- iii. Options to site 6th/7th bunker (including a CT SIM if outside of current SWWCC footprint) to house up to two (maximum) Linacs, linked to the existing Linac Replacement Programme.
- iv. Satellite Centre (expansion beyond five Linac model) - longer term aspiration, however this is referenced in the paper as an option which needs to be considered in line with the above priorities, given the interdependencies.

There is an urgent need to progress with implementation of the 5th Linac which is required to be operational by 2026/2027, as demonstrated by recent demand and capacity modelling. However, given the complexity of the steps involved (i.e. the development requires a formally approved Joint Health Board revenue and WG major capital business case, and then capital build/ clinical commissioning), there is a significant risk that this timeline may not be met. As a consequence, backlogs in the Radiotherapy treatment pathway will occur and would impact on delivery of the WG reported quality measure, Time to Radiotherapy. This would adversely affect patient safety and quality. Furthermore, the 5th Linac machine carries substantial revenue costs. At this point, the indicative revenue costs have been supported in principle by both SBUHB and HDdUHB, however this is subject to full business case scrutiny by Health Boards through respective governance processes.

Key Issues

- Radiotherapy treatment is becoming more suitable for increased numbers of patients with cancer. This supports improved patient outcomes; however, together with increased complexity of treatments, this is generating increased demand for radiotherapy which current capacity in South West Wales is struggling to keep up with.
- An additional (5th) Radiotherapy treatment machine, known as a Linac, for the South West Wales region should be operational by 2026/2027, as shown by demand and capacity modelling.
- An options appraisal undertaken in 2024 demonstrated the preferred site for the 5th Linac is in the South West Wales Cancer Centre, Singleton Hospital.
- Progressing implementation of the 5th Linac requires development of a joint Health Board (SBUHB and HDdUHB) revenue and WG major capital business case.
- Regional work has taken place in 2024/25 to commence the 5th Linac Business Case prior to approaching WG for scoping and formal initiation of the major capital project. This includes production of estimated revenue costs which have been supported in principle by both Health Boards and provisionally taken into account for future financial planning purposes.
- There are key interdependent capital radiotherapy developments which need to be considered and included as subsequent phases to the 5th Linac business case, these being the construction of an additional bunker in the South West Wales and the existing Linac replacement programme in SWWCC.

Given the significant revenue implications and the complexities, it is necessary that both Boards are fully appraised and have provided formal approval to progress to the next phase, i.e. to approach Welsh Government to commence the major capital project.

This report sets out the brief for the 5th Linac Business Case, which the Health Board is required to approve prior to approaching WG for a capital scoping meeting, in order to formally initiate this major capital project. In addition, this report highlights the proposed phased approach to progressing the linked capital developments, such as construction of spare bunkers and the ongoing Replacement Linac programme. Please note the report is not seeking approval for the revenue costs, which will be subject to a further business case (capital and revenue) and will be considered through the respective governance routes.

Cefndir / Background

The South-West Wales Cancer Centre at Singleton Hospital in Swansea is a vital healthcare facility serving almost a third of Wales' population. It is one of three specialist cancer centres in the country, providing non-surgical oncology services to the region. In 2023, both SBUHB and HDdUHB approved a 10-year strategic plan (SPC) to improve these services. An essential element of the SPC is the delivery of radiotherapy (RT).

RT is a key treatment for cancer, to achieve cure while maintaining good quality of life. Radiotherapy uses radiation to kill cancer cells and may be used in the early stages of cancer or after it has started to spread. Approximately 50% of all patients require radiotherapy as part of their cancer treatment and this is projected to increase to 60% over the next year. The SWWCC provides radiotherapy treatment using Linacs. The SWWCC currently operates with four Linacs and one decant bunker, which is essential for replacing equipment without loss of treatment capacity, as replacement can take up to a year. Radiotherapy is delivered in small portions known as 'fractions' and advancements in RT techniques now enable more precise treatment over fewer attendances. However, more complex approaches, such as Stereotactic Body RT (SBRT) and hypo fractionated RT require more time, typically two to three 30-minute slots per attendance. As a result, 'slots' have become the new more accurate metric for measuring activity. On average 1 fraction = 1 attendance = 1.4 slots, 12.8 slots per patient RT course.

Demand is outstripping capacity, necessitating the addition of a new (5th) Linac by 2026/27. Two key factors are driving this increased demand: growth and adaptive radiotherapy.

- **Demand & Capacity** - The current capacity of the four Linacs is 32,525 slots which equates to an average of 8,131 slots per Linac per annum.

Pre-COVID, there was an urgent need to move to a 5th Linac model due to demand exceeding capacity. In 2018 and 2019, two cohorts of prostate patients were outsourced to Rutherford Cancer Centre to mitigate this issue. Based on 2019 data, this cost circa £188k to outsource one cohort of 40 urology patients. Fortunately, it was the new developments in (primarily breast) hypofractionation which became mainstream during COVID that was able to release Linac capacity to maintain the four Linac model. This resulted in the single CTSIM becoming the rate limiting step in machine infrastructure capacity and Time to RT workflow, which necessitated the priority capital development of the second CTSIM development.

Based on the updated modelled demand and using 8,131 slots per Linac the table below shows the 5th Linac will need to be in place for 2026/27 and an additional Linac will be needed in South West Wales almost every two years up to 2030/31; seven Linacs in total required by 2030/31.

Future Linacs Timeline	Activity	Year 0 24/25	Year 1 25/26	Year 2 26/27	Year 3 27/28	Year 4 28/29	Year 5 29/30	Year 6 30/31
Total Demand	Slots	32,141	34,067	41,495	47,235	52,934	56,615	58,487
Current SWWCC Activity (4 Linacs)								
Current Average Activity per Linac (32,525/4)	Slots	8,131	8,131	8,131	8,131	8,131	8,131	8,131
Number of Linacs Required	Slots	4.0	4.2	5.1	5.8	6.5	7.0	7.2
Number of Linacs Timeline		4 Linacs		5 Linacs		6 Linacs		7th

Based on the national recommendation of 7,500 slots per Linac the number of Linac and timeframe increases (per the table below):

National Recommendation	Activity	24/25	25/26	26/27	27/28	28/29	29/30	30/31
Total Demand	Slots	32,141	34,067	41,495	47,235	52,934	56,615	58,487
Recommended 7,500 slots per Linac	Slots	7,500	7,500	7,500	7,500	7,500	7,500	7,500
Number of Linacs Required	Slots	4.3	4.5	5.5	6.3	7.1	7.5	7.8

NB: For context Velindre NHS Trust serve a population of c1.5m and currently have 10 Linacs (including two new satellite Linacs based in Nevill Hall which will be fully operational by June 2025). SWWCC serving a population of c0.9million currently has four Linacs and North Wales serving a population of c0.6million has four Linacs

- **Adaptive Radiotherapy** is an advanced approach to radiation treatment that adjusts the therapy plan in response to changes in a patient's anatomy or tumour characteristics over time. Unlike conventional radiotherapy, which relies on a static treatment plan, adaptive radiotherapy continuously monitors and modifies the dose and targeting to improve precision and effectiveness. Consequently, the most complex treatment, requires daily adaptation of the RT which in turn increases Linac demand – this is driving the need to expand the Linac model to seven total required by 2030/31.

Asesiad / Assessment

Regional Radiotherapy Requirements

5th Linac, Progress to date:

In Summer 2024, a high-level strategic options appraisal for the siting of 5th Linac was completed with stakeholders in SBUHB/HDdUHB. This demonstrated that the SBUHB site (specifically, using the space in place of existing, currently empty 5th bunker on SWWCC site) is the preferred option for the 5th Linac development, due to feasibility within the 2026/2027 timeline. Appendix 1 provides the Options Appraisal document. Summary papers were shared with SWWCC Regional Strategic Group, ARCH Regional Strategic Group, SBUHB Cancer Programme & Information Group and HDdUHB Sustainable Resources Committee (SRC) and Strategic Development and Operational Delivery Committee (SDODC). On this basis, estimated revenue costs have been prepared, circa total £2m split equally between Health Boards – see finance implications section for details. In terms of the programme timelines, SBUHB Capital have indicated the capital timeline for programme of works is around 19-month end to end – see **Governance and Risks section** for detail on implications of this.

6th Bunker to be in place by 2027/28

As the preferred option is for the 5th Linac to go into the existing spare (5th) bunker on SWWCC site, this will leave no spare bunker, until a 6th (void space) bunker is constructed. There are risks to not having a spare bunker, including service interruptions, limited flexibility, delayed treatments and impact on patient outcomes. However, the risk of not progressing with the 5th Linac outweighs the risk of not having a spare bunker in the short term.

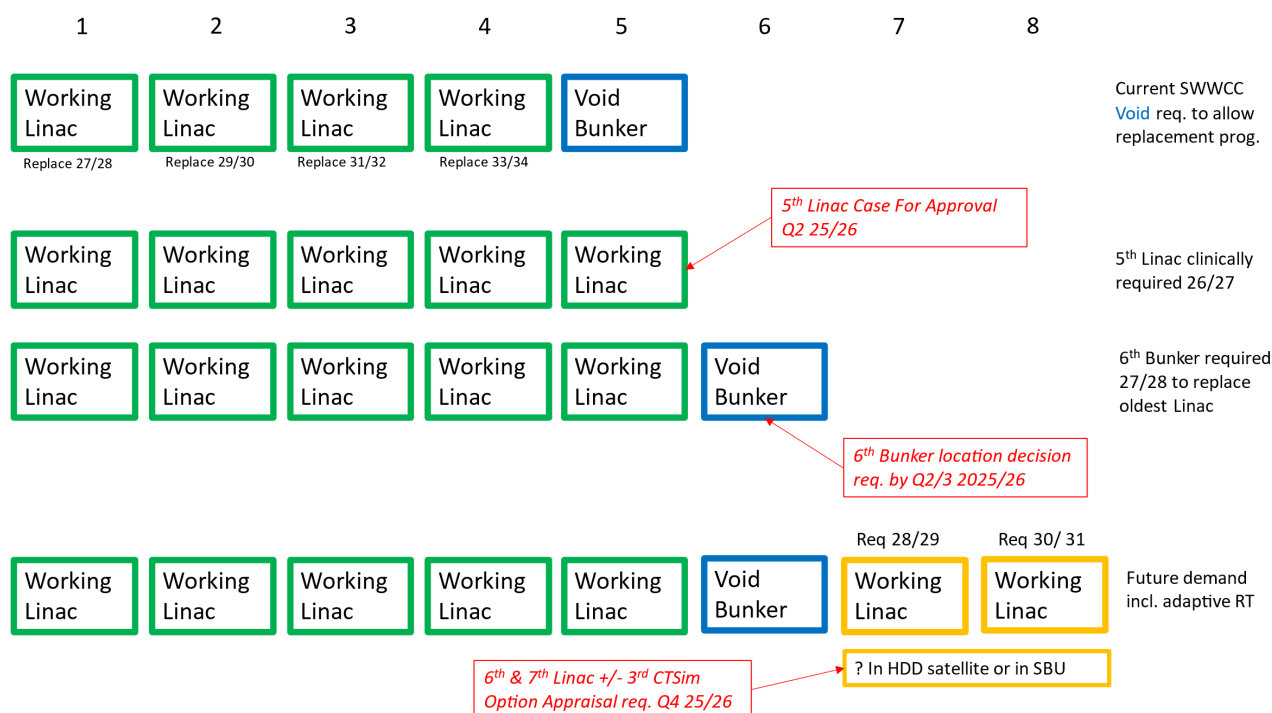
The 6th (void space) bunker must be in place by 2027/28, as this is when one of the existing Linacs is due for replacement. The replacement schedule is a national requirement as set out by the Service Specification for External Beam Radiotherapy Services in Wales approved by all Health Boards and NHS Trusts in Wales, as Linacs have a lifespan of approximately 10 years. The replacement of the next 'oldest' machines in Singleton Hospital will take place every two years from 2027/28. There are options to site the new (6th) bunker in the SWWCC, Singleton Hospital, or within HDdUHB which will need to be progressed at pace in parallel to the development of the 5th Linac Business Case.

Expansion to Seven Linac Model across South West Wales

There needs to be consideration of an option for expanding to a seven Linac model on a phased basis to enable six Linacs to be operational from 2028/29. This would meet the demand and capacity projections for the region, as outlined above. It would ensure the South West Wales region has equitable provision of radiotherapy in line with the South East (i.e Velindre and Neville Hall Satellite Centre opening May/June 2025 will have a total of 10 Linacs; seven Linacs is a proportionate equivalent for the South West population). The development of this option will be progressed at pace, in parallel to the development of the 5th Linac Business Case.

Summary

The following schematic sets out the proposed phases, timelines and key decision points for the developments outlined above:



Governance And Risk Issues

Risks and Mitigations

Risks: As per the Demand and Capacity (D&C) modelling the 5th Linac should be in situ by 2026/27, however due to the timescales involved with capital planning, internal governance routes, onward submission to WG, capital build and clinical commissioning lead-in time, there is a risk that this timeline will not be met. The indicative programme is approximately 19 months end to end. Consequently, patients will be waiting longer for access to radiotherapy, impacting on Time to RT performance.

Mitigation: There are a number of options to be considered, however financials and feasibility assessments will need to be identified and worked through jointly. At this point, these could include:-

- Outsourcing (Private and NHS) – Costs likely to exceed that of the 5th Linac development revenue costs (early calculations suggest outsourcing equivalent activity would equate to £2.3m per annum, while also being poorer for patients in terms of experience and outcomes. Currently the Rutherford Cancer Centre is not operational.

- Mobile LINAC machine (to be confirmed if feasible).
- Increased hours/weekend working (extended working) of existing Linac machines – would need to fit in with maintenance.

All of the above are short term solutions only and at this point are felt to be unfeasible to deliver. However, a thorough appraisal of these options will be included in the full business case. Given the likely limited deliverability of mitigation, the Board must consider the seriousness of adverse patient safety and outcomes including the mortality risk, if the 5th Linac does not proceed at pace. Time to Radiotherapy is currently on the SBUHB Risk Register with a score of 20; this is likely to increase to 25 should the 5th Linac not be in place by 2026/27.

Quality and Patient Outcomes

The latest performance for Time to RT (reporting March 2025 period) is demonstrated in the table below. This shows the Time to Radiotherapy Quality Performance Indicator (QPI) (scheduled priority – the vast majority of patients) is not achievable with the existing Linac capacity. Inevitable increasing demand will lead to delayed Time to Radiotherapy and increase the risk of harm to patients.

See Appendix 2 for the full report including reasons for breach, which was presented to the SBUHB Cancer Programme & Information Group in April 2025.

RT Time to Tx - % pts within target												
Pathway	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
Urgent SC Pathway Target – 7 Days 100%	64%	49%	58%	75%	70%	67%	74%	88%	88%	67%	68%	90%
Urgent SC Pathway Target – 2 Days 80%	15%	20%	3%	28%	30%	37%	26%	28%	47%	17%	35%	41%
Emergency Pathway Target - 2 days 100%	100%	100%	100%	100%	92%	100%	100%	96%	90%	100%	100%	91%
Emergency Pathway Target – 1 day 80%	88%	75%	80%	100%	67%	100%	100%	96%	90%	100%	80%	82%

It is critical to consider the real life consequences of increasing time to RT. There is evidence to show this may increase the chance of recurrence, decrease chance of survival and decrease quality of life¹. As referenced in the British Medical Journal (BMJ) article (Appendix 3), the below shows the hazard ratios for death with an additional four weeks delay to radiotherapy. This is equivalent to starting at six weeks after decision to treat as opposed to two weeks (the Wales Key Performance Indicator (KPI) target for time to RT). If these delays were incurred, it would trigger an institutional duty of candour with individual patients as there would be an increased risk of significant harm having occurred if this was the reason for delay for at least some tumour sites (radical Head and Neck (H&N) for example) where this would equate to a 9% or greater increased risk of death.

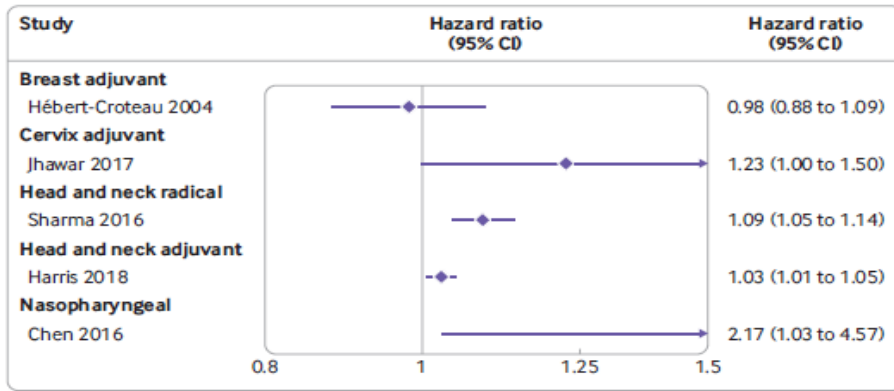


Fig 4 | Forest plot of hazard ratios for association of each four week delay in radical and adjuvant radiotherapy and overall survival by cancer site. Purple diamonds represent the hazard ratio for each study and whiskers represent 95% confidence interval

Additionally, it is felt that any deterioration on time to RT delivery would damage staff morale and lower our attractiveness as a high-quality radiotherapy centre for recruitment and retention, of which Oncology is known as a national shortage profession, and this is a particular issue in South West Wales given the proximity to the Velindre Cancer Centre.

FINANCIAL IMPLICATIONS

5th LINAC – revenue costs (indicative)

The table below provides an initial estimated revenue cost of £2m for the 5th Linac. A more detailed breakdown of the costs is available, however in summary the 5th LINAC requires an additional 21.30 whole time equivalents (WTEs) which costs c£1.44m per annum and non-pay totals £0.53m (of which £0.3m relates to new adaptive RT non pay costs).

Indicative Costings (NB. pay based on top of scale 2024/25 pay scales)	Current Baseline 4 Linacs		Additional 5th Linac	
	WTE	£000s	WTE	£000s
Pay Costs - Medical Physics	19.70	1,516	6.80	466
Pay Costs - Radiotherapy*	43.75	2,440	13.50	829
Pay Costs - Oncology Consultants	4.00	579	1.00	145
Total Indicative Pay Costs	67.45	4,535	21.30	1,440
Non Pay - Medical Physics & Radiotherapy		697		213
Non Pay - New Adaptive RT		0		314
Total Indicative Non Pay Costs		697		527
Facilities Management Costs		159		40
Total Indicative Cost	67.45	5,391	21.30	2,007

* Radiotherapy Pay costs above include 2.5wte advance practitioner posts (£194k) that is not specific to 5th Linac

A version of this paper was presented to the Executive Team in March 2025, they noted the cost implications and confirmed support in principle for the development of a 5th LINAC at Singleton Hospital, enabling further planning (including robust revenue and capital costs).

Finalised costings will be subject to the development of the full business case, when this has been agreed to proceed by WG. Scrutiny on the detail of costings will be undertaken through the respective governance organisations as required for formal approval of the revenue costs, which would be split (50/50) jointly between SBUHB and HDdUHB in line with agreed commissioning principles set out in the SPC.

Please note – the contractual mechanism between the organisations for radiotherapy treatment is based on staffing model as opposed to a cost and volume. The current cost sharing mechanism will continue to exist, albeit recognising the increased costs which would be borne between the two Health Boards. Costs will only start to be incurred when staffing posts have been recruited.

Workforce – SBUHB are currently working on the workforce strategy and will share once completed. However, they do not envisage any issues with the staffing of the 5th LINAC. SBUHB are already working on strategies for alternative routes to registration (to ensure the workforce) and training for advanced and Consultant Radiographers. They are working with Health Education and Improvement Wales (HEIW) on funded training at all levels.

Argymhelliad / Recommendation

Members are asked to:

- **RECOMMEND**, for onward ratification by Board on 29 May 2025 the 5th Linac brief in order to approach WG for a scoping meeting, in view of formally initiating the capital project.
- **NOTE** the risk that the 5th Linac may not be fully operational by 2026/27, and that limited interim solutions (e.g. outsourcing) will need to be explored, and these have significant revenue consequences.
- **NOTE** the seriousness of adverse patient safety and outcomes including the mortality risk if the 5th Linac development does not proceed at pace.

Amcanion: (rhaid cwblhau)

Objectives: (must be completed)

Committee ToR Reference: Cyfeirnod Cylch Gorchwyl y Pwyllgor:	3.1.17.Review revenue expenditure implications relating to capital and provide assurance to the Board that arrangements for capital expenditure and management are robust.
Cyfeirnod Cofrestr Risg Datix a Sgôr Cyfredol: Datix Risk Register Reference and Score:	Not Applicable
Parthau Ansawdd: Domains of Quality Quality and Engagement Act (sharepoint.com)	7. All apply
Galluogwyr Ansawdd: Enablers of Quality: Quality and Engagement Act (sharepoint.com)	5. Whole systems perspective

Amcanion Strategol y BIP: UHB Strategic Objectives:	All Strategic Objectives are applicable
Amcanion Cynllunio Planning Objectives	All Planning Objectives Apply 10 Population health 6 Clinical services plan 4 Planned care, diagnostics and cancer Recovery
Amcanion Llesiant BIP: UHB Well-being Objectives: Hyperlink to HDdUHB Well-being Objectives Annual Report 2021-2022	9. All HDdUHB Well-being Objectives apply

Gwybodaeth Ychwanegol: Further Information:	
Ar sail tystiolaeth: Evidence Base:	Contained in the body of the report
Rhestr Termau: Glossary of Terms:	Contained in the body of the report
Partïon / Pwyllgorau â ymgynhorwyd ymlaen llaw y Pwyllgor Strategaeth a Chynllunio Parties / Committees consulted prior to Strategy and Planning Committee:	Version of paper discussed at the Executive Team meeting on 19 March 2025. <ul style="list-style-type: none"> Noted the indicative cost implications and confirmed support in principle for the development of a 5th LINAC at Singleton Hospital, enabling further planning (including robust revenue and capital costs) to progress.

Effaith: (rhaid cwblhau) Impact: (must be completed)	
Ariannol / Gwerth am Arian: Financial / Service:	As set out in the paper. Full business case (revenue and capital) to follow, which will be subject to QIA and EQIA
Ansawdd / Gofal Claf: Quality / Patient Care:	Improving Radiotherapy is linked to improved patient quality, safety and experience
Gweithlu: Workforce:	As set out in the paper
Risg: Risk:	As set out in the paper
Cyfreithiol: Legal:	Full business case will be subject to QIA and EQIA
Enw Da: Reputational:	There would be a reputational risk if HDdUHB did not jointly approve to progress with 5 th LINAC case
Gyfrinachedd: Privacy:	Not Applicable
Cydraddoldeb: Equality:	Full business case will be subject to QIA and EQIA

Detail the specifications/ requirements for the Radio

Capa
Suggested headings
Anticipated number of Linear Accelerators (Linacccs)
Number of fractions per hour
Number of operating hours per day
Number of operating days per week
Number of operating weeks per year
Anticipated total number of fractions available per year
Maximum capacity utilisation
Service p
All Palliative Radiotherapy, Radical Radiotherapy (including H (WHSSC Commissioned), Adaptive RT
Workforce Assumptions (1 Linac, 50
Staff Group
Medical
Locum junior medical cover
Nursing (Registered and HCAs) ?Local Cover
Advanced Radiographer
Band 7 Radiographer
Band 6 Radiographer
Band 5 Radiographer
Radiotherapy HCSW
Radiotherapy HCSW
Radiotherapy Physics (MPE)
Radiotherapy Physics Technologist
Radiotherapy Physics Advanced Practice Technologist
Radiotherpay Physics Clinical Scientist
Radiotherapy Physics Engineers
Radiotherapy Physics IT
Admin and Clerical
Est Pay costs
Other considerations:
Non Pay Revenue - AI software (reduces Medical staff ask), IT additional licenses, increased Service contacts (Mosaiq), Staff travel from SBU, single use immobilisation equipment, Mould Room per patient use equipment, possibly Elekta parts contract

non-pay capital costs - Laptops, immobilisation equipment, IT Hardware

Capital cost est

Technical and equipment assumptions

Elekta Linacs, able to house MR Linac, other spec

Physical / Estates assumptions

MR-Linac ready Bunkers, clinic accomodation(Rad Review, patient transport, in-patient bed accessible, equipment bays, oxygen/su rooms, training hubs, access to Oncolgy IT syster

Quality/ Safety/ Regulatory assumptions

IRR and IRMER compliance, BSI Certification, Training certification

South West Wales Radiotherapy 5th Linac Options

therapy 5th Linac

city Assumptions	
Response	Additional information
	Using existing 5th/ spare bunker space in SWWCC
1	
4	<4 due to average treatment time ~18mins
8.75	Current model treat 8.30 to 17.45
5	sun, also weekend working from >5 years,
52	Some PPM and QA needed
7,500	Matched Linac
9,000	

provision assumptions	
hypofractionated treatments), Specialised Stereotactic Radiotherapy	

0 patients, spec'd on full use/ 7,500 attendances)

Est. WTE	Band
3	Consultant
tbc	
1	6
1	8A
2	7
3	6
3	5
1	4
1	3
1	8A
1.2	5
1.2	7
1.8	7
1.2	7
0.8	6
0.4	3

£ to be provided for a high level estimate	

£5m est capital as per recent Linac replacement work. Expected that a new site would cost multiple times more, .e.g £50m capital cost for Satelite Centre build in Nevill Hall (2 x linac + 1 CT sim).	
cialist equipment. CT-Sim/MR-Sim, SGRT, Electrons, Kilovoltage	
assessment, Clinics, nursing, Privacy rooms), Rest facilities, access for ambulance ction, Engineers facility, IT hub, recepiton and waiting room, parking, breakout ns. Accessible to hospital crash team, cardiac monitoring team,	

Appraisal - SERVICE SPECIFICATION

Assessment Criteria		Assessment Questions	Information for consideration when testing options	OPTION 1: SITE 5TH LINAC IN SBUHB		OPTION 2: SITE 5TH LINAC IN HDdUHB	
				Yes/No	Rationale / Comments	Yes/No	Rationale / Comments
Desirability	Strategic fit	Does the option align with the Health Boards' strategic objectives/ Clinical Services Plan/ IMTPs/ Annual Plan?	<p>Regional Clinical Services Plan principles - SBU and HDd (agreed in 2019)</p> <ul style="list-style-type: none"> • Ensure that there is a focus on equitable care and excellent experience, no matter where in the region a patient lives • Provide a clear focus on improving population health at a regional level • Enable integration of a range of health services to support the needs of smaller and more rural communities in a sustainable way • Deliver joined up decisions about what services can be provided where within the region; taking in to account population needs, workforce availability, changing clinical practice and technology • Confirm which specialist/tertiary services can be sustained and how they about how should be organised – Take in to account deliverables within national programmes to ensure best access for the regional population • Provide an opportunity to explore whether value based healthcare can be realised on a regional basis <p>Interdependencies with other key HB programmes of work</p>	Yes	Aligns with HB Strategic ambitions. Singleton Hospital is considered the Centre of Excellence for Cancer Services/ Oncology, as set out in the HB Changing for the Future public consultation (2022). There are no issues foreseen in terms of dependency on other strategic or operational programmes of work in the HB.	Yes	This remains a strategic ambition for HDdUHB. Siting in HDd would improve equity of access to treatment for HDd population.
		Does option improve the current and future capacity for radiotherapy in the South West Wales region?	<ul style="list-style-type: none"> •Impact on service provision including that of current cancer centre •Potential for further expansion for additional linacs as required •Wider associated benefits, e.g. e local hospital development and clinical expertise, educational and teaching developments and ability to support service development & research 	Yes	Option improves the capacity to deliver radiotherapy treatment in line with demand expected. The service would be able to provide complex treatments/ technologies. However there are limited options in the SWWCC footprint to extend the provision beyond a 5 Linac model due to space constraints.	Yes	Siting in HDd offers greater overall benefit for patients in terms of access. It was highlighted the ability to deliver the higher level of specialised services in HDd site may be reduced as complex work would not be possible in single bunker site.
	Patient benefit	Does the option demonstrate patient benefit/ improvements in patient experience, for example in terms of accessibility to the radiotherapy facility/ site?	<ul style="list-style-type: none"> •Assessment of average car travel times to the facility; •Availability of car parking facilities; •Alternative public transport availability e.g. bus and rail; •Access to Patient accomodation for overnight / long stays (not inpatient facility) 	No	Yes for SBUHB population, however siting in SBUHB would provide limited improvement to HDd patients as this remains the status quo.	Yes	This would significantly improve access for HDd patients for radiotherpay treatment. There is anecdotal evidence of unmet demand in HDd, e.g. patients who choose to not take up recommended RT treatment due to travel time barriers. Following repatriation of SABR lung to Swansea from Cardiff (WHSSC business case 2022), there has been an uptake in patients undergoing the treatment.
Feasibility	Site logistics/ Ability to fit within the available footprint	Has a potential site been identified that provides the space, facilities and equipment requirements (as per service spec)?	<ul style="list-style-type: none"> •Space •Facilities/ Estates •Technical capacity/ Equipment/ Digital infrastructure •Access to the full range of acute services required to support patients attending a radiotherapy facility/ site 	Yes	Clear identified site using the the existing 5th bunker space in SWWCC site. However this will constrain opportunity to replace the next oldest linacs as per the All Wales replacement programme, as there will be no spare bunker to decant the facilities.	No	Nothing identified to date due to timeline of 26/27. The new urgent and planned care hospital if approved (currently at SOC stage) would be site for the facility, however this is not within the 26/27 timeline. There are space constraints in existing sites on HDd footprint, there may be some opportunities to expand site, but this would require permission to proceed/ scope from WG.
	Time taken to complete/ deliver	Can the development be considered deliverable end to end by 26/27?	<ul style="list-style-type: none"> •Considerations of the facility/ site in terms of ability for 5th Linac to be In situ in FY 26/27 •Buildability •Planning risks/ restrictions 	Yes	Option is considered deliverable within the timelines.	No	Not within timelines required for service to expand to 5th linac model, as per above.
Viability	Cost to deliver	<p>Estimated costs for capital, equipment and technical facilities are in line with financial planning parameters and have the potential to demonstrate value for money (to be tested at business case stage)</p> <p><i>Acknowledged as not a Yes/ No question, however this domain is considered an essential one to provide comment particularly given the All Wales financial constraints, especially concerning capital funding.</i></p>	<p>Estimates in terms of capital and revenue costs</p> <p>The capital costs should include refurbishment as well as any new build costs and ordinarily we would also include opportunity costs for all assets employed</p> <p>The revenue implications should include potential benefits, cost savings and efficiencies as well as costs, (including any knock-on costs/benefits to other parts of SBU/HD). If there are savings or efficiencies it should be clear whether this relates to cash-releasing or redeployment of resources. We would want to understand revenue consequences by year with clarity around inflation assumptions.</p>		Capital cost to deliver est £5m (based on last 4 linac replacements).		Economies of scale would expect to see significantly increased costs for new build plus running costs, Recent Satellite in Neville Hall approx. £50M capital costs.
	Workforce implications	Does the option enable the workforce required to deliver the service highly likely to be available at time of completion?	<ul style="list-style-type: none"> •Ability to staff and bring into operation •Reliance on recruitment of multiple additional roles and/or skills where there are known shortfalls. •Accessibility (eg. transport, parking) and amenities for staff •Ability to encourage recruitment & retention •Education facilities - alignment with Universities/ teaching provision 	Yes	Highly likelihood of the workforce being available. Good past history of recruiting into such posts, e.g recent CTSIM cases.	Yes	Considered likely to acquire staff as a number of existing staff who work in SWWCC live in the area. A number of existing staff have expressed interest in travelling. Supports HDd in becoming an Anchor Institute for the area. Highlighted some potential technicalities and legal requirements for employment. Legally under Irmer Regulations, staff would need to be aligned to SBUHB. However noted that legal structure to employ being tested out with Regional Path work, eg ODN which is creating regional posts, and lessons learnt could be shared. Rotational opportunities would be needed from training perspective to avoid staff being deskilled if working in satellite centre that does not offer the more complex treatments.



General Information

	Oct-24	Nov-24
Attendances	2438	2160
Exposures	4721	4192

Time to Radiotherapy

		Oct-24	Nov-24
Scheduled	Number of treatments	116	
	Average Wait		
	% within 14 days (target 80%)	29	25%
	% within 21 days (target 100%)	87	75%
	% Out of Target	29	25%
Urgent SC	Number of treatments	39	
	Average Wait		
	% within 2 days (target 80%)	10	26%
	% within 7 days (target 100%)	29	74%
	% Out of Target	10	26%
Emergency	Number of treatments	17	
	Average Wait		
	% within 1 day (target 80%)	17	100%
	% within 2 days (target 100%)	17	100%
	% Out of Target	0	0%
Elective Delay	Number of treatments	64	
	Average Wait		
	% within 7 days (target 80%)	57	89%
	% within 14 days (target 100%)	63	98%
	% Out of Target	1	2%

Total number of new courses

236	183
-----	-----

Total treated in 21 days

207	172
-----	-----

% treated in 21 days

88%	94%
-----	-----

Most significant reason for breach

		Oct-24	Nov-24
Scheduled	Admin	2	
	CT - Breakdown		
	CT - Capacity	1	
	CT - Plan not localised		
	CT - rescan required	5	

	CT - Tattoo error		
	CDU - Capacity	5	3
	Delayed - external procedures	1	1
	Delay in planning	4	1
	Delay in Mouldroom		
	DR - Late Ebooking		
	DR - Late Peer Review		
	DR - Plan not approved		
	DR - Plan not localised	5	4
	DR - Plan Query		
	DR - Request		
	E-booking error		
	Further investigations needed		
	Replan required	2	1
	Pathway Design	4	1
	Scheduling error		
	Transport		
	TRT - Staff Shortage		
	TRT - Machine Breakdown		
	TRT - Machine Capacity		
Urgent SC	Admin error	1	1
	Changed to planned pathway		
	CT - Breakdown		
	CT - Capacity		
	CT - Delay in writing up plan	1	1
	CT - Import to Prosoma delay		
	CT - rescan required		
	Delay in booking		
	DR - Plan not localised	7	2
	DR - Plan Query		
	DR - Late Ebooking		
	E-booking error		
	Replan required		
	Pathway Design		
	Scheduling error		
	Transport		
	TRT - Machine Breakdown		
	TRT - Machine Capacity	1	
Emergency	Staff shortage - booking		
	Awaiting Histology		1
	Planning required		
	Plan not approved		
	Plan not localised		
	Prosoma Error		
	Plan Query		
	Patient refused		
	Transport failure		
Elective	Admin error		
	CT - Breakdown		
	CT - Capacity		

CT - Plan not localised		
CT - Delay in plan checking		
CT - rescan required		
CT - Tattoo error		
Delayed - external procedures		
Delay in CTX/W12 BED		
Delay in planning		
Delay in Mouldroom		
DR - Late Ebooking		
DR - Plan not approved		
DR - Plan not localised		
DR - Plan Query		
E-booking error		
ECAD date not supplied/known		
Further investigations needed		
Replan required	1	
Trial Patient		
TRT - RCC Delay		
TRT - Machine Breakdown		
TRT - Machine Capacity		

Total number of breaches

40	16
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Consultant breach

		Oct-24	Nov-24
RB	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
CB	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
PB	E-booking Delay		
	Peer Review		
	Plan Query		
	Plan not approved		
DB	Plan not localised		
	E-booking Delay		
	Plan Query		
	Plan not approved		
AB	Plan not localised	1	
	E-booking Delay		
	Plan Query		
	Plan not approved		
STC	Plan not localised	1	
	E-booking Delay		
	Plan Query		

	Plan not localised		
ECC	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
RD	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
S Gwynne	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		1
S Gupta	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
AK	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
JK	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
JFL	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised	1	1
ON	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
MDP	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised	3	2
DP	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		
MR	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised	3	
RET	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised		

MAT	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised	2	
VV	E-booking Delay		
	Plan Query		
	Plan not approved		
	Plan not localised	1	2

Capacity and Demand

	Oct-24	Nov-24
Future Demand (Booking office)	3359	2577
Lin 1 Usage	90%	85%
Lin 2 Usage	90%	85%
Lin 3 Usage	88%	82%
Lin 5 Usage	83%	87%

Total Linac Capacity	3320		3019	
Capacity used for treatment	2730	82.2%	2394	79.3%
Capacity used for staff training	63	1.9%	40	1.3%
Capacity used for servicing	32	1.0%	16	0.5%
Capacity used for cleaning	11	0.3%	10	0.3%
Capacity lost to staff shortages	21	0.6%	41	1.4%
Capacity lost to breakdowns	44	1.3%	50	1.7%
Capacity lost -DNA/TITA	10	0.3%	4	0.1%
Capacity lost to machine upgrade	0	0.0%	0	0.0%
Total	87.7%		84.6%	

Total CT Capacity (Slots)	322		294	
Average Slot Length	43 mins		41mins	
Slots used for scanning	233	72.4%	205	69.7%
Slots lost to breakdown	3	0.9%	0	0.0%
Slots lost to service	5	1.6%	0	0.0%
Slots lost to staff shortages	0	0.0%	0	0.0%
Slots used for staff training	5	1.6%	0	0.0%
Slots used for upgrade	0	0.0%	0	0.0%
Slots lost to patients not receiving appt	0	0.0%	0	0.0%
Unsuitable Machine (CT1)	0	0.0%	0	0.0%
DNA/TITA	12	3.7%	6	2.0%
Total	80.1%		71.8%	

Average CT slot (mins)

Oct-24	Nov-24
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General Comments	Additional CT slot times reviewed and reduced	
Breakdowns		

es Cancer Centre
Performance

Dec-24	Jan-25	Feb-25	Mar-25
1940	2395	2044	1837
3854	4545	4092	3551

Dec-24		Jan-25		Feb-25		Mar-25	
83		103		90		77	
17 Days		20 Days		18 Days		18 Days	
29	35%	22	21%	24	27%	28	36%
67	81%	74	72%	73	81%	64	83%
16	19%	29	28%	17	19%	13	17%
32		36		31		39	
4 Days		6 Days		6 Days		4 Days	
15	47%	6	17%	11	35%	16	41%
28	88%	24	67%	21	68%	35	90%
4	12%	12	33%	10	32%	4	10%
10		6		5		11	
1 Day		1 Day		1 Day		1 Day	
9	90%	6	100%	4	80%	9	82%
9	90%	6	100%	5	100%	10	91%
1	10%	0	0%	0	0%	1	9%
35		72		56		51	
1 Day		1 Day		1 Day		0 Days	
35	100%	70	97%	54	96%	49	96%
35	100%	72	100%	56	100%	51	100%
0	0%	0	0%	0	0%	0	0%

160	217	182	178
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144	188	165	164
90%	87%	91%	92%

Dec-24	Jan-25	Feb-25	Mar-25
	6		
	3		2

5	3	8	2
		1	
3	5	1	1
5	2	3	3
	1		1
2	2	1	2
	1	1	1
1			1
		1	
	6	1	
1	1		
2	3	1	2
		2	1
	7	4	1
	1		
1		2	
1			
			1

		2	
			1
	2	1	
1			
		1	
	2		
			1
1		1	
	1		
			2
1	1		
1	1		

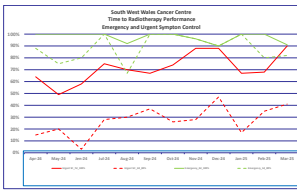
Dec-24	Jan-25	Feb-25	Mar-25
2486	2998	2689	2367
78%	90%	83%	72%
82%	91%	98%	84%
79%	96%	96%	81%
76%	85%	96%	73%

2911		3228		2917		2996	
2164	74.3%	2799	86.7%	2475	84.8%	2225	74.3%
4	0.1%	4	0.1%	0	0.0%	3	0.1%
32	1.1%	32	1.0%	96	3.3%	32	1.1%
36	1.2%	6	0.2%	15	0.5%	10	0.3%
23	0.8%	3	0.1%	21	0.7%	25	0.8%
9	0.3%	35	1.1%	86	2.9%	29	1.0%
33	1.1%	27	0.8%	29	1.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
79.0%		90.0%		93.3%		77.6%	

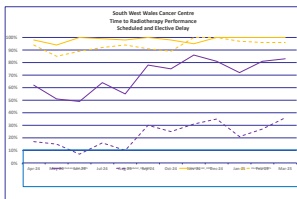
280		308		280		294	
43 mins		43 mins		40 mins		42 mins	
200	71.4%	233	75.6%	166	59.3%	183	62.2%
0	0.0%	0	0.0%	23	8.2%	0	0.0%
14	5.0%	0	0.0%	0	0.0%	14	4.8%
0	0.0%	0	0.0%	1	0.4%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	1	0.3%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
21	7.5%	12	3.9%	7	2.5%	5	1.7%
83.9%		79.5%		70.4%		69.0%	

Dec-24	Jan-25	Feb-25	Mar-25
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	CT1 decomissioned	Lin 5 annual service 5 days	Treatment slots altered to 20mins
		CT2 - 2 partial days	



Month	15-30 min	30-60 min	60-90 min	90-120 min
Sep 20	85	95	90	80
Oct 20	80	90	85	75
Nov 20	85	95	90	80
Dec 20	80	90	85	75
Jan 21	85	95	90	80
Feb 21	80	90	85	75
Mar 21	85	95	90	80



Month	15-30 min	30-60 min	60-90 min	90-120 min
Sep 20	95	98	95	90
Oct 20	95	98	95	90
Nov 20	95	98	95	90
Dec 20	95	98	95	90
Jan 21	95	98	95	90
Feb 21	95	98	95	90
Mar 21	95	98	95	90



Month	15-30 min	30-60 min	60-90 min	90-120 min
Sep 20	95	98	95	90
Oct 20	95	98	95	90
Nov 20	95	98	95	90
Dec 20	95	98	95	90
Jan 21	95	98	95	90
Feb 21	95	98	95	90
Mar 21	95	98	95	90

Prostates

No. of prostate referrals

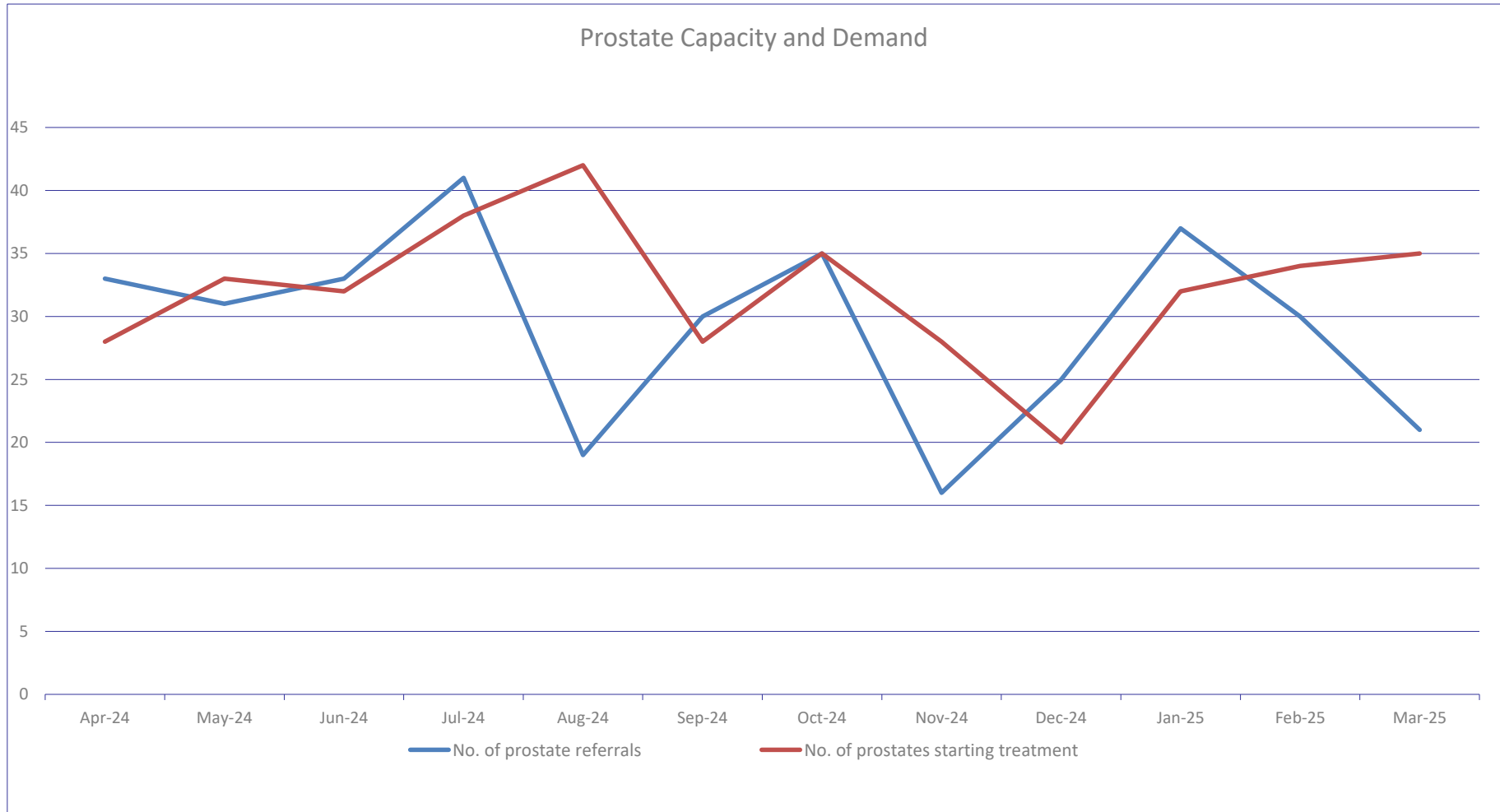
Ultra Hypofractionated

No. of prostates starting treatment

Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
33	31	33	41	19	30	35	16	25	37	30	21
2	6	3	4	5	1	1	6	4	2	5	6
28	33	32	38	42	28	35	28	20	32	34	35

Ave wait beyond ECAD (Target = 14 days)

3	5	5	1	7	8	2	1	1	1	3	4
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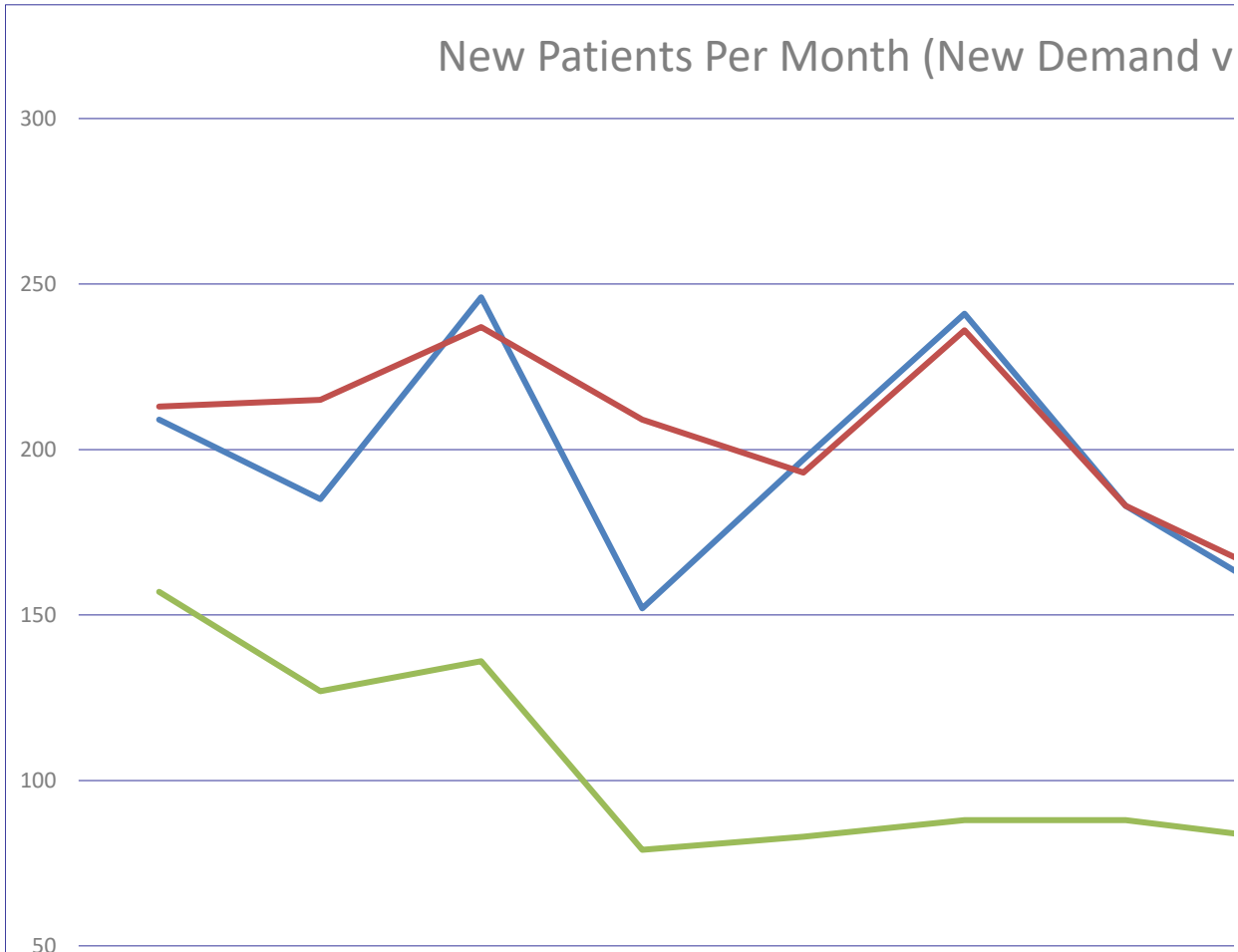


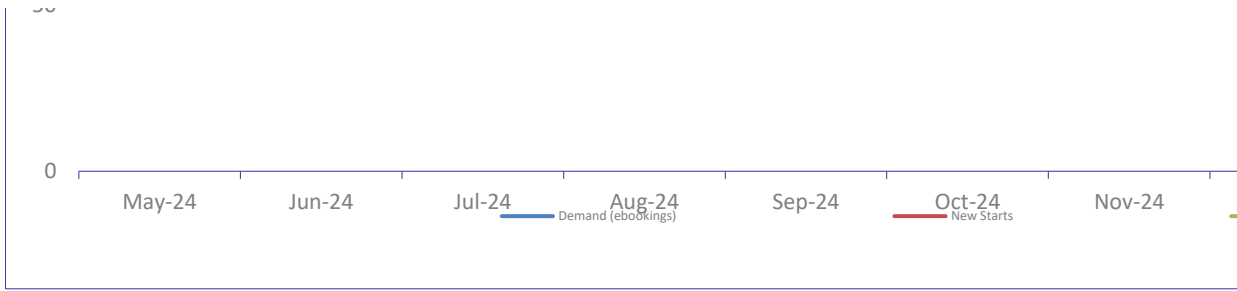
New Patients Per Month (New Demand vs New Starts)

Month	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24
Demand (ebookings)	209	185	246	152	197	241
New Starts	213	215	237	209	193	236
Difference (Demand - Starts)	-4	-30	9	-57	4	5
Wait List (Work in progress)	157	127	136	79	83	88

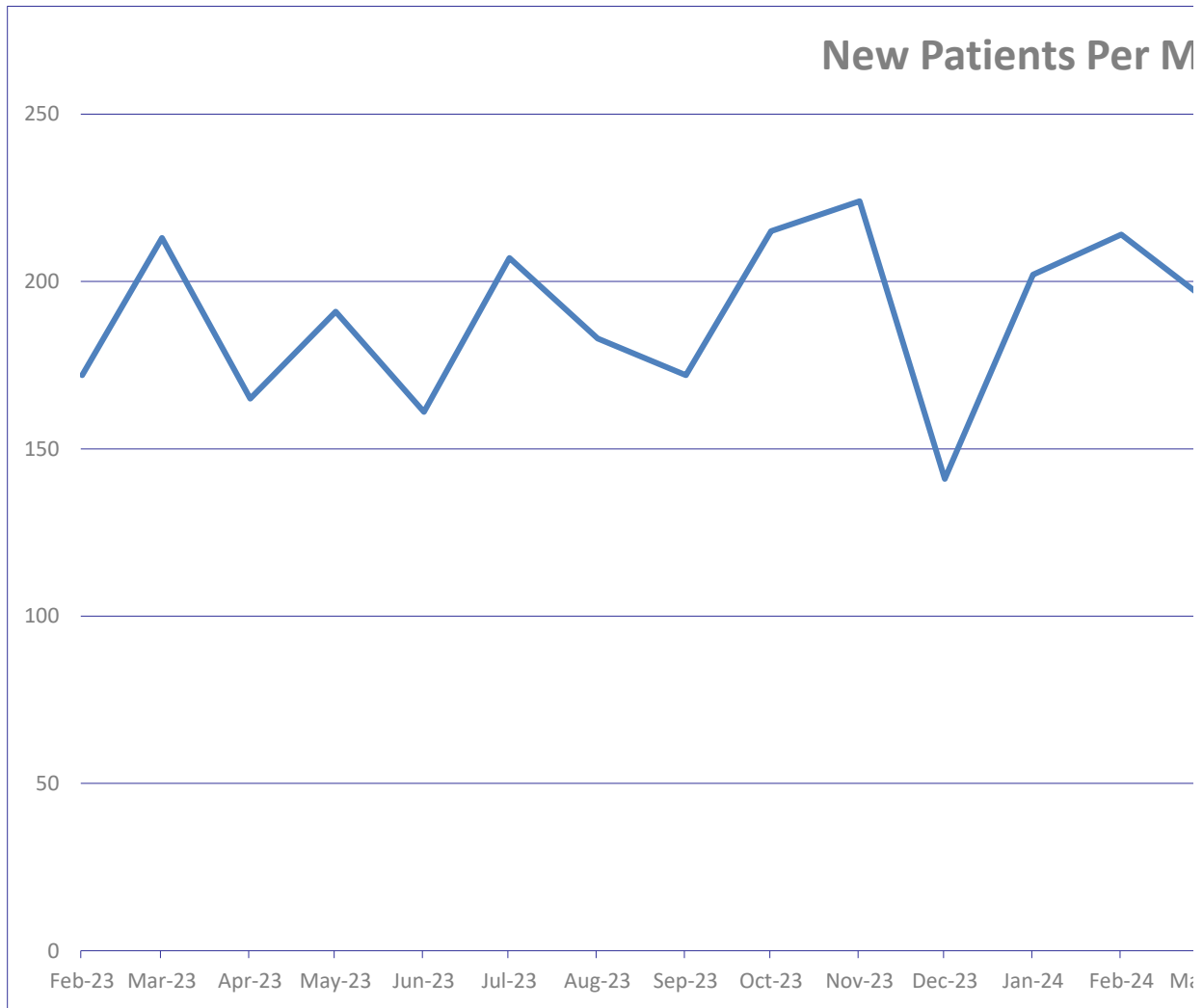
Demand By Site

Site	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24
Brain	0	0	6	1	4	0
Breast	42	32	56	28	50	53
Gynae	7	5	5	4	10	11
H&N	23	24	25	9	14	31
Lower GI	16	15	12	12	16	15
Lung	11	6	11	10	11	10
Lymph	3	3	11	3	3	7
Urgent/Emergency	50	44	56	43	44	52
SABR Lung	5	0	3	6	6	2
SABR Other	1	0	1	2	3	5
Sarcoma	0	3	0	0	0	3
Skin	13	5	12	10	2	2
Upper GI	5	6	7	3	4	8
Urology	33	42	41	21	30	42
Total	209	185	246	152	197	241





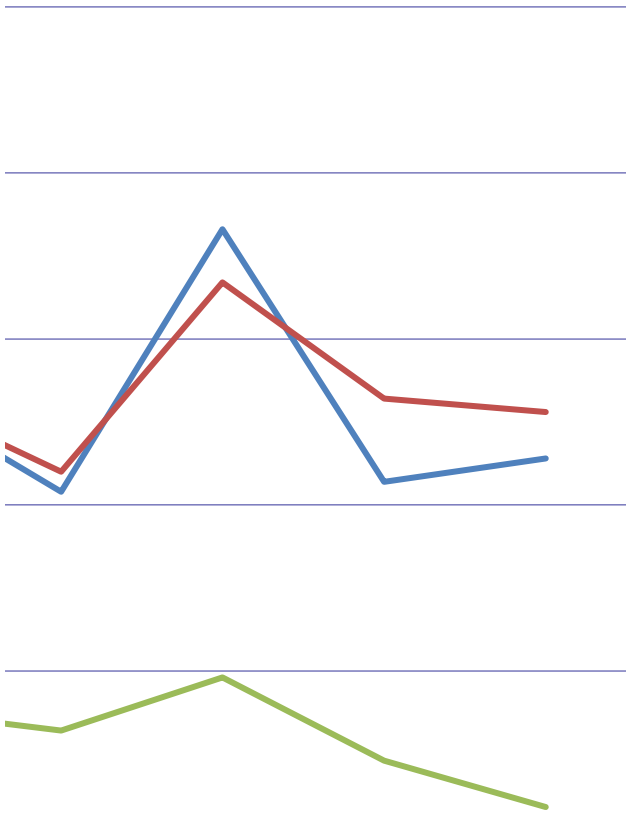
Month	Feb-23	Mar-23	Apr-23	May-23	Jun-23	Jun-23
New Starts	172	213	165	191	161	161

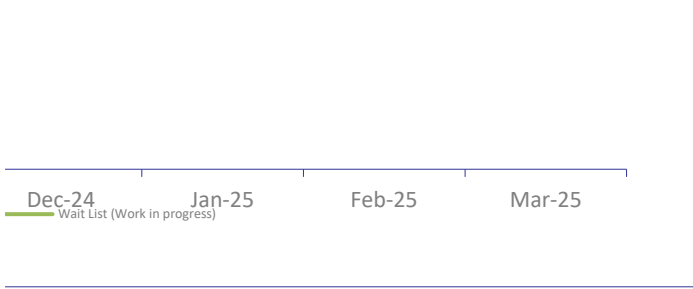


Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
183	154	233	157	164
183	160	217	182	178
0	-6	16	-25	-14
88	82	98	73	59

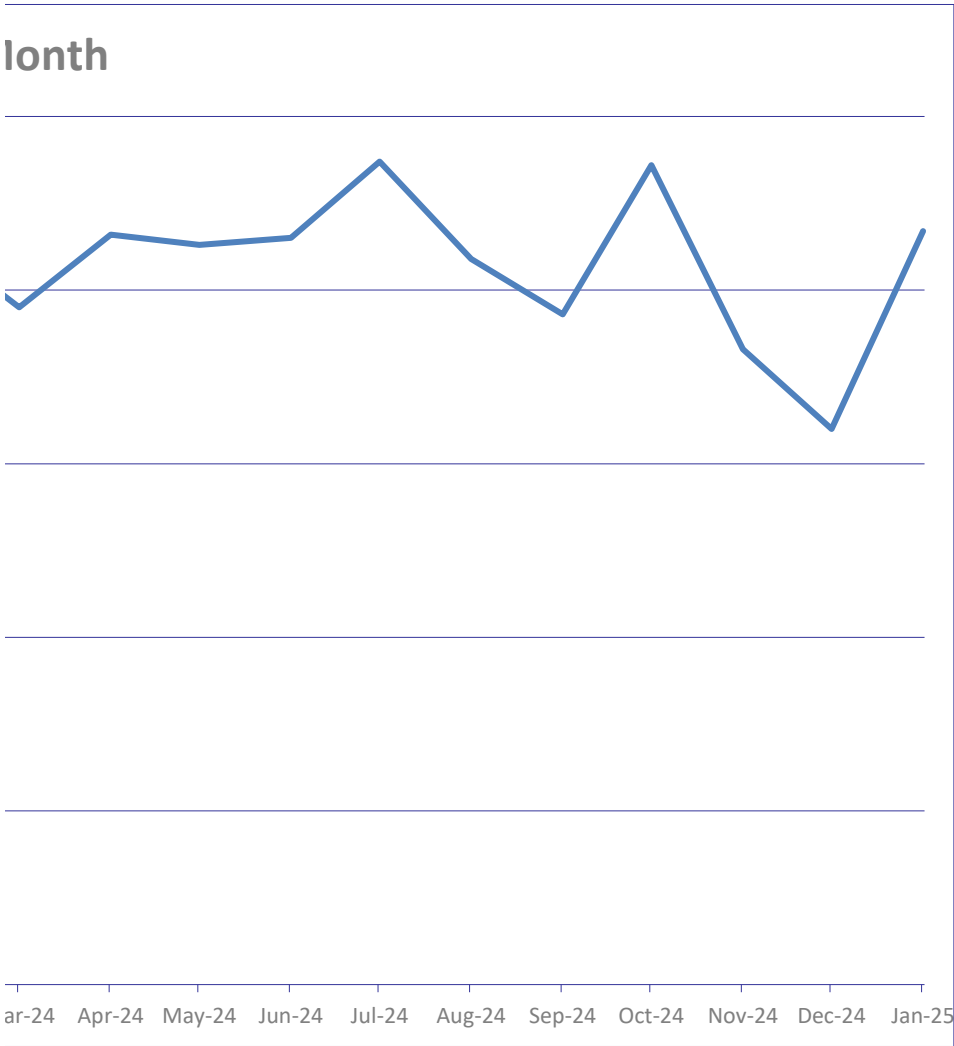
Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
3	3	1	1	4
38	34	52	39	38
7	9	8	9	9
22	13	28	11	9
4	10	16	9	7
10	4	13	3	8
3	4	3	3	1
66	41	50	38	53
4	3	4	1	3
2	1	6	2	4
0	4	0	2	0
1	4	8	5	5
2	5	5	3	2
21	19	39	31	21
183	154	233	157	164

s New Starts)





Jul-23	Aug-23	Aug-23	Aug-23	Sep-23	Oct-23	Nov-23	Dec-23	Jan-24
207	183	183	183	172	215	224	141	202



Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24
214	195	216	213	215	237	209	193	236

Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
183	160	217	157	164

Cancer Centre	Measure	May-24	Jun-24	Jul-24
SWWCC	Total number of curative patients who died within 90 days of RT	2	0	1
SWWCC	Total number of patients receiving RT who have curative treatment intent	132	147	148
SWWCC	%	2%	0%	1%
SWWCC	Total number of palliative patients who died within 30 days of RT	6	5	5
SWWCC	Total number of patients receiving RT who have palliative treatment intent	82	57	88
SWWCC	%	7%	9%	6%

Aug-24	Sep-24	Oct-24	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25
2	0	1	0	0	2	1	0
135	119	155	107	92	143	119	110
1%	0%	1%	0%	0%	1%	1%	0%
1	3	7	6	4	5	6	2
75	74	81	76	68	74	63	68
1%	4%	9%	8%	6%	7%	10%	3%



OPEN ACCESS



FAST TRACK

Mortality due to cancer treatment delay: systematic review and meta-analysis

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Accepted: 16 October 2020

ABSTRACT

OBJECTIVE

To quantify the association of cancer treatment delay and mortality for each four week increase in delay to inform cancer treatment pathways.

DESIGN

Systematic review and meta-analysis.

DATA SOURCES

Published studies in Medline from 1 January 2000 to 10 April 2020.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES

Curative, neoadjuvant, and adjuvant indications for surgery, systemic treatment, or radiotherapy for cancers of the bladder, breast, colon, rectum, lung, cervix, and head and neck were included. The main outcome measure was the hazard ratio for overall survival for each four week delay for each indication. Delay was measured from diagnosis to first treatment, or from the completion of one treatment to the start of the next. The primary analysis only included high validity studies controlling for major prognostic factors. Hazard ratios were assumed to be log linear in relation to overall survival and were converted to an effect for each four week delay. Pooled effects were estimated using DerSimonian and Laird random effect models.

RESULTS

The review included 34 studies for 17 indications (n=1 272 681 patients). No high validity data were found for five of the radiotherapy indications or for cervical cancer surgery. The association between delay and increased mortality was significant (P<0.05) for 13 of 17 indications. Surgery findings were consistent, with a mortality risk for each four week delay of 1.06-

1.08 (eg, colectomy 1.06, 95% confidence interval 1.01 to 1.12; breast surgery 1.08, 1.03 to 1.13). Estimates for systemic treatment varied (hazard ratio range 1.01-1.28). Radiotherapy estimates were for radical radiotherapy for head and neck cancer (hazard ratio 1.09, 95% confidence interval 1.05 to 1.14), adjuvant radiotherapy after breast conserving surgery (0.98, 0.88 to 1.09), and cervix cancer adjuvant radiotherapy (1.23, 1.00 to 1.50). A sensitivity analysis of studies that had been excluded because of lack of information on comorbidities or functional status did not change the findings.

CONCLUSIONS

Cancer treatment delay is a problem in health systems worldwide. The impact of delay on mortality can now be quantified for prioritisation and modelling. Even a four week delay of cancer treatment is associated with increased mortality across surgical, systemic treatment, and radiotherapy indications for seven cancers. Policies focused on minimising system level delays to cancer treatment initiation could improve population level survival outcomes.

Introduction

Delay in the treatment of cancer can have adverse consequences on outcome. However, despite its foundational importance, we lack standardised estimates of the effect of treatment delay on survival for most treatment indications. Previous meta-analyses have found evidence supporting a continuous association between delay and mortality^{1 2} or local control.³ A wide variation in reporting of delay estimates has limited meta-analysis.⁴ Understanding the impact of delay on mortality and other outcomes such as recurrence or financial impact on patients is essential to designing cancer care systems, pathways, and models of care that deliver affordable and equitable outcomes.⁵

The need for an in-depth understanding of the impact of treatment delay on outcomes has come sharply into focus during the coronavirus 2019 (covid-19) pandemic. Many countries have experienced deferral of elective cancer surgery and radiotherapy, and reductions in the use of systemic treatments^{6 7} because systems have reassigned healthcare resources to pandemic preparedness.⁸ The lack of high quality data on the impact of deferred and delayed cancer treatment has meant that the impact of covid-19 lockdown measures on patterns of care and subsequent outcomes has not been robustly quantified. More broadly, in non-pandemic times, health systems have developed pathways and targets for intervals from

WHAT IS ALREADY KNOWN ON THIS TOPIC

Delay in the treatment of cancer can have adverse consequences on outcome
Previous meta-analyses of high validity studies have found evidence supporting a continuous relation between delay and mortality or local control
Despite its foundational importance, we lack standardised estimates of the effect of treatment delay for most treatment indications

WHAT THIS STUDY ADDS

This systematic review considered seven major cancer types (bladder, breast, colon, rectum, lung, cervix, and head and neck) and three treatment modalities (surgery, systemic treatment, and radiotherapy)
The data consistently show that a four week treatment delay is associated with increased mortality; further mortality was reported with longer delays
Policies focused on minimising system level delays in cancer treatment initiation could improve population level survival outcomes

the time of diagnosis to receipt of treatment within National Cancer Control Plan frameworks that do not have a strong empirical basis.⁹

Our analysis aims to provide robust evidence to guide national policy making, specifically the prioritisation and organisation of cancer services, by investigating the association between delays in receipt of cancer treatment and mortality. We considered seven common cancers across all three curative modalities: surgery, systemic treatment, and radiotherapy delivered in the radical, neoadjuvant, and adjuvant setting.

Methods

Population

We investigated seven cancers that together represent 44% of all incident cancers globally¹⁰: five common cancers (bladder, breast, colon, rectum, lung); cervical cancer, given its global importance as the fourth most common cancer diagnosis among women; and head and neck cancer (a major burden in middle income settings), for which there is an established association between delay and mortality.¹⁰ We selected these cancers by balancing representativeness with comprehensiveness. We also considered rectal and colon cancer separately given that radiotherapy is an integral part of treatment for rectal cancer but not colon cancer. Because of the generally indolent nature of prostate cancer (particularly for low and intermediate risk disease) compared with other cancers, and a preliminary review of the delay literature, this cancer was excluded because delays

of the magnitude considered in our analysis were probably not associated with increased mortality.

Exposure

Treatment delay was defined as time from diagnosis to treatment for the first treatment (definitive surgery or radiation), and from time of surgery to treatment for adjuvant indications (chemotherapy or radiation after surgery). For neoadjuvant treatments (those delivered before primary curative therapy, eg, surgery), delay was defined as the time from diagnosis to the start of neoadjuvant treatment, or from the end of neoadjuvant treatment to time of surgery. Delay of curative treatments was investigated (surgery, systemic treatment, and radiotherapy).

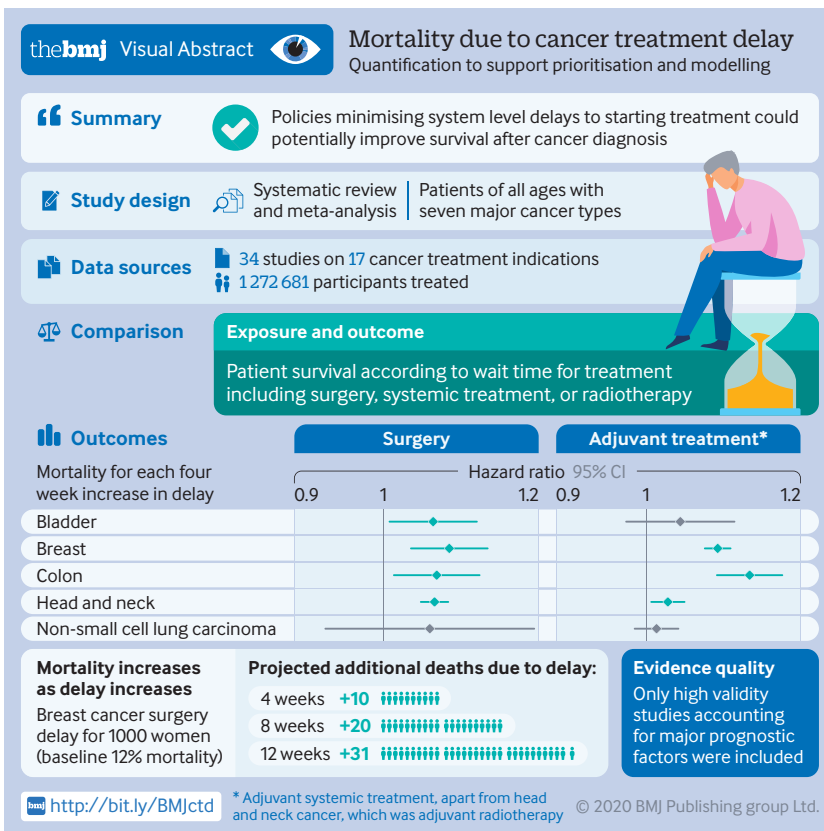
Outcome

A hazard ratio for overall survival was estimated for each four week increase in delay. The hazard ratio represents the risk of death from any cause for patients experiencing the observed treatment delay compared with those treated without the delay.

Systematic review

We undertook a systematic review to identify high validity studies quantifying the impact of treatment delay on mortality. The PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines were followed.¹¹ We used Ovid Medline to carry out the search (appendix 1). To fully assess the validity of included studies, we did not search the literature for studies in abstract form only. Studies were limited to English language publications, from 2000 to present, and those reporting specifically on treatment delay and survival for the seven cancers being analysed. The year 2000 was selected to be comprehensive, while limiting reports to those reflective of contemporary practice as much as possible. We included studies if they specifically reported on the impact of delay for a well defined cancer indication. Studies that reported predominantly on patients receiving neoadjuvant treatments were excluded when evaluating the impact of treatment delay from diagnosis to definitive surgery. Studies that investigated the therapeutic benefit of intentional moderate delay between completion of neoadjuvant therapy for rectal cancer and surgery were excluded given potential confounding by indication. We did not exclude any studies based on design, except that the study needed to quantify the hazard ratio for overall survival because of treatment delay. The search was run on 10 April 2020, except for the bladder cancer search which was performed on 22 April 2020. Two reviewers screened abstracts by using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). Searches of reference lists and Google were also performed.

We reviewed studies for evidence of control for major prognostic factors to assess risk of bias. The criteria used were consistent with those used by our group in other systematic reviews of delay and outcomes.¹⁻³



Firstly we asked “was the distribution of the relevant prognostic factors adequately described in the groups of patients which were compared?” Relevant prognostic factors for all studies were considered to be age, stage, treatment description, and comorbidity or functional status. If no, the study was classified as not of high validity. If yes, we proceeded to the next question “Were the comparison groups balanced with respect to the relevant prognostic factors?” If yes, the study was classified as high validity. We qualitatively assessed the magnitude of observed differences, and the P value was considered when interpreting these differences. If no, we asked “Were the reported results appropriately adjusted for any differences in the relevant prognostic factors?” If yes, the study was classified as high validity; if no, the study was classified as not high validity. Only studies meeting these criteria were included for subsequent meta-analysis.

For some definitive indications (colon cancer, lung cancer, cervical cancer), it was possible that observed associations between treatment delay and risk of death were attenuated because patients with poorer outcomes might present more quickly with symptomatic disease through emergency or urgent referral pathways (often referred to as the waiting time paradox).¹² To qualify as high validity, such studies were required to have also performed an analysis or subanalysis to investigate the impact of this factor in the observed associations. Similar to Neal and colleagues, this was defined as an analysis or subanalysis of patients clearly including or excluding patients with short diagnosis to treatment interval (eg, less than four weeks) or poor outcomes (eg, death within four to eight weeks of diagnosis).¹²

Converting hazard ratios to four week delay estimates

There was heterogeneous reporting of results, with time intervals reported as dichotomous, ordinal categories or as continuous variables. Results were converted to a common unit—hazard ratio for each four week delay with the assumption of a log linear relation across waiting times based on the findings of other meta-analyses.¹⁻³ A log linear relation predicts, for example, that patients waiting eight weeks rather than four weeks have a doubling in their risk of death. A unit of four weeks was chosen based on the magnitude of waiting times reported in the literature. We emphasise that the hazard ratio calculated in this study might be converted to shorter (eg, each week or each day) or longer units. Appendix 2 provides further information on the conversion of hazard ratios to each four week delay estimates or other units, and compares the log linear model to the linear model.

Meta-analysis

We obtained the summary hazard ratio estimate by pooling hazard ratios for each four week delay with inverse variance weighting in DerSimonian and Laird random effect models. Heterogeneity between studies was evaluated using the I^2 test. We performed the statistical analysis using the R package metafor

(R Foundation for Statistical Computing, Vienna, Austria). We considered a two tailed P value less than 0.05 to be statistically significant. Publication bias was not tested given the small number of studies identified for each indication.

Sensitivity analysis

We undertook a post hoc sensitivity analysis to evaluate the impact of the stringent validity criteria on findings. Studies that had been excluded in the main analysis because of a lack of information on comorbidities or functional status were included in this analysis because other factors such as increasing age could be proxies for these.

Patient and public involvement

The research was informed by patient groups and cancer charities that were concerned about the impact of cancer treatment deferral and delays during the covid-19 pandemic.

Results

Our search identified 2543 articles for review (fig 1).¹¹ After we added records identified through additional sources, and removed duplicates, 2843 records were screened. The primary reason for exclusion at the screening stage was lack of relevance to the study question. We obtained 275 articles to assess for eligibility. Of these, 241 were excluded, most commonly because they were not high validity studies (n=100), they included the wrong patient population (n=36), or the wrong study design (n=26). This left 34 studies with unique populations for inclusion (fig 1, table 1, table 2).¹³⁻⁴⁶ These studies included 1 272 681 patients, with a sample size ranging from 174 to 420 792 (appendix 3). Twenty eight studies were population or registry based, and six were institutional reports. All studies were retrospective observational comparisons. Abstracted data on delay were dichotomous in eight, continuous in nine, and categorical in 17 studies. Waiting time data generally covered from three to four weeks, to 16 weeks (appendix 3). Appendix 3 presents the association between treatment delay and survival for individual studies. In addition to adjustments for age, stage, and comorbidity or functional status, 91% of studies accounted for one or more socioeconomic variables in their analysis, 82% accounted for insurance status, 65% for year of treatment or year of diagnosis, and 88% for institutional or geographical factors (appendix 4). We did not find any high validity data for five radiotherapy indications or cervical cancer surgery (table 1, table 2).

Figure 2, figure 3, figure 4 show summary results for all indications, with pooled estimates displayed for treatment site combinations where more than one high validity study exists. The random effects models showed a consistent association of surgical delay with increased mortality, with all indications showing a hazard ratio for each four week delay of between 1.06 and 1.08 (6-8% increased chance of death for each four week delay in treatment). For example,

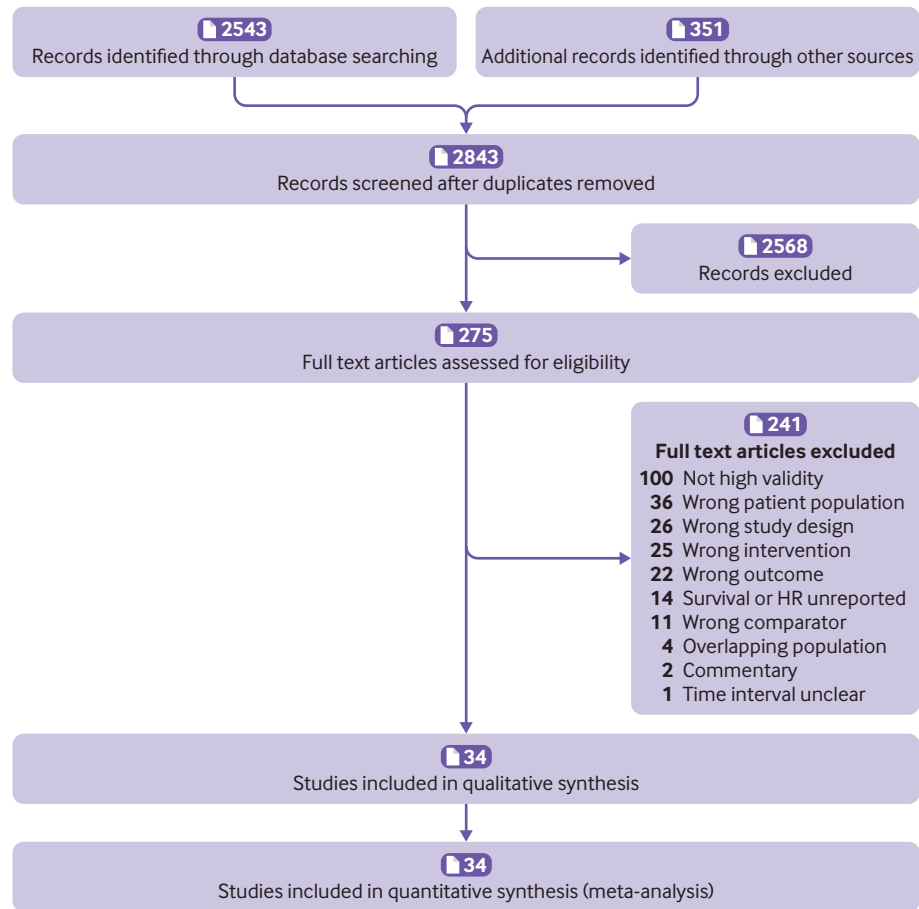


Fig 1 | PRISMA (preferred reporting items for systematic reviews and meta-analyses) 2009 flow diagram for systematic review of treatment delay and survival for curative surgery, systemic treatment, and radiotherapy for bladder, breast, colon, rectum, lung, cervix, and head and neck cancer. HR=hazard ratio

for head and neck surgery the hazard ratio was 1.06 (95% confidence interval 1.04 to 1.08) and for breast partial or complete mastectomy the hazard ratio was 1.08 (1.03 to 1.13). The results for lung surgery were consistent with other sites, though not statistically significant (1.06, 0.93 to 1.19).

Adjuvant and neoadjuvant systemic treatment indications varied more widely in effect (hazard ratio range 1.01-1.28). We observed significant associations for bladder neoadjuvant systemic treatment (hazard ratio 1.24, 95% confidence interval 1.03 to 1.50), breast adjuvant (1.09, 1.07 to 1.11) and neoadjuvant systemic treatment (1.28, 1.05 to 1.56), and colon and rectal adjuvant chemotherapy (1.13, 1.09 to 1.17). Associations were non-significant for non-small cell lung cancer adjuvant chemotherapy (1.01, 0.99 to 1.04) and bladder adjuvant chemotherapy (1.04, 0.98 to 1.11).

High validity data on curative radiotherapy were limited, but supported a mortality impact of delay for head and neck cancer (eg, radical radiotherapy: 1.09, 1.05 to 1.14) and for cervical cancer adjuvant radiotherapy (1.23, 1.00 to 1.50; $P=0.045$). We found no significant effect for the single high validity study of adjuvant radiotherapy after breast conserving

surgery (0.98, 0.88 to 1.09). No high validity studies were found for delay between diagnosis and start of neoadjuvant therapy for rectal cancer or for four other curative radiotherapy indications (table 2).

Sensitivity analysis

To evaluate the impact of our validity criteria on study findings, we undertook a sensitivity analysis and included studies that could be considered of borderline validity. For this analysis, we included 12 studies that were excluded in the primary analysis solely because of the lack of reporting or adjustment for comorbidity or functional status. We found little change in our estimates, except for breast cancer neoadjuvant systemic treatment (appendix 5).

Discussion

Principal findings

This analysis reports the impact of delay in curative treatment on the risk of death across the seven major tumour types: bladder, breast, colon, rectum, lung, cervix, and head and neck, and across all three major treatment modalities (surgery, systemic treatment, and radiotherapy). Across all three modalities, we found that a treatment delay of four weeks is associated

Table 1 | Summary of characteristics for studies investigating surgical treatment

Indication: surgery	Source	Study design	Dataset (dates)	Median age (years)	Stage	Other study details
Bladder	Chu 2019 ¹³	Retrospective observational comparison	SEER Medicare database (2004-2012)	75.2 (mean)	II	—
	Gore 2009 ¹⁴	Retrospective observational comparison	SEER Medicare database (1992-2001)	≤12 weeks=73.8, >12 weeks=73.6 (mean)	II	—
	Kulkarni 2009 ¹⁵	Retrospective observational comparison	Ontario Cancer Registry (1992-2004)	≤90 days 67.4, >90 days 69.2 (mean)	Tx, T0, Ta, Tis, T1-T4	—
Breast	Bleicher 2016 ¹⁶	Retrospective observational comparison	SEER Medicare database (1992-2009), NCDB (2003-2005) databases	75.2 (mean), 60.3 (mean)	I-III, I-III	Both cohorts were included in meta-analysis as overlap was limited owing to years considered in two cohorts, wider geographical population coverage of NCDB with ≥18 years represented (SEER was ≥66 years)
	Eaglehouse 2019 ¹⁷	Retrospective observational comparison	CCR, MDR databases (1998-2010)	54.5 (mean)	I-III	—
	Polverini 2016 ¹⁸	Retrospective observational comparison	NCDB (2004-2012)	59.4 (mean)	I-III	—
	Shin 2013 ¹⁹	Retrospective observational comparison	KCCR database (2006)	49.3 (mean)	Local and regional (SEER)	—
	Mateo 2020 ²⁰	Retrospective observational comparison	NCDB (2010-2014)	NR	I-III	—
Colon	Bagaria 2019 ²¹	Retrospective observational comparison	Multicentre, US (1990-2012)	71 (range 18-99)	I-IV (pathological)	—
	Flemming 2017 ²²	Retrospective observational comparison	OCR, CIHI DAD, OHIP databases (2002-2008)	71 (IQR 62-78)	I-IV (pathological)	—
NSCLC	Kanarek 2014 ²³	Retrospective observational comparison	Institutional US (2003-2009)	61% ≥65	1A, 1B/2A, 2B	—
	Samson 2015 ²⁴	Retrospective observational comparison	NCDB (1998-2010)	<8 weeks: 67.63 (±10.1), ≥8 weeks: 68.73 (±9.8) (mean (±SD))	I (clinical)	—
Cervix	No high validity data found					
Head and neck	Murphy 2016 ²⁵	Retrospective observational comparison	NCDB (2003-2005)	NR	I-IVB	Oral tongue, oropharynx, larynx, hypopharynx
	Liao 2017 ²⁶	Retrospective observational comparison	Taiwanese Cancer Registry database (2004-2010)	52.8 (mean)	I-IVB (clinical)	Oral cavity

CCR=Department of Defence Central Cancer Registry; CIHI DAD=Canadian Institute for Health Information Discharge Abstract Database; IQR=interquartile range; KCCR=Korean Central Cancer Registry; MDR=Military Health System Data Repository; NCDB=National Cancer Database (US); NR=not reported; NSCLC=non-small cell lung cancer; OCR=Ontario Cancer Registry; OHIP=Ontario Health Insurance Plan; SEER=Surveillance, Epidemiology, and End Results.

with an increase in the risk of death. For surgery, this is a 6-8% increase in the risk of death for every four week delay. This impact is even more marked for some radiotherapy and systemic indications, with a 9% and 13% increased risk of death for definitive head and neck radiotherapy and adjuvant systemic treatment for colorectal cancer, respectively. The one high validity study for breast cancer adjuvant radiotherapy did not show an effect, although a clear effect of delay on local control has been described (hazard ratio for each month of delay 1.08, 95% confidence interval 1.02 to 1.14); longer delays (eg, >20 weeks) have been associated with worse breast cancer specific survival.^{47 48}

Policy implications and comparison to other studies

Our analysis builds on the foundations of Mackillop and colleagues, who investigated the mortality impact per one month delay for radiotherapy indications (eg, head and neck, breast) and similarly for systemic treatment (adjuvant colon, breast).^{1-3 47} Our study provides a strong empirical basis for estimating the mortality impact of system level delays for different treatment modalities and cancers.

Delays of up to eight weeks and 12 weeks further increase the risk of death. For example, an eight week

delay in breast cancer surgery would increase the risk of death by 17% ($=1.08^{8\text{weeks}/4\text{weeks}}$) and a 12 week delay would increase the risk by 26% ($=1.08^{12\text{weeks}/4\text{weeks}}$). Such figures translate into significant population level excess mortality. A surgical delay of 12 weeks for all patients with breast cancer for a year (eg, during covid-19 lockdown and recovery) would lead to 1400 excess deaths in the United Kingdom, 6100 in the United States, 700 in Canada, and 500 in Australia, assuming surgery is the first treatment in 83%, and mortality without delay is 12%.^{10 16 49} These results are sobering and suggest that the survival gained by minimising the time to initiation of treatment is of similar (and perhaps greater) magnitude of benefit as that seen with some novel therapeutic agents.⁵⁰ Furthermore, our results do not consider the impact of treatment delay on local control rates, functional outcomes (eg, continence, swallowing), complications from more extensive treatments because of progression during delays, quality of life,⁵¹ or the greater economic burden because of higher direct care costs and productivity losses because of premature mortality and morbidity.⁵² Therefore, the impact of treatment delay is probably far greater for patients and society than that reflected in our results.

Table 2 | Summary of characteristics for studies investigating systemic treatment and radiotherapy

Indication	Source	Study design	Dataset (dates)	Median age (years)	Stage	Other study details
Systemic treatment						
Neoadjuvant chemotherapy, bladder	Chu 2019 ¹³	Retrospective observational comparison	SEER Medicare database (2004-2012)	72.9 (mean)	II	Same study as Chu 2019 ¹³ bladder surgery
Adjuvant chemotherapy, bladder	Corbett 2019 ²⁷	Retrospective observational comparison	NCDB (2006-2013)	NR	pT3-T4 or pN+	—
	Booth 2014 ²⁸	Retrospective observational comparison	OCR	38% were ≥70	18% <T3, 82% T3-T4, 68% node positive	—
Neoadjuvant chemotherapy, breast	Sanford 2016 ²⁹	Retrospective observational comparison	Research database at University of Texas (1995-2007)	50 (range 24-83)	I-III (clinical)	Time from end of neoadjuvant chemotherapy to surgery
Adjuvant chemotherapy, breast	Gagliato 2014 ³⁰	Retrospective observational comparison	MD Anderson Cancer Center institutional database. (1997-2011)	50 (range 19-85)	I-III	—
	Mateo 2020 ²⁰	Retrospective observational comparison	NCDB (2010-2014)	NR	I-III	—
	Hershman 2006 ³¹	Retrospective observational comparison	SEER Medicare database (1992-1999)	NR	I-II	—
Adjuvant chemotherapy, colon, rectum	Hershman 2006 ³²	Retrospective observational comparison	SEER Medicare database (1992-1999)	NR	III Colon	—
	Cheung 2009 ³³	Retrospective observational comparison	SEER Medicare database (1991-2002)	73.3 (IQR 69.8-77.4)	II- III Rectal	—
	Bayraktar 2011 ³⁴	Retrospective observational comparison	Jackson Memorial Hospital and University of Miami Sylvester Comprehensive Cancer Center (2000-2008)	55.7±1.1 for ≤60 days and 56.9±1.8 for >60 days (mean±SE)	II-III Colon	—
	Lima 2011 ³⁵	Retrospective observational comparison	Alberta Cancer Registry, ambulatory care classification system, discharge abstract database (2000-2005)	NR	III Colon	—
	Becerra 2017 ³⁶	Retrospective observational comparison	New York State Registry, SPARCS (2004-2009)	NR	III Colon	—
	Turner 2018 ³⁷	Retrospective observational comparison	NCDB (2006-2014)	NR	III Colon	—
	Xu 2014 ³⁸	Retrospective observational comparison	SEER Medicare database (1992-2005)	73.6 (IQR 69.8-77.6)	II Colon	—
	Massarweh 2015 ³⁹	Retrospective observational comparison	NCDB (2003-2010)	60.8 (±11.6) (mean (±SD))	III Colon	—
Adjuvant chemotherapy, NSCLC	Booth 2013 ⁴⁰	Retrospective observational comparison	OCR (2004-2006)	62 (28-85) (mean (range))	I-IV (pathological)	—
	Salazar 2017 ⁴¹	Retrospective observational comparison	NCDB (2004-2012)	64 (IQR 57-70)	I-III (pathological)	—
Radiotherapy						
Definitive radiotherapy/ neoadjuvant, bladder	No high validity data found					
Adjuvant radiotherapy, post breast conserving surgery	Hébert-Croteau 2004 ⁴²	Retrospective observational comparison	Random population based sample of five regions of Quebec, Canada for periods covering 1988-1994	NR	I-II	—
Neoadjuvant (chemo)radiation, rectum*	No high validity data found					
NSCLC, stage III chemoradiation	No high validity data found					
SCLC, limited stage chemoradiation	No high validity data found					
Adjuvant chemoradiation, cervix	Jhawar 2017 ⁴³	Retrospective observational comparison	NCDB (2004-2013)	46 (IQR 38-56)	IB1-IIIB	No stratified wait group table but adjusted analysis
Definitive chemoradiation, cervix	No high validity data found					
Radical chemoradiation, head and neck	Sharma 2016 ⁴⁴	Retrospective observational comparison	NCDB (2003-2006)	57.6 (9.9) (mean (SD))	III-IV (clinical, non-metastatic)	Oropharynx chemoradiation
Adjuvant (chemo)radiation, head and neck	Harris 2018 ⁴⁵	Retrospective observational comparison	NCDB (2004-2013)	59 (10.9) (mean (SD))	III-IV (non-metastatic)	Interaction between subsite and outcome observed
Radical (chemo)radiation, nasopharyngeal carcinoma	Chen 2016 ⁴⁶	Retrospective observational comparison	Sun Yat-Sen University Cancer Center, institutional series (2009-2012)	NR, 45% ≤45 (primary cohort)	I-IV (non-metastatic)	99.6% World Health Organization histology type II/III, treated with IMRT

IMRT=intensity modulated radiation therapy; IQR=interquartile range; NCDB=National Cancer Database (US); NR=not reported; NSCLC=non-small cell lung cancer; OCR=Ontario Cancer Registry; SCLC=small cell lung cancer; SD=standard deviation; SE=standard error; SEER=Surveillance, Epidemiology, and End Results; SPARCS=Statewide Planning and Research Cooperative System. *Delay studies primarily investigating therapeutic benefit of usually short delay between completion of neoadjuvant treatment and surgery for rectal cancer are excepted. No high validity studies investigating time from diagnosis to start of neoadjuvant therapy were found for rectal cancer.

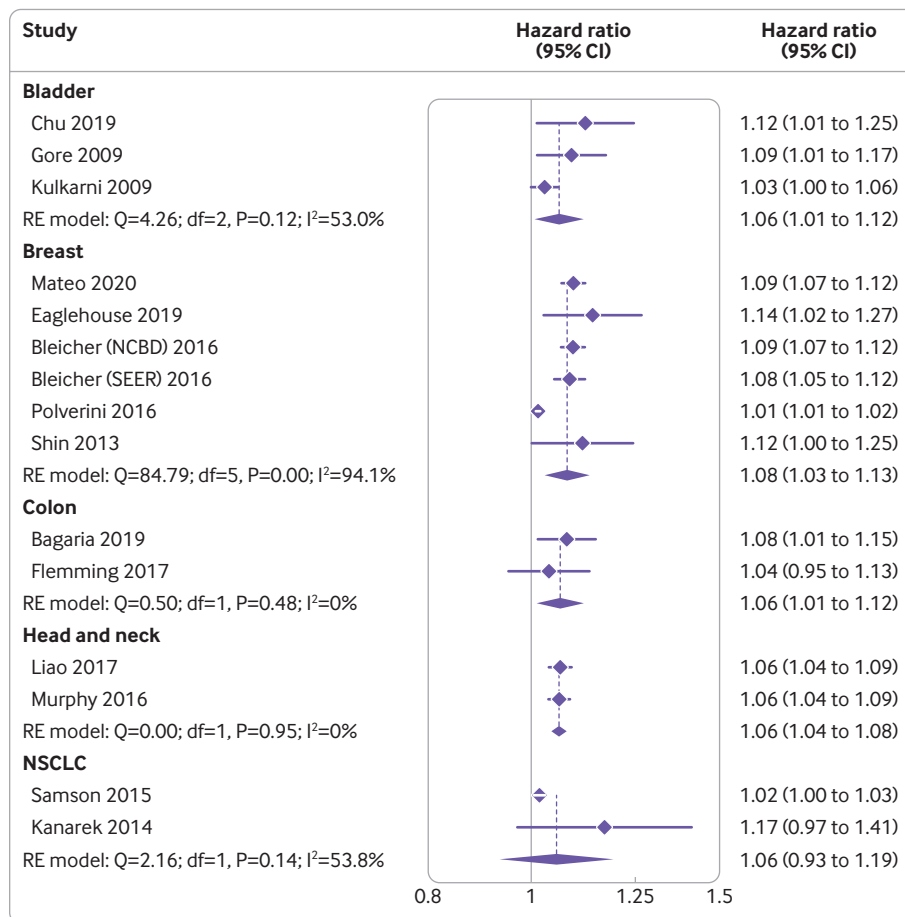


Fig 2 | Forest plot and pooled hazard ratios for association of each four week delay in surgery and overall survival by cancer site. Small purple diamonds represent the hazard ratio for each study and whiskers represent 95% confidence interval. Large purple diamonds represent summary effect estimates with the centre being the estimate and the ends representing 95% confidence intervals. NSCLC=non-small cell lung cancer

Treatment delays could be due to patient factors (eg, need for cardiac workup, postoperative wound infection), disease factors (eg, need for additional imaging investigations), or system factors (eg, waiting for an operating room date, a central line insertion, or a specialist consultation). The main purpose of this discussion is to highlight the need to minimise system level delays. We strongly emphasise that patients should not start surgery, systemic treatment, or radiotherapy until they are medically fit to do so, and have completed appropriate investigations. We also acknowledge that for rectal cancer, for instance, an increasing body of evidence shows that deferral of surgery after radiotherapy might not confer a survival disadvantage for those having a complete response.⁵³

A major finding from our study is the paucity of high quality data for several tumour specific indications for radiotherapy, including chemoradiation for non-small cell lung cancer and definitive cervical cancer treatment. Two high validity studies providing delay estimates across multiple treatment modalities for these tumour types suggest an impact of delay in treatment initiation in these settings (cervical cancer mortality for each four week delay: hazard ratio 1.04,

95% confidence interval 1.02 to 1.07⁵⁴; stage III non-small cell cancer: 1.03, 1.01 to 1.06).⁵⁵ While the negative impact of treatment interruptions on survival outcomes is well documented for these tumours,⁵⁶⁻⁵⁸ evidence is insufficient about the exact impact of a delay in starting treatment, which given its importance, should be an urgent research priority.

The study results are timely in light of the current covid-19 pandemic. Internationally, some countries have released national guidance on prioritisation of surgical treatments for cancer, which do not appear to be supported by the results of this study. For example, at the beginning of the pandemic the UK NHS⁵⁹ created a short term surgical prioritisation algorithm. Several indications were considered safe to be delayed by 10-12 weeks with no predicted impact on outcome, including all colorectal surgery. Therefore, our results can help to directly inform policy—we found that increasing the wait to surgery from six weeks to 12 weeks would increase the risk of death in this setting by 9%.

We note that a delay of less than four weeks should not be justified as safe based on our findings. For example, our results suggest a 4% increased risk of death for a two week delay for breast cancer surgery (1.08^{2weeks/4weeks};

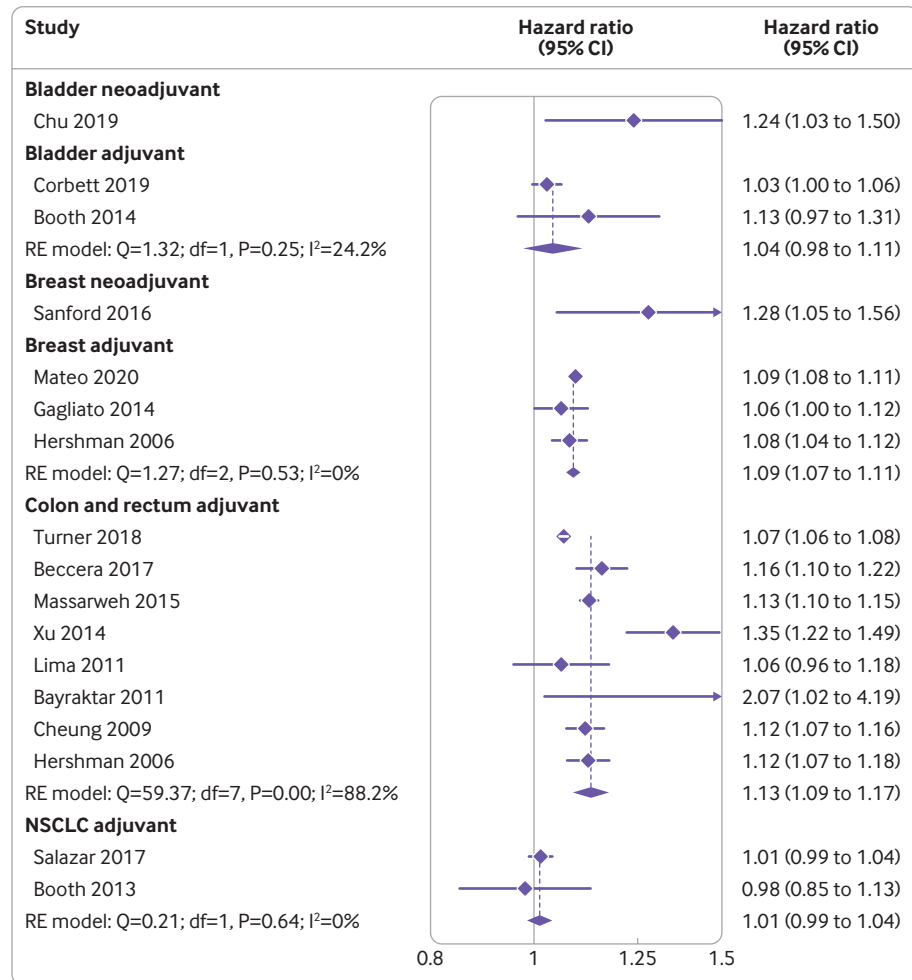


Fig 3 | Forest plot and pooled hazard ratios for association of each four week delay in adjuvant and neoadjuvant systemic treatment and overall survival by cancer site. Small purple diamonds represent the hazard ratio for each study and whiskers represent 95% confidence interval. Large purple diamonds represent summary effect estimate with the centre being the estimate and the ends representing 95% confidence intervals. NSCLC=non-small cell lung cancer

appendix 2). Taken as a whole, these results suggest there is an urgent need to reconsider how we organise our cancer services. The prevailing paradigm has been around access to new treatments to improve outcomes, but from a system level, gains in survival might be achieved by prioritising efforts to minimise the time from cancer diagnosis to initiation of treatment from weeks to days. We acknowledge that treatment delays are multifactorial in cause and that patients should not start treatment before they are medically fit to do so, and have had completed all appropriate evaluations, however these data strongly support efforts to minimise system level delays. For example, national quality indicators around cancer waiting times from diagnosis to treatment are widely used across different health systems. In the UK NHS, current targets for the initiation of primary definitive treatment have been set at 31 days from the decision to treat date; this does not include the lag between receiving a diagnosis and having a surgical or radiation oncology consultation for treatment.^{9 60} At a population level, differences in lead times to

treatment of even two or three weeks could be a factor in why survival outcomes differ across health systems and needs further investigation. However, these delays need to be balanced with the necessity to be medically fit for treatment. Additionally, potential opportunities for second opinions could result in more effective or appropriate care, especially where variation in practice or outcomes exist across providers.

Options for decreasing delay after diagnosis include increasing specialist workforce capacity through training initiatives or overcoming these challenges through technological developments. For example, automated treatment contouring and planning is increasingly standardised and reduces the radiotherapy preparation time to hours rather than days.⁶¹ Satellite centres might improve capacity for treating patients, as can reconfiguration of existing infrastructure to high volume super specialised services, or single entry models and team based care.⁶² Innovations in surgical technique could also minimise morbidity and reduce time to adjuvant therapy.^{63 64}

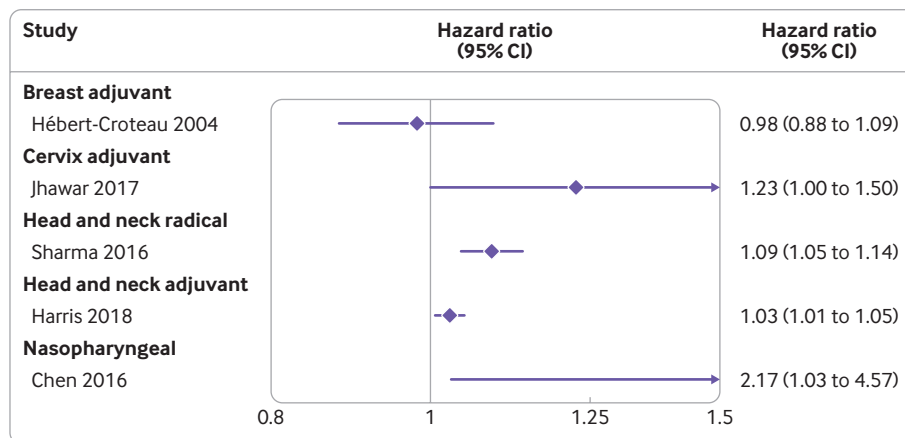


Fig 4 | Forest plot of hazard ratios for association of each four week delay in radical and adjuvant radiotherapy and overall survival by cancer site. Purple diamonds represent the hazard ratio for each study and whiskers represent 95% confidence interval

Strengths and limitations of this study

Our study provides evidence on the association of treatment delay and mortality, covering seven cancer types and three treatment modalities. Our study was based on observational data, and we therefore restricted our sample to high validity studies given the biases inherent to this study design. Our approach provides high level evidence on system delay because randomised trials in this context are not appropriate or feasible.

The most fundamental limitation of our study is the risk of residual confounding. Patients with longer treatment delays could be destined to have inferior outcomes for reasons of comorbidity, treatment morbidity, or performance status. In evaluating the validity of our findings, we note the coherence of overall mortality and cancer specific endpoints (local control, cancer specific survival, disease-free survival) for all past meta-analyses of high validity studies.^{1-3 47} We also note major detrimental effects of prolonged waiting times on cancer specific survival outcomes in 13 of 15 studies included in our meta-analysis that reported cancer survival outcomes alongside overall survival.^{14 16 22 28 29-36 38 39 46} These studies span seven treatment indications. Factors associated with medical status such as elements of socioeconomic status or insurance status might also be confounding factors; we found that 91% and 82% of identified studies accounted for these, respectively, though this does not completely rule out the possibility of residual confounding. Twenty five of 34 identified studies were from the USA, though no significant heterogeneity was detected compared with other countries.

Our findings cannot be directly applied to other cancer specific treatment indications, or to subgroups or single patients with treatment indications considered here. For example, limited evidence suggests that the impact of delay can vary according to stage, often with consistently greater mortality impact with earlier stage disease.^{16-18 25 55} Additionally, our results can only be applied to the range of delay considered in

the studies we evaluated. Given evidence derived from cancers representing almost half of all patients, the precautionary principle (acting to avoid or diminish harm in the face of scientific uncertainty) should be used when determining acceptable waiting times for treatment where data are limited.⁸ Too few studies were found for most indications to perform a risk of publication bias assessment with funnel plots. For previous meta-analyses where enough studies existed to do so, findings were not explained by publication bias.^{1 2}

We acknowledge that the assumption of a log linear relation between waiting time and mortality could be an oversimplification. This assumption was required to estimate per unit time mortality impact of delay from studies that use a variety of wait time representations. However, there is support for this assumption in the primary studies we used. A continuous exposure from nine primary studies assumed (log) linearity. Six studies undertook cubic spline analysis and the results are compatible with log linear effects with the range of wait times considered here (four weeks to 16 weeks).^{15 19 21 26 41 45} Moreover, the previous meta-analyses by Biagi and colleagues and Raphael and colleagues suggest a reasonable fit of a log linear relation to delay.^{1 2} If a linear relation with delay exists (rather than log linear), the degree of difference in the two models is expected to be sufficiently small to allow use of a log linear model for the specific purposes of modelling the impact of delay on mortality between four and 16 weeks (appendix 2). We emphasise that assuming log linearity outside of the range of wait times used in this analysis is inappropriate. Our findings should also not be used to evaluate whether there is a minimal safe delay, or to estimate the impact of delay beyond 16 weeks.

Our results reflect the impact of delay on large and expectedly heterogeneous populations with varying risks of recurrence. Therefore, these estimates are best used at a policy and planning level for modelling, rather than for individual risk prediction. We also

emphasise that few studies considered the impact of immortal time bias on delay; this could be done through a landmark analysis for survival. Patients that survived a longer wait might have less aggressive tumours, biasing the delay effect towards the null. Our findings could therefore underestimate the impact of delay on mortality.

Conclusions

A four week delay in treatment is associated with an increase in mortality across all common forms of cancer treatment, with longer delays being increasingly detrimental. In light of these results, policies focused on minimising system level delays in cancer treatment initiation could improve population level survival outcomes.

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Web appendix: Appendices