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Drivers of Improvement in Observed Survival in Cancer Sites: A Cancer Registry Analysis

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Aim & Background

To investigate drivers of improvement in median overall survival (OS) over three decades across malignant tumour sites. Despite substantial progress in cancer treatment, survival outcomes vary widely across tumour sites. Understanding the factors driving improvements in OS can inform future research priorities and public health strategies. This study leverages long-term cancer registry data to explore temporal trends in OS and their association with disease incidence and clinical trial activity.

Method

- The incidence of malignant tumours and the median OS were derived using the Surveillance, Epidemiology, and End Results Program (SEER) database for tumours diagnosed between 1975 and 2022. Data were collated according to malignant tumour sites by regrouping the International Classification of Diseases 10th Edition (ICD-10) C codes by site according to the International Agency for Research on Cancer (IARC) summary list in SEER.
- To enable robust analysis on the change in trajectory of OS over time, tumours with median OS well captured over a period of at least 25 diagnostic years were eligible for inclusion. The number of Phase 0 – 4 clinical trials across the cancer tumour sites was extracted using Cortellis Clinical Trial Intelligence (a Clarivate™ solution).
- An analysis of the trends in median OS according to diagnostic year was conducted for each tumour site. The absolute change in median OS per year was calculated as the difference between the median OS in the first and last observed diagnostic periods, divided by the interval width. The coefficient of annual change (ß) in median OS was estimated by fitting a linear regression model of median OS against diagnostic year; ß represents the estimated increase (or decrease) in median OS per year increment in diagnostic year. This statistic incorporates all observed data, providing a more robust measure of temporal change relative to the simple difference calculation, which utilised the first and last observation only.
- Correlation coefficient and 95% confidence interval (CI) between disease risk (incidence per 100,000 people per year [SEER]) and the change in median OS were estimated using Spearman's rank (ρ) and Kendall's tau (τ), to account for the non-normal distribution in the data. The uncertainty around the coefficient of annual change calculated from the linear regression models (lower and upper bounds of the 95% CI [ß]) was utilised to approximate the 95% CI of the correlation.

Results

- The median OS over at least 25 diagnostic years (from 1975 up to 2022) was extracted from the SEER database for 48 malignant tumour sites. Median OS was not observed in more recent years due to improved survival; <50% of patient have died for certain tumour sites during this time period.
- According to the absolute change per year, the greatest improvement in OS by diagnostic year was observed for prostate, tonsil, bones and joints, breast and chronic myeloid leukaemia, and the smallest improvement was observed for salivary gland, corpus uteri, vulva, ureter and vagina.
- Based on the linear regression of the median OS by diagnostic year, bones and joints, prostate, breast, tonsil and renal tumour sites demonstrated the greatest yearly improvement in median OS; coefficient of change in median OS in months per diagnostic year, ß (95%CI) = 5.99 (4.84,7.14), 5.05 (4.64, 5.46), 4.03 (3.71, 4.34), 3.99 (3.38, 4.6) and 2.92 (2.59, 3.25) respectively, (p<0.001) for each site.
- Ureter, larynx, vulva, uterus and peritoneum cancers experienced the smallest advancement in median OS, and there was even significant evidence (p<0.001) of a decline in the OS by diagnostic year for ureter and larynx tumours; ß (95%CI) = -0.66 (-0.84, -0.47) and -0.39 (-0.53, -0.26) months per diagnostic year, respectively.
- There was statistically significant evidence that the tumour incidence was positively correlated with the absolute yearly change in median OS according to both Spearman's rank (ρ=0.30 [p=0.039]) and Kendall's Tau (τ=0.20 [p=0.045]).
- When the correlation between the coefficient of annual change in median OS by diagnostic year was investigated relative to the tumour site incidence, there persisted significant evidence of a positive correlation (ρ(95%CI) =0.36 (0.22, 0.4) and τ(95%CI) =0.23 (0.15,0.28)).
- Smooth trends in median OS were not observed for all tumour sites, as shown for bone and joint tumours in Figure 2. The instabilities could be explained by changes in cancer code groupings and the expansion of the SEER registry coverage (additional registries merging over time). Rarer cancers will also be more sensitive to inconsistent median OS, since the lower incidence means each event has a greater impact on the median OS.

Figure 2. Median OS (months) according to diagnostic year for the five tumour sites with the greatest improvement in OS over time.

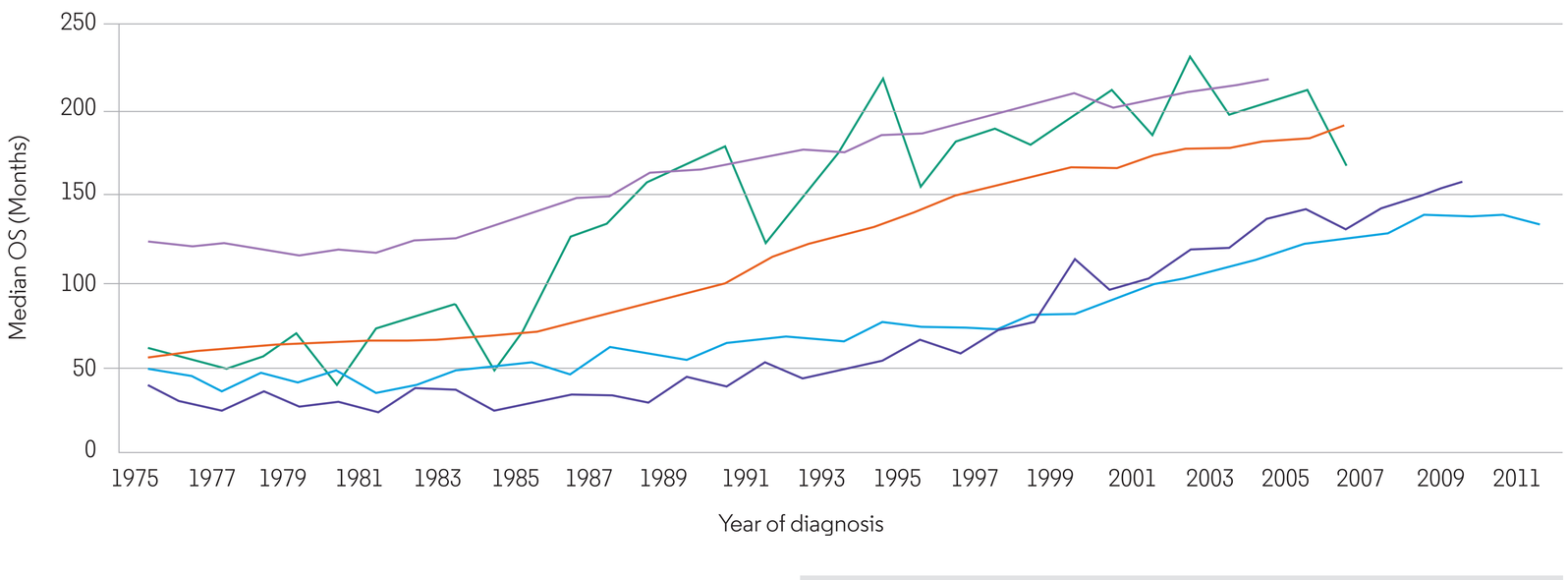
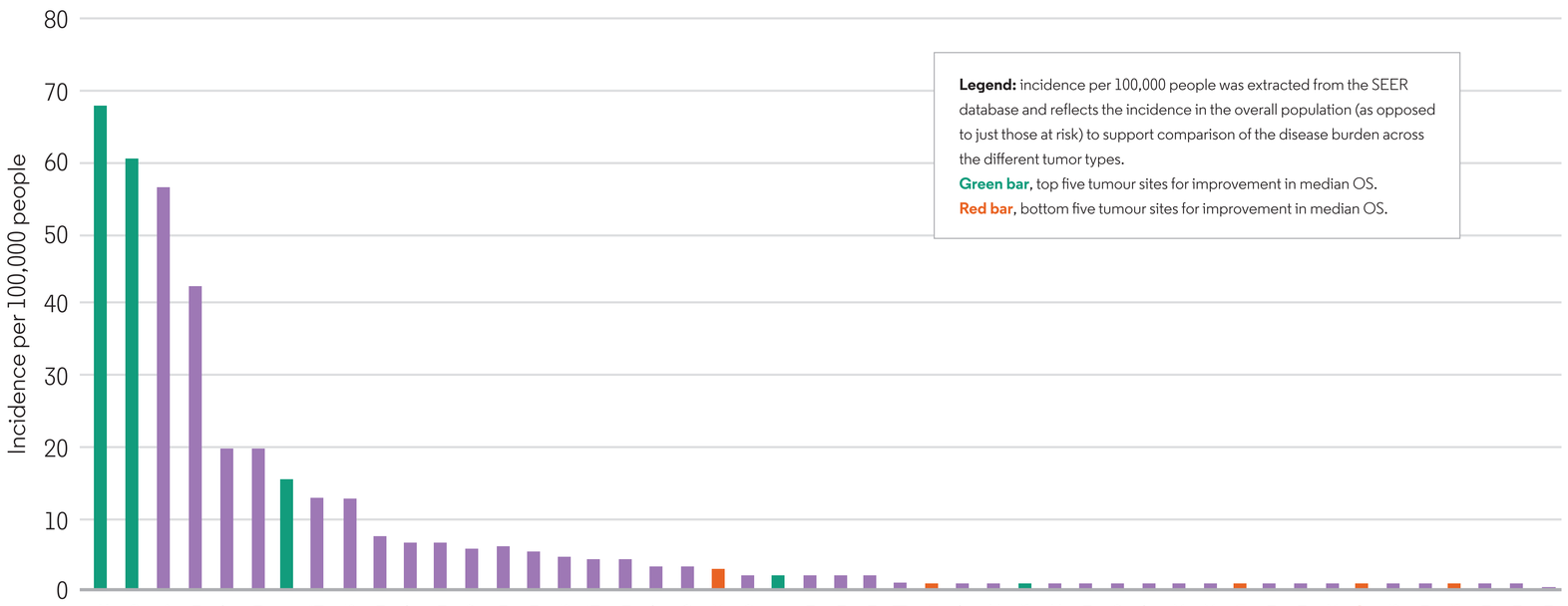


Figure 1. Incidence (per 100,000 people) across the 48 tumour sites investigated.



Discussion points from our experts

- **Therapeutic innovation as a key driver of improved survival** – top-performing tumour sites (bones and joints, prostate, breast, tonsil, and renal) have benefited from novel therapies, including: targeted therapies and PD-1/PD-L1 inhibitors (especially in breast and renal cancers), androgen receptor inhibitors and radioligand therapy in prostate cancer, multimodal treatment approaches in bones and joint (surgery, chemotherapy, radiotherapy) and widespread implementation of the HPV vaccine improved prognosis for many head and neck cancers (including tonsil) where HPV is a risk factor.
- These advances highlight the impact of drug development and clinical trial activity on survival outcomes. Notably, tumour sites with higher incidence also tend to have more clinical trials, suggesting a feedback loop between disease burden and research investment.
- **The role of screening and public awareness in driving survival gains** – high incidence cancers like breast and prostate have shown some of the most significant improvements in median OS over the past decades. This is likely attributable not only to therapeutic advances but also to widespread screening programs and greater public awareness, which facilitate earlier diagnosis and treatment.
- On the contrary, cancers with low incidence, such as ureter, uterus and vulva, have shown the smallest change in median OS. These rare cancers do not benefit from the same education campaigns and screening programs which improve outcomes for high-profile cancers.

Table 1. Tumour sites with the greatest and smallest advancement in median OS over time.

Rank	Tumour type	Interval start	Interval end	Interval width	No. data points	First median OS (months)	Last median OS (months)	Absolute change in OS (months per year)	Annual change in median OS by diagnostic year from linear regression		Incidence (events per 100,000 people)	Number of RCTs
									ß (months) [95%CI]	p-value		
Tumour sites with the most improvement in median OS according to the coefficient of annual change												
1st	Bones & Joints	1975	2006	31	28	61	167.99	3.45	5.99 (4.84, 7.14)	<0.001	1.0	1,462
2nd	Prostate	1975	2006	31	32	55.49	192.28	4.41	5.05 (4.64, 5.46)	<0.001	60.9	6,596
3rd	Breast	1975	2004	29	30	122.96	218.57	3.30	4.03 (3.71, 4.34)	<0.001	68.3	11,943
4th	Tonsil	1975	2009	34	35	38.2	158.99	3.55	3.99 (3.38, 4.6)	<0.001	1.9	NA
5th	Renal	1975	2011	36	37	50.41	133.55	2.31	2.92 (2.59, 3.25)	<0.001	15.4	2,602
Tumour sites with the least improvement in median OS according to the coefficient of annual change												
44.5th	Peritoneum	1975	2020	45	46	5	28.92	0.53	-0.08 (-0.42, 0.25)	0.622	0.6	1,873
44.5th	Uterus	1975	2022	47	48	6.67	7.64	0.02	-0.08 (-0.21, 0.05)	0.223	0.4	274
46th	Vulva	1975	2014	39	40	117.85	97.55	-0.52	-0.09 (-0.39, 0.21)	0.553	1.3	88
47th	Larynx	1975	2017	42	43	67.38	70.65	0.08	-0.39 (-0.53, -0.26)	<0.001	3.1	639
48th	Ureter	1975	2020	45	46	46.5	33.35	-0.29	-0.66 (-0.84, -0.47)	<0.001	0.5	159

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