THE LANCET
Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Clark JJ, Dwyer D, Pinwill N, Clark P, Johnson P, Hackshaw A. The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: a retrospective analysis. *Lancet Oncol* 2020; published online Nov 27. http://dx.doi.org/10.1016/S1470-2045(20)30619-7.

Online Supplementary Appendix

Figure S1: The number of SACT registrations between September 2019 and June 2020, according to type of therapy.

Figure S2: The number of SACT registrations between September 2019 and June 2020, for all solid tumours and all haematological malignancies, and gynaecological and colorectal cancers.

Figure S3: The number of SACT registrations between September 2019 and June 2020 for breast, prostate, lung, skin, renal, head and neck, and others (neuroendocrine tumours, thyroid, sarcoma, gastrointestinal stromal tumours and central nervous system).

Figure S4: The number of SACT registrations between September 2019 and June 2020, for selected haematological malignancies.

Figure S5: The total number of SACT registrations between April 2019 and June 2020.

Figures are only provided for specific tumour types where the mean monthly number of registrations during the control period was ≥50.

Table S1. New indications introduced by the NHS via the Cancer Drugs Fund in April and May 2020 in response to the COVID pandemic

Table S2: Data used to create Figures 1-4 and Figures S1-S4.

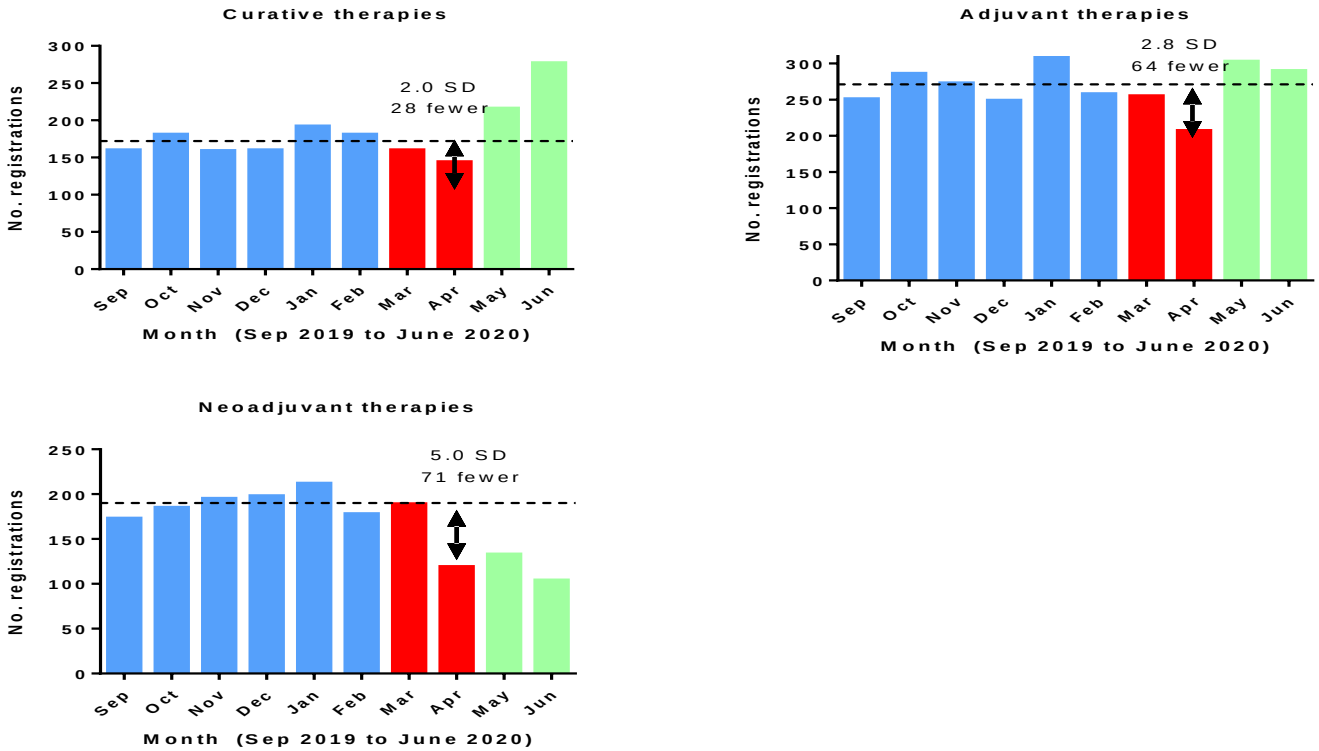


Figure S1. The number of SACT registrations observed per month, according to type of therapy. The number seen in April 2020 is compared with the mean number between September 2019 and February 2020 (dashed horizontal line). The arrow shows the difference between April 2020 and the mean value, and also expressed as number of standard deviations (SD) from the mean. All reductions in April had $p \leq 0.0001$ (all differences and p-values for May and June are in Supplementary Table 2).

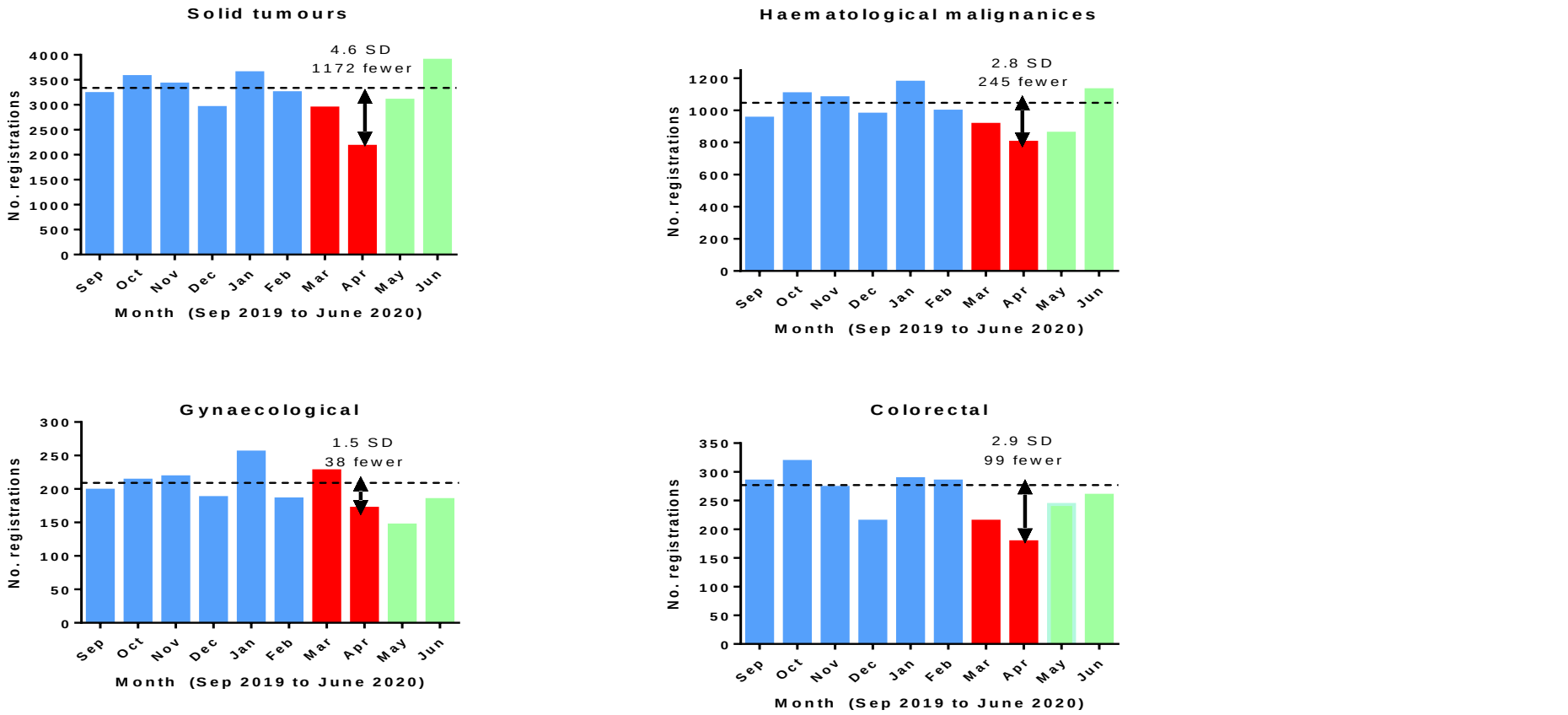
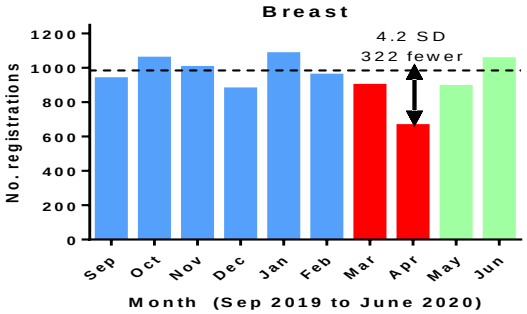
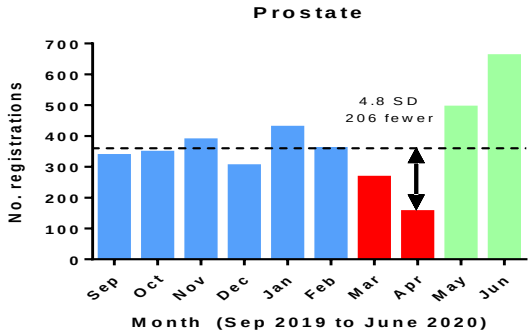
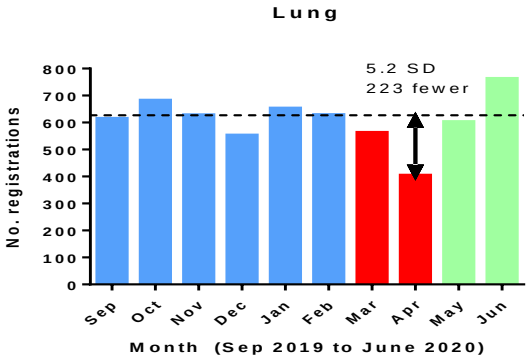
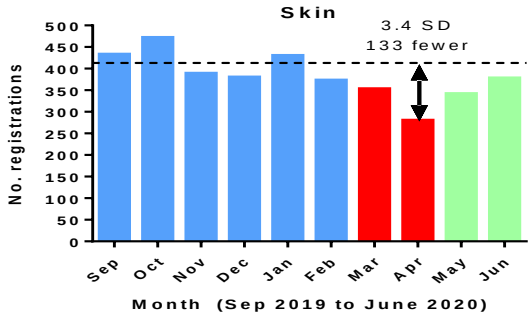


Figure S2. The number of SACT registrations observed per month, for all solid tumours and haematological malignancies, and gynaecological and colorectal cancers. The number seen in April 2020 is compared with the mean number between September 2019 and February 2020 (dashed horizontal line). The arrow shows the difference between April 2020 and the mean value, and also expressed as number of standard deviations (SD) from the mean. All reductions in April had $p \leq 0.0001$ (all differences and p-values for May and June are in Supplementary Table 2).


Breast
4.2 SD
322 fewer
No. registrations
1200
1000
800
600
400
200
0
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Month (Sep 2019 to June 2020)


Prostate
4.8 SD
206 fewer
No. registrations
700
600
500
400
300
200
100
0
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Month (Sep 2019 to June 2020)


Lung
5.2 SD
223 fewer
No. registrations
800
700
600
500
400
300
200
100
0
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Month (Sep 2019 to June 2020)


Skin
3.4 SD
133 fewer
No. registrations
500
450
400
350
300
250
200
150
100
50
0
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Month (Sep 2019 to June 2020)

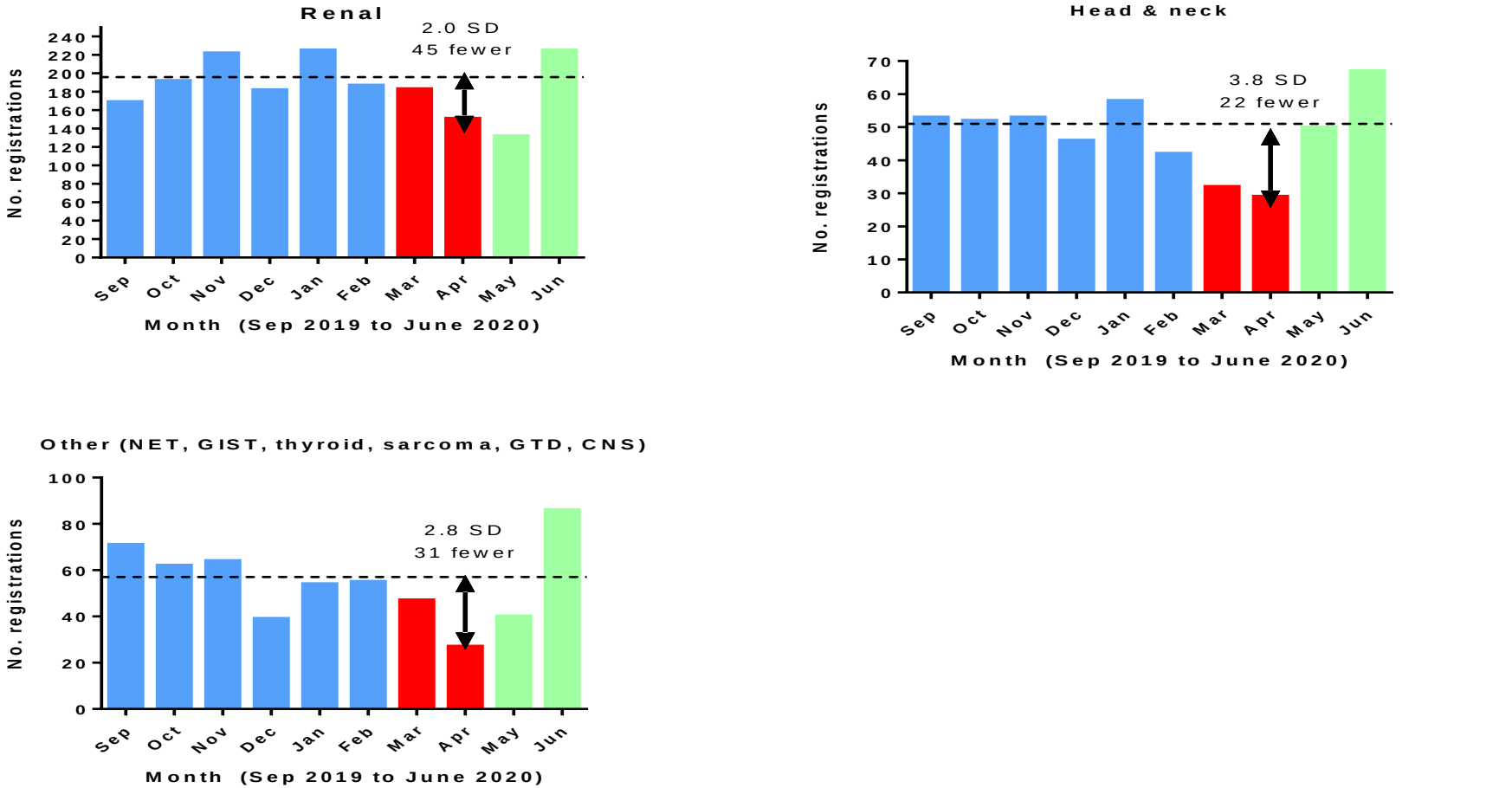


Figure S3. The number of SACT registrations observed per month for several solid tumour types. The number seen in April 2020 is compared with the mean number between September 2019 and February 2020 (dashed horizontal line). The arrow shows the difference between April 2020 and the mean value, and also expressed as number of standard deviations (SD) from the mean. All reductions in April had $p \leq 0.0001$ (all differences and p-values for May and June are in Supplementary Table 2).
Abbreviations: NET (neuroendocrine tumours), GIST (gastrointestinal stromal sarcomas), GTD (gestational trophoblastic disease), CNS (central nervous system tumours)

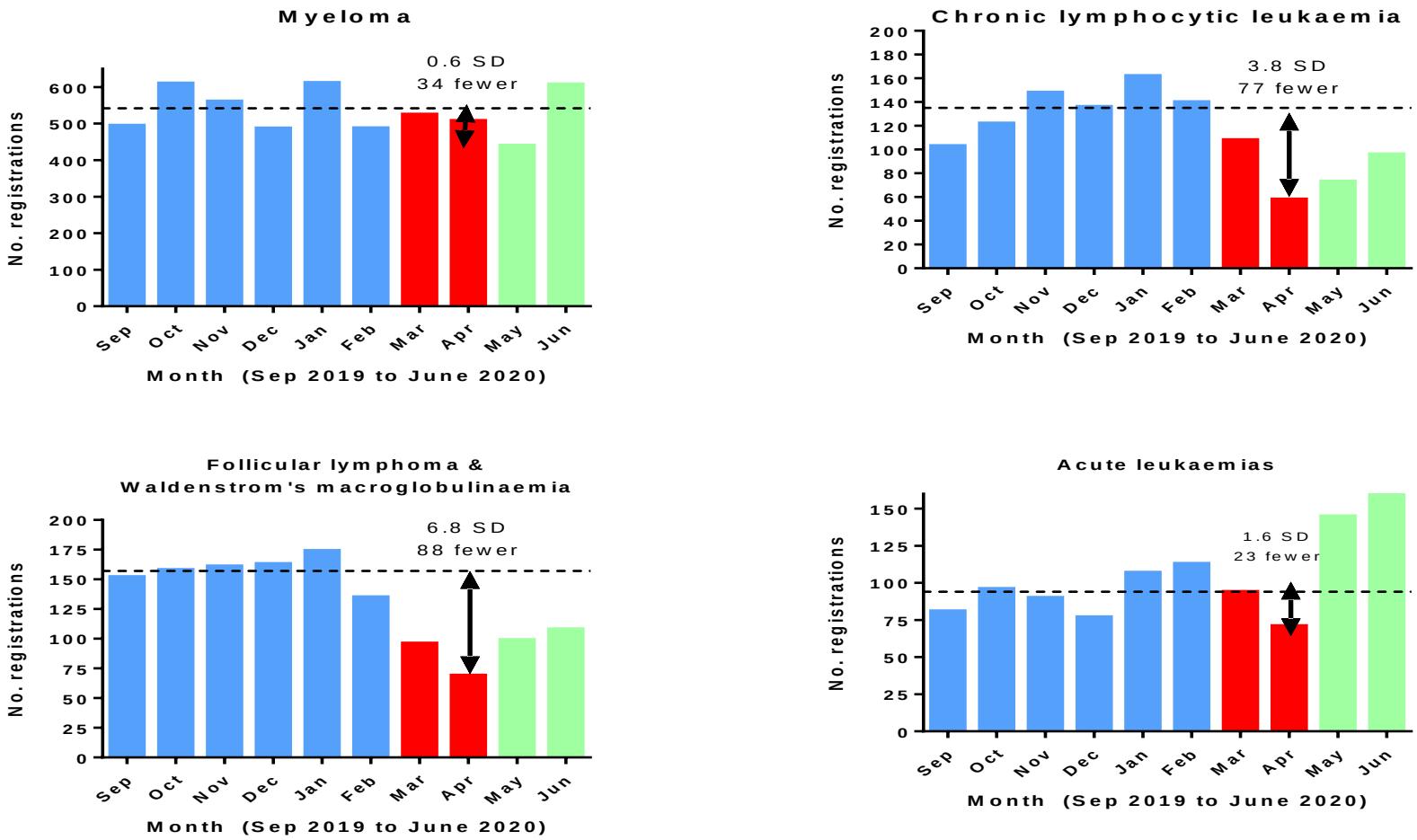


Figure S4. The number of SACT registrations observed per month, for haematological malignancies. The number seen in April 2020 is compared with the mean number between September 2019 and February 2020 (dashed horizontal line). The arrow shows the difference between April 2020 and the mean value, and also expressed as number of standard deviations (SD) from the mean. All reductions in April had $p \leq 0.0001$ except acute leukaemias ($p=0.001$) and myeloma ($p=0.27$) (all differences and p-values for May and June are in Supplementary Table 2).

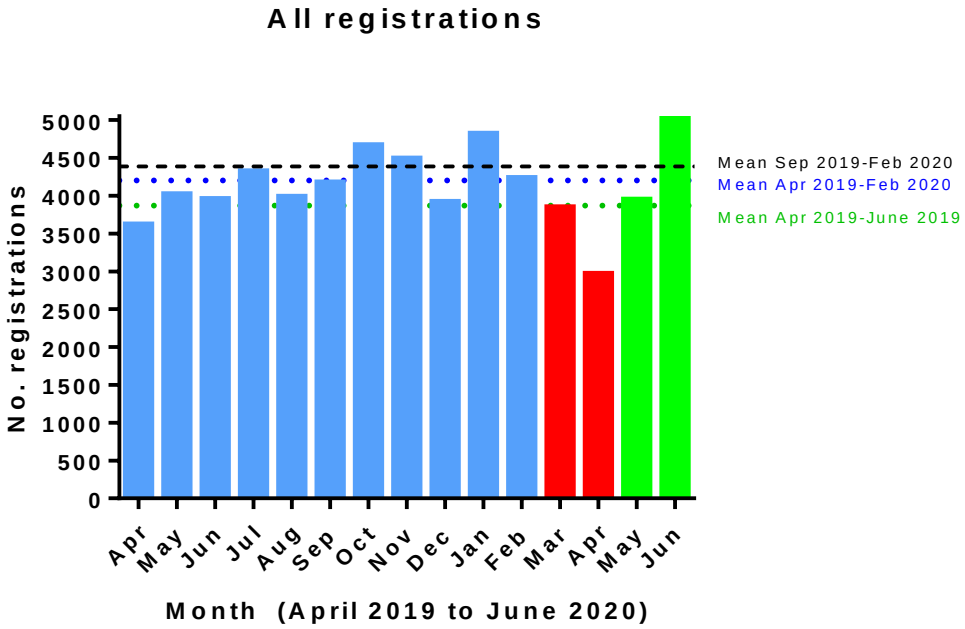


Figure S5. The total number of new SACT registrations from April 2019 to June 2020. The horizontal black dashed line represents the mean number of registrations for the control period used in the analyses (4386, for September 2019 to February 2020); the horizontal blue line represents the mean number for April 2019 to February 2020 (4203); the horizontal green line represents the mean number for April 2019 to June 2020 (3868).

Supplementary Table S1: New COVID indications introduced by the NHS via the Cancer Drugs Fund in April and May 2020 (available from https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/ - note this list is regularly updated)

Drug	Indication	Date Available via CDF
Abiraterone in combination with androgen deprivation therapy (ADT	*For the treatment of newly diagnosed high risk metastatic hormone-sensitive prostate cancer in patients either in whom enzalutamide is contraindicated or who are intolerant of enzalutamide and cannot or should not or have chosen not to receive docetaxel or would have received docetaxel had the COVID19 pandemic not occurred*	May 5th 2020
Atezolizumab	*As first line treatment for locally advanced or metastatic urothelial cancer instead of chemotherapy (as a consequence of the COVID19 pandemic)*	April 28th 2020
Brentuximab	*For brentuximab-naïve relapsed/refractory Hodgkin lymphoma following 1 prior therapy when cytotoxic chemotherapy is not a treatment option (because of the Covid19 pandemic) in adult patients*	April 28th 2020
Brentuximab	*For brentuximab-naïve relapsed/refractory Hodgkin lymphoma following at least 1 prior therapy when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option in child patients*	April 28th 2020
Enzalutamide in combination with androgen deprivation therapy (ADT)	*For the treatment of newly diagnosed metastatic hormone-sensitive prostate cancer in patients who cannot or should not or have chosen not to receive docetaxel or would have received docetaxel had the COVID19 pandemic not occurred*	May 5th 2020
Gilteritinib	*For treating relapsed/refractory FLT3 mutation positive acute myeloid leukaemia in adults*	April 28th 2020
Ibrutinib	*For the 1st line treatment, instead of chemotherapy, of mantle cell lymphoma in patients who have not previously received any prior systemic therapy*	April 28th 2020
Ixazomib with lenalidomide and dexamethasone	*For treating relapsed or refractory multiple myeloma in patients who have had 1 prior line of therapy*	May 22nd 2020
Lenalidomide (in combination with dexamethasone)	*As 1st line treatment in transplant eligible patients with multiple myeloma*	April 12th 2020
Lenalidomide (in combination with dexamethasone)	*As 2nd line treatment in patients with multiple myeloma previously not treated with a 1st line bortezomib-containing regimen*	April 12th 2020
Lenalidomide in combination with subcutaneous (SC) rituximab	*For previously treated follicular lymphoma (grades 1-3a)*	April 28th 2020
Nab-paclitaxel	*Paclitaxel as albumin-bound nanoparticles (nab-paclitaxel) instead of either paclitaxel or docetaxel in breast cancer regimens*	April 14th 2020
Niraparib	*As treatment without preceding chemotherapy in patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent FIRST RELAPSE of platinum-sensitive disease*	April 14th 2020
Nivolumab	*For the treatment of advanced renal cell carcinoma as a first line single agent without ipilimumab*	April 14th 2020
Nivolumab	*For the treatment of relapsed or refractory classical Hodgkin lymphoma in adults following treatment with brentuximab and with no previous stem cell transplantation*	April 28th 2020
Nivolumab	*For treating relapsed or refractory classical Hodgkin Lymphoma in paediatric patients following treatment with brentuximab and with no previous stem cell transplantation*	April 28th 2020
Nivolumab (in combination with ipilimumab)	*For the 2nd line treatment of intermediate or poor risk advanced renal cell carcinoma*	April 12th 2020
Nivolumab	*For treating metastatic colorectal cancer for patients with high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR)*	April 28th 2020
Olaparib (in its tablet formulation)	*As treatment without preceding chemotherapy as treatment in patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent first*	April 14th 2020

	relapse of platinum-sensitive disease	
Osimertinib	*For the first-line treatment of locally advanced or metastatic epidermal growth factor receptor mutation-positive non-small-cell lung cancer in adults*	April 28th 2020
Pembrolizumab	*For treating untreated PD-L1-positive metastatic non-small-cell lung cancer for patients with a PD-L1 tumour proportion score [TPS] between 1% and 49%*	April 12th 2020
Pembrolizumab (in combination with pemetrexed based combination chemotherapy)	*For treating untreated PD-L1-positive or negative locally advanced or metastatic non-squamous non-small-cell lung cancer followed by single agent pembrolizumab maintenance without pemetrexed maintenance*	April 12th 2020
Pembrolizumab	*As treatment for Gestational Trophoblastic Neoplasia instead of chemotherapy*	April 28th 2020
Pembrolizumab	*For the 1st line treatment of PD-L1 positive metastatic or unresectable recurrent squamous cell carcinoma of the head and neck (instead of 1st line chemotherapy)*	April 28th 2020
Pertuzumab (in combination with trastuzumab only)	*For the first line treatment of locally advanced or metastatic breast cancer*	April 12th 2020
Pertuzumab (neoadjuvant)	*In node positive patients for the neoadjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence*	April 12th 2020
Pertuzumab (neoadjuvant)	*In patients who are node negative or of unknown nodal status for the neoadjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence*	April 12th 2020
Pertuzumab (in combination with intravenous trastuzumab)	*As adjuvant therapy for axillary node positive HER2-positive early breast cancer and with NO preceding neoadjuvant therapy*	April 12th 2020
Pertuzumab (in combination with intravenous trastuzumab)	*As adjuvant therapy for patients with HER2-positive early breast cancer which was diagnosed as being node positive prior to neoadjuvant treatment and has now completed neoadjuvant pertuzumab in combination with trastuzumab and surgery*	April 12th 2020
Pertuzumab (in combination with intravenous trastuzumab)	*As adjuvant therapy for HER2-positive early breast cancer patients thought to be node negative or of unknown nodal status prior to neoadjuvant pertuzumab plus trastuzumab and found to be axillary node positive after completion of neoadjuvant pertuzumab plus trastuzumab and surgery*	April 12th 2020
Polatuzumab vedotinin combination with either bendamustine and rituximab or rituximab as bridging therapy	*For CAR T cell therapy in diffuse large B cell lymphoma and primary mediastinal B cell lymphoma patients formally accepted by the National CAR-T cell Clinical Panel for CAR-T cell therapy*	May 4th 2020
Pomalidomide (in combination with dexamethasone)	*For the treatment of relapsed and refractory multiple myeloma after a lenalidomide-containing regimen*	April 12th 2020
Rucaparib	*Without preceding chemotherapy treatment in patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have had a recent first relapse of platinum-sensitive disease*	April 14th 2020
Venetoclax with either azacitidine or cytarabine	*For untreated adult acute myeloid leukaemia (AML) instead of standard induction chemotherapy with daunorubicin and cytarabine*	April 28th 2020

Supplementary Table S2. Data used to create the figures

	Sept 2019 – Feb 2020 (control period)		March 2020	April 2020				May 2020				June 2020			
	Mean	SD	Number	Number	% change	SD difference	P-value	Number	% change	SD difference	P-value	Number	% change	SD difference	P-value
Total	4385.8	334.9	3847	2969	-32	-4.2	<0.0001	3950	-10	-1.3	<0.0001	5022	15	1.9	<0.0001
Curative	172.2	14.3	160	144	-16	-2.0	0.012	216	25	3.1	<0.0001	277	61	7.3	<0.0001
Adjuvant	270.8	23.0	255	207	-24	-2.8	<0.0001	303	12	1.4	0.071	290	7	0.8	0.512
Neoadjuvant	190.2	14.4	189	119	-37	-5.0	<0.0001	133	-30	-4.0	<0.0001	104	-45	-6.0	<0.0001
Non-curative (total)	3739.7	299.9	3223	2449	-35	-4.3	<0.0001	3196	-15	-1.8	<0.0001	4233	13	1.6	<0.0001
Non-curative 1st line	1797.0	110.3	1612	1265	-30	-4.8	<0.0001	1780	-1	-0.2	0.936	2291	27	4.5	<0.0001
Non-curative 2nd line	1200.7	131.2	1006	774	-36	-3.3	<0.0001	896	-25	-2.3	<0.0001	1256	5	0.4	0.213
Non-curative 3rd or more line	742.0	69.5	605	410	-45	-4.8	<0.0001	520	-30	-3.2	<0.0001	686	-8	-0.8	0.028
Oral drugs	1762.3	152.0	1685	1453	-18	-2.0	<0.0001	1812	3	0.3	0.490	2263	28	3.3	<0.0001
Immunotherapies	821.5	59.3	661	500	-39	-5.4	<0.0001	736	-10	-1.4	<0.0001	879	7	1.0	0.052
Chemo-immunotherapy	201.5	13.4	193	124	-38	-5.8	<0.0001	195	-3	-0.5	0.915	334	66	9.9	<0.0001
Chemotherapies	1089.0	108.9	825	533	-51	-5.1	<0.0001	770	-29	-2.9	<0.0001	1068	-2	-0.2	0.838
Intravenous drugs	2621.2	185.2	2157	1515	-42	-6.0	<0.0001	2137	-18	-2.6	<0.0001	2758	5	0.7	0.001
Solid tumours	3338.7	255.8	2934	2167	-35	-4.6	<0.0001	3092	-7	-1.0	<0.0001	3893	17	2.2	<0.0001
Haematological malignancies	1047.2	86.7	913	802	-23	-2.8	<0.0001	858	-18	-2.2	<0.0001	1129	8	0.9	0.002

- Mean and SD: mean and standard deviation (SD) of the number of registrations between Sep 2019 and Feb 2020 (the control period)
- Number: number of registrations in the month.
- Percentage change: number of registrations in the month expressed as a percentage of the mean for the control period (relative change)
- SD difference is the number of registrations minus mean number for the control period, divided by the SD (control period).
- P-values comes from a chi-squared test for comparing two counts: comparing the number registrations with the mean number for the control period. No adjustment was made for multiple analyses (3 time points and 35 rows in the table). However, those that are <0.0001 would be largely unaffected by not being adjusted with regards to statistical significance because p=0.0001 multiplied by 3x35 analyses still yields p=0.01 which is <0.05.

Supplementary Table S2 continued

	Sept 2019 – Feb 2020 (control period)		March 2020	April 2020				May 2020				June 2020			
	Mean	SD	Number	Number	% change	SD difference	P-value	Number	% change	SD difference	P-value	Number	% change	SD difference	P-value
Breast	985.0	76.9	897	663	-33	-4.2	<0.0001	891	-10	-1.2	<0.0001	1053	7	0.9	0.023
Prostate	360.0	43.2	266	154	-57	-4.8	<0.0001	493	37	3.1	<0.0001	660	83	6.9	<0.0001
Lung	626.7	43.2	563	404	-36	-5.2	<0.0001	603	-4	-0.5	0.649	763	22	3.2	<0.0001
Renal	196.2	22.5	183	151	-23	-2.0	<0.0001	132	-33	-2.8	<0.0001	225	15	1.3	0.048
Colorectal	276.8	34.3	214	178	-36	-2.9	<0.0001	243	-12	-1.0	0.028	259	-6	-0.5	0.553
Hepato-, pancreas and biliary tract	105.5	11.9	102	71	-33	-2.9	<0.0001	78	-26	-2.3	<0.0001	126	19	1.7	0.069
Gynaecological	209.3	26.1	227	171	-18	-1.5	<0.0001	146	-30	-2.4	<0.0001	184	-12	-1.0	0.103
Head & neck	50.7	5.7	32	29	-43	-3.8	<0.0001	50	-1	-0.1	0.996	67	32	2.9	0.023
Urothelial	58.2	11.1	50	39	-33	-1.7	<0.0001	72	24	1.3	0.142	91	56	3.0	<0.0001
Skin	412.8	38.6	353	280	-32	-3.4	<0.0001	342	-17	-1.8	<0.0001	378	-8	-0.9	0.125
Other (NET, GIST, Thyroid, Sarcoma, CNS)	57.5	11.0	47	27	-53	-2.8	<0.0001	40	-30	-1.6	0.002	86	50	2.6	<0.0001
Myeloma	542.2	60.1	525	508	-6	-0.6	0.266	440	-19	-1.7	<0.0001	608	12	1.1	<0.0001
Non-Hodgkins lymphoma, diffuse large B cell lymphoma	28.8	4.1	19	20	-31	-2.1	0.110	34	18	1.3	0.671	40	39	2.7	0.070
Acute leukaemias	94.0	14.2	94	71	-24	-1.6	0.001	145	54	3.6	<0.0001	160	70	4.6	<0.0001
Chronic lymphocytic leukaemia	135.2	20.6	108	58	-57	-3.8	<0.0001	73	-46	-3.0	<0.0001	96	-29	-1.9	<0.0001
Follicular lymphoma, Waldenstrom's macroglobulinaemia	157.2	13.0	96	69	-56	-6.8	<0.0001	99	-37	-4.5	<0.0001	108	-31	-3.8	<0.0001
Hodgkins lymphoma	20.8	5.9	22	25	20	0.7	0.705	12	-42	-1.5	0.017	44	111	3.9	<0.0001
Chronic myeloid leukaemia	34.7	6.0	21	23	-34	-1.9	0.018	19	-45	-2.6	<0.0001	28	-19	-1.1	0.478
Mantle cell lymphoma	31.2	2.4	25	25	-20	-2.6	0.498	35	12	1.6	0.824	39	25	3.3	0.382
Myelodysplastic syndromes	3.2	1.5	3	3	-5	-0.1	-	1	-68	-1.5	0.260	6	89	1.9	-

- NET (neuroendocrine tumours), GIST (gastrointestinal stromal tumors), GTD (gestational trophoblastic disease), CNS (central nervous system)