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Socio-demographic inequalities in stage of cancer diagnosis: evidence from patients with female breast, lung, colon, rectal, prostate, renal, bladder, melanoma, ovarian and endometrial cancer

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Background: Understanding socio-demographic inequalities in stage at diagnosis can inform priorities for cancer control.
Patients and methods: We analysed data on the stage at diagnosis of East of England patients diagnosed with any of 10 common cancers, 2006–2010. Stage information was available on 88 657 of 98 942 tumours (89.6%).
Results: Substantial socio-demographic inequalities in advanced stage at diagnosis (i.e. stage III/IV) existed for seven cancers, but their magnitude and direction varied greatly by cancer: advanced stage at diagnosis was more likely for older patients with melanoma but less likely for older patients with lung cancer [odds ratios for 75–79 versus 65–69 1.60 (1.38–1.86) and 0.83 (0.77–0.89), respectively]. Deprived patients were more likely to be diagnosed in advanced stage for melanoma, prostate, endometrial and (female) breast cancer: odds ratios (most versus least deprived quintile) from 2.24 (1.66–3.03) for melanoma to 1.31 (1.15–1.49) for breast cancer. In England, elimination of socio-demographic inequalities in stage at diagnosis could decrease the number of patients with cancer diagnosed in advanced stage by ~5600 annually.
Conclusions: There are substantial socio-demographic inequalities in stage at diagnosis for most cancers. Earlier detection interventions and policies can be targeted on patients at higher risk of advanced stage diagnosis.
Key words: cancer, demographic, diagnosis, inequalities, socio-economic, stage

introduction

Eliminating population exposure to known lifestyle and environmental risk factors would only prevent up to 45% of all new diagnoses of cancer, and this potential may not be achievable for many years [1]. Therefore, in addition to primary prevention efforts to decrease cancer incidence, current cancer control policies aim to reduce the proportion of patients diagnosed at advanced disease stage. Early-stage detection renders currently available treatments more effective and can therefore amplify the impact of primary prevention initiatives to help decrease cancer-related deaths [2, 3].

However, the evidence about how to achieve earlier stage detection is still developing [3]. The great majority of cancer patients are diagnosed after first presenting to a general practitioner with symptoms relating to their cancer [4]. In those patients, interventions to improve awareness and appraisal of cancer symptoms could help to decrease the time interval between symptom onset and presentation to a doctor [5]. Such interventions could be further targeted and tailored on population groups at higher risk of advanced stage diagnosis, for example older women (who are at higher risk of late-stage diagnosis of breast cancer compared with younger women) [6, 7] or men (who are at higher risk of late-stage diagnosis of melanoma compared with women) [8]. For cancers with large socio-demographic inequalities in stage at diagnosis, such targeting may be judged particularly appropriate. However, for most common cancers, up-to-date UK evidence about whether socio-demographic inequalities in stage at diagnosis exist and their magnitude and direction is limited.

Against this background, we set out to examine socio-demographic inequalities in stage at diagnosis for 10 common cancers. Our aim was to explore and characterise variation in

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advanced stage at diagnosis for different cancers and patient groups to help inform priorities for cancer control.

methods

data

We analysed information on the stage at diagnosis of East of England patients with cancer aged 30 years or over with a new diagnosis of (International Classification of Diseases–10 code): colon (C18), rectal (C19–20), lung (C34), melanoma (C43), female breast (C50), endometrial (C54), ovarian (C56), prostate (C61), renal (C64) and bladder (C67) cancer during 2006–2010. This represents the longest most recent period for which stage information was available with high completeness for all 10 cancers. Together, the respective cancer sites represent 67% of new cancer diagnoses in England (2009) and 57% of all cancer deaths. Anonymous data were extracted from the Eastern Cancer Registration and Information Centre (ECRIC), a cancer registry covering a population of ~5.7 m. This registry has an excellent record of registration quality as indicated by measures, such as death-certificate only registrations of 0.02% in 2010 compared with an average national rate of 1.6% [9]. Uniquely among English cancer registries, currently it holds stage at diagnosis information for a high proportion of tumours [10]. As part of the registration process, stage at diagnosis was assigned by CHB and BAR, based on clinical, imaging and pathological information according to the TNM classification [11]. Information on the income domain of the Index of Multiple Deprivation (IMD) 2004 score of the Lower Super Output Area of patients' residence at diagnosis was available as part of the registration record and was subsequently used to define socio-economic status quintiles (1 = least deprived, or 'affluent'; 5 = most deprived) [12]. The use of this index (i.e. of the income domain of IMD) is standard practice in UK cancer statistics and research because it avoids the potential for endogeneity between health outcomes (e.g. cancer stage at diagnosis) and composite (multidimensional) deprivation measures already incorporating measures of health deprivation.

analysis

The main analysis was confined to patients with known stage (complete case analysis). We defined advanced stage at diagnosis as diagnosis in stages III/IV. We used a two-step modelling approach, which allows us to examine overall socio-demographic differences before investigating how they vary by cancer [13].

Initially, a logistic regression model was used to predict advanced stage diagnosis, adjusting for age group (65–69-year olds used as reference), gender (men as reference), deprivation quintile (least deprived group as reference), cancer (rectal cancer as reference); tumour type (morphology); and for breast, colon and rectal cancers, whether the cancer was detected symptomatically or by screening (diagnosis of cancer within 90 days from a screening episode defined screening-detected cancers). We used this initial model which only included main effect variables to summarise overall associations between age, gender and deprivation with advanced stage at diagnosis across all studied cancers. Because of interactions between socio-demographic variables and cancer ($P < 0.001$ for all), in subsequent analysis we used a series of separate logistic regression models for each cancer.

We assessed the robustness of the findings using different sensitivity analyses. We re-ran the initial model using different definitions of advanced stage categories, i.e. diagnosis in stages II–IV versus stage I; or in stage IV versus stages I–III. We also explored potential confounding of gender, deprivation and age inequalities by ethnicity by repeating the analysis adjusting for ethnic group in the two-thirds of all patients for whom ethnicity information was available. We explored potential bias arising from missing stage information using multiple imputation of missing stage repeating the analysis in a complete dataset including patients with imputed stage [7, 14, 15]. All exposure variables included in the analysis models were complete, and data were only missing for the outcome variable (stage). In this case, the analysis model will provide unbiased estimates of associations under the missing at random (MAR) assumption (that outcome data are MAR given the exposure variables). However, the MAR assumption can be made more reasonable if stage is imputed on additional variables to those used in the analysis. We therefore imputed stage using an imputation model including information on survival, tumour histological grade, basis of diagnosis (i.e. whether the diagnosis was verified with histology or not), and oestrogen receptor status (for patients with breast cancer only) in addition to all the variables used in the analysis models. Imputation variables were complete, except for grade and oestrogen receptor status (used in imputation models only). Survival was censored at 365 days so that a reasonably consistent approach was applied to patients of any age regarding competing mortality risk. For the imputation model to be congenial with the analysis, model imputation was stratified by cancer. Multiple imputation was conducted using chained equations which created 20 imputed datasets.

We illustrate the potential population health impact of the findings by estimating the number of cancers diagnosed in advanced stage in England annually that could be prevented by eliminating gender, deprivation and old age inequalities. Potential improvements were estimated only where there was significant variation. For the prediction of potential proportions, the odds ratio values for patients belonging to patient groups with higher probability of advanced stage diagnosis were set to that of the relevant group with the lowest odds ratios. As more deprived patients with cancer are under-represented in the East of England compared with the England average, we used inverse probability weights calculated using the national deprivation group-specific incidence of each cancer. We focused on the impact of eliminating age inequalities on patients aged 65 or over because this age group includes about two-thirds of all patients with cancer and because of concerns about poorer relative survival and avoidable excess cancer deaths in older patients [16, 17]. Confidence intervals for these impact values were estimated using a bootstrap with 1 000 replications, accounting for both the uncertainty in stage inequalities and the uncertainty in the distribution of different patient groups.

In order to account for the fact that patients may attend the same health care organisation and that some tumours occur in the same patient, we use a sandwich estimator throughout. All analysis was conducted in STATA 11 (StataCorp. 2009, College Station, TX), including using the *ice* and *mim* commands used for multiple imputation [18]. See also supplementary file S1, for additional details on methods, available at *Annals of Oncology* online.

results

In total, there were 98 942 patients diagnosed with a relevant cancer during the study period. Information on stage at diagnosis was available for 88 657 (89.6%) of all patients, and among those patients the proportion of those diagnosed in stages III/IV varied substantially by cancer (Table 1 and supplementary file S2, available at *Annals of Oncology* online).

Considering socio-demographic inequalities for all cancers together, there was strong evidence that advanced stage at diagnosis was less likely in women and more likely with increasing level of deprivation ($P = 0.003$ for gender and $P < 0.001$ for deprivation, Table 2). Advanced stage also varied by age ($P < 0.001$), being more likely in older age. There was strong evidence that the associations between advanced stage at

Table 1. Distribution of stage, gender, age and deprivation categories by cancer ($n = 98\,942$)[a]

	Bladder $n = 4924$	Breast $n = 22\,447$	Colon $n = 12\,019$	Endometrial $n = 3644$	Renal $n = 3476$	Lung $n = 16\,714$	Melanoma $n = 5693$	Ovarian $n = 2744$	Prostate $n = 20\,372$	Rectal $n = 6909$	Total $n = 98\,942$
Stage I	2219	8595	1489	2612	1208	1949	3536	524	2111	1460	25 703
	45%	*38%*	*12%*	*72%*	*35%*	*12%*	*62%*	*20%*	*10%*	*21%*	*26%*
Stage II	1403	9124	3661	315	395	901	1142	136	11 815	1451	30 343
	28%	*41%*	*30%*	*9%*	*11%*	*5%*	*20%*	*5%*	*58%*	*21%*	*30%*
Stage III	277	1999	2917	321	552	4339	629	1323	2323	1807	16 487
	6%	*9%*	*24%*	*9%*	*16%*	*26%*	*11%*	*48%*	*11%*	*26%*	*17%*
Stage IV	551	1030	2374	167	977	6360	77	461	2958	1169	16 124
	11%	*5%*	*20%*	*5%*	*28%*	*38%*	*1%*	*17%*	*15%*	*17%*	*16%*
Unknown stage	474	1699	1578	229	344	3165	309	300	1165	1022	10 285
	10%	*8%*	*13%*	*6%*	*10%*	*19%*	*5%*	*11%*	*6%*	*15%*	*10%*
Stage I/II	3622	17 719	5150	2927	1603	2850	4678	660	13 926	2911	56 046
	81%	*85%*	*49%*	*86%*	*51%*	*21%*	*87%*	*27%*	*73%*	*49%*	*63%*
Stages III/IV	828	3029	5291	488	1529	10 699	706	1784	5281	2976	32 611
	19%	*15%*	*51%*	*14%*	*49%*	*79%*	*13%*	*73%*	*27%*	*51%*	*37%*
All known stage	4450	20 748	10 441	3415	3132	13 549	5384	2444	19 207	5887	88 657
Men	3625		6069		2207	9627	2855		20 372	4207	48 962
	74%		*51%*		*63%*	*58%*	*50%*		*100%*	*61%*	*49%*
Women	1299	22 447	5950	3644	1269	7087	2838	2744		2702	49 980
	26%	*100%*	*49%*	*100%*	*37%*	*42%*	*50%*	*100%*		*39%*	*51%*
30–49	111	4245	446	178	293	447	1261	291	171	316	7759
	2%	*19%*	*4%*	*5%*	*8%*	*3%*	*22%*	*11%*	*1%*	*5%*	*8%*
50–54	119	2574	342	244	224	566	461	189	441	285	5445
	2%	*11%*	*3%*	*7%*	*6%*	*3%*	*8%*	*7%*	*2%*	*4%*	*6%*
55–59	247	2412	638	492	355	1117	563	264	1345	523	7956
	5%	*11%*	*5%*	*14%*	*10%*	*7%*	*10%*	*10%*	*7%*	*8%*	*8%*
60–64	418	3119	1270	650	451	1950	748	387	2760	901	12 654
	8%	*14%*	*11%*	*18%*	*13%*	*12%*	*13%*	*14%*	*14%*	*13%*	*13%*
65–69	601	2724	1602	546	432	2197	635	379	3686	1020	13 822
	12%	*12%*	*13%*	*15%*	*12%*	*13%*	*11%*	*14%*	*18%*	*15%*	*14%*
70–74	766	1873	1859	547	467	2722	636	377	3900	1136	14 283
	16%	*8%*	*15%*	*15%*	*13%*	*16%*	*11%*	*14%*	*19%*	*16%*	*14%*
75–79	919	1963	2113	428	536	2970	571	319	3746	1068	14 633
	19%	*9%*	*18%*	*12%*	*15%*	*18%*	*10%*	*12%*	*18%*	*15%*	*15%*
80–84	896	1652	1968	323	394	2641	442	262	2506	916	12 000
	18%	*7%*	*16%*	*9%*	*11%*	*16%*	*8%*	*10%*	*12%*	*13%*	*12%*
85+	847	1885	1781	236	324	2104	376	276	1817	744	10 390
	17%	*8%*	*15%*	*6%*	*9%*	*13%*	*7%*	*10%*	*9%*	*11%*	*11%*
Affluent	1143	6031	2902	809	712	3093	1696	686	5601	1709	24 382
	23%	*27%*	*24%*	*22%*	*20%*	*19%*	*30%*	*25%*	*27%*	*25%*	*25%*
Deprivation group 2	1154	5837	3164	943	920	3943	1552	703	5629	1756	25 601
	23%	*26%*	*26%*	*26%*	*26%*	*24%*	*27%*	*26%*	*28%*	*25%*	*26%*
Deprivation group 3	1273	5453	3036	958	949	4313	1417	682	4935	1747	24 763
	26%	*24%*	*25%*	*26%*	*27%*	*26%*	*25%*	*25%*	*24%*	*25%*	*25%*
Deprivation group 4	1003	3881	2211	700	677	3834	800	493	3175	1282	18 056
	20%	*17%*	*18%*	*19%*	*19%*	*23%*	*14%*	*18%*	*16%*	*19%*	*18%*
Deprived	351	1245	706	234	218	1531	228	180	1032	415	6140
	7%	*6%*	*6%*	*6%*	*6%*	*9%*	*4%*	*7%*	*5%*	*6%*	*6%*

[a]For each cancer, column percentages for patient groups in each category are presented in italics.

diagnosis and gender, age and deprivation varied between cancers ($P < 0.001$ for all).

In separate models (by cancer), women were less likely to be diagnosed in advanced stage compared with men for melanoma and lung cancer [odds ratios (OR) for women versus men 0.68 (0.57–0.81) $P < 0.001$ and 0.88 (0.81–0.96) $P = 0.003$, respectively] (Table 3). There was evidence ($P \leq 0.007$ for all) for deprivation gradients in patients with 4 of the 10 cancers (i.e. for melanoma, breast, endometrial and prostate cancer), with most deprived patients having a higher probability of advanced stage diagnosis (Figure 1). Among patients aged 65 or over, the strength and direction of

Table 2. Independent associations of gender, deprivation and age with advanced stage at diagnosis (stage III/IV versus stage I/II)* ($n = 88\,657$)

	Adjusted odds ratio* (95% confidence intervals)	*P*
Men	Reference	0.003
Women	0.93 (0.89, 0.98)	
Affluent	Reference	<0.001
2	1.10 (1.05, 1.15)	
3	1.11 (1.06, 1.16)	
4	1.15 (1.09, 1.21)	
Deprived	1.21 (1.12, 1.30)	<0.001
30–49	0.90 (0.83, 0.98)	
50–54	1.03 (0.94, 1.12)	
55–59	1.09 (1.01, 1.17)	
60–64	1.01 (0.95, 1.08)	
65–69	Reference	
70–74	1.00 (0.94, 1.06)	
75–79	1.01 (0.96, 1.08)	
80–84	1.08 (1.01, 1.15)	
85+	1.28 (1.19, 1.37)	

*From a model which also adjusted for breast, colon and rectal screening detection status, cancer and tumour type (all cancers).

associations between age and stage at diagnosis varied greatly between cancers (Figure 2). Older patients with melanoma, prostate, endometrial and breast cancer were more likely to be diagnosed in advanced stage compared with patients aged 65–69 ($P = 0.01$ for endometrial and $P < 0.001$ for others). Conversely, older patients with bladder, lung and renal cancer were less likely to be diagnosed in advanced stage compared with 65–69-year-old patients ($P = 0.002$, $P < 0.001$, and $P = 0.009$, respectively).

The sensitivity analysis (carried out using the initial model) produced overall similar findings (supplementary files S3–S6, available at *Annals of Oncology* online). Multiple imputation produced similar findings to those obtained by complete case analysis for gender, deprivation and age inequalities, although it indicated a slight underestimation of associations with advanced stage diagnosis in older patients.

In England, there are ∼186 000 new diagnoses for the 10 studied cancers every year (2009), and we estimated (see Methods) that ∼73 000 (39%) of those cancers are diagnosed in advanced stage currently. For the seven cancers with evidence of socio-demographic variation in stage at diagnosis there are ∼146 000 new diagnoses, and we estimated that ∼52 000 (36%) of those cancers are diagnosed in advanced stage currently. If it were possible to eliminate all gender, deprivation and old age inequalities in stage at diagnosis, there would be ∼5600 fewer cases diagnosed in advanced stage in England annually (Table 4) representing ∼3% of all diagnoses of the 10 studied cancers. Alternatively, this figure represents an ∼8% reduction in the advanced stage cases of all 10 studied cancers, or an ∼11% reduction in the advanced stage cases of the seven cancers for which there was evidence of potential gains in early stage diagnosis. Prostate, melanoma and endometrial cancer have the largest proportional early diagnosis gains. About 5000 of those tumours (∼90%) comprise reductions in advanced stage at diagnosis for prostate (∼2000 cancers), breast (∼1000 cancers), lung (∼1300 cancers) and melanoma (∼700 cancers), with colon, rectal and ovarian cancer contributing no cases.

discussion

We found substantial and potentially avoidable gender, deprivation and age inequalities in advanced stage diagnosis of seven common cancers and relatively limited socio-demographic variation in stage at diagnosis of three other cancers. Among cancers with substantial inequalities, the size and direction of differences in advanced stage diagnosis varied greatly by cancer. The results were robust to various assumptions investigated with sensitivity analyses, including adjustment for ethnic group. Multiple imputation of missing stage indicated that the effect of age in older patients may have been slightly underestimated. Potential elimination of socio-demographic inequalities could help diagnose a substantial number of patients with cancer in earlier stage. Although, in absolute terms, most of these earlier detection gains relate to four common cancers, there are also notable relative gains for endometrial cancer.

The findings should be interpreted taking into account evidence about the socio-demographic differences in awareness and appraisal of cancer symptoms; and on the promptness by which cancer is suspected in symptomatic patients with different cancers. For melanoma, breast and endometrial cancers the observed socio-demographic inequalities in advanced stage at diagnosis are unlikely to reflect delays in suspecting and investigating cancer after symptomatic presentation to a doctor: these cancers are among the 'easiest to suspect and diagnose' and delays after presentation are limited [13, 19]. Therefore, inequalities in stage at diagnosis for those three cancers are likely to reflect socio-demographic differences in awareness and interpretation of cancer symptoms which have been previously described [20–22].

For lung, renal and bladder cancer, we observed 'negative' age gradients in advanced stage at diagnosis among patients aged 65 or over (older patients having lower probability of diagnosis at advanced stage). Similar associations between older age and stage at diagnosis of lung cancer have been reported previously in both related and other patient populations [7, 19, 23]. These findings are unlikely to reflect improved awareness and appraisal of cancer symptoms for lung, renal and bladder cancer in older compared with younger patients. Healthcare factors however may be implicated. Older patients tend to have more co-morbidities, which may lead to incidental identification of lung or renal cancers through imaging investigations (e.g. by chest X-ray or abdominal ultrasound, respectively, for symptoms unrelated to cancer). This may reflect a paradoxical apparent benefit of increasing level of co-morbidity, similar to other improvements in care reported for patients with multiple conditions [24]. An alternative explanation may be that these patterns reflect cognitive or psychological barriers by the doctors in suspecting cancer in middle-aged patients. Strong inverse age patterns in the number of consultations with a general practitioner with cancer

Table 3. Association between gender, deprivation and age and advanced stage at diagnosis by cancer (using stratified models for each cancer)

	Bladder*		Breast*		Colon*		Rectal*		Endometrial†	
	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a
Men	Reference	0.065	n/a		Reference	0.372	Reference	0.362	n/a	
Women	1.19 (0.99, 1.43)				1.04 (0.96, 1.12)		0.95 (0.86, 1.06)			
Affluent	Reference	0.126	Reference	<0.001	Reference	0.391	Reference	0.915	Reference	0.007
2	1.05 (0.99, 1.13)		1.07 (1.04, 1.10)		1.01 (0.98, 1.05)		1.00 (0.96, 1.04)		1.37 (1.11, 1.68)	
3	1.11 (0.97, 1.27)		1.14 (1.07, 1.22)		1.03 (0.96, 1.10)		1.00 (0.91, 1.08)		1.59 (1.19, 2.12)	
4	1.17 (0.96, 1.43)		1.22 (1.11, 1.35)		1.04 (0.95, 1.15)		0.99 (0.87, 1.13)		1.56 (1.16, 2.10)	
Deprived	1.23 (0.94, 1.61)		1.31 (1.15, 1.49)		1.06 (0.93, 1.20)		0.99 (0.84, 1.17)		1.31 (0.89, 1.92)	
30–49	1.50 (1.00, 2.24)	<0.001[b]	0.79 (0.69, 0.90)	<0.001[b]	1.78 (1.48, 2.14)	<0.001[b]	1.78 (1.43, 2.22)	<0.001[b]	1.21 (0.78, 1.87)	0.032[b]
50–54	1.35 (1.00, 1.83)		0.84 (0.76, 0.92)		1.54 (1.34, 1.77)		1.54 (1.31, 1.82)		1.15 (0.83, 1.60)	
55–59	1.22 (1.00, 1.50)		0.89 (0.83, 0.95)		1.33 (1.22, 1.46)		1.33 (1.19, 1.49)		1.10 (0.89, 1.37)	
60–64	1.11 (1.00, 1.22)		0.94 (0.91, 0.97)		1.16 (1.10, 1.21)		1.16 (1.09, 1.22)		1.05 (0.94, 1.17)	
65–69	Reference		Reference		Reference		Reference		Reference	
70–74	0.90 (0.84, 0.96)	0.002[c]	1.07 (1.03, 1.11)	<0.001[c]	1.01 (0.98, 1.04)	0.618[c]	1.01 (0.97, 1.06)	0.585[c]	1.13 (1.03, 1.24)	0.010[c]
75–79	0.81 (0.71, 0.92)		1.15 (1.06, 1.24)		1.02 (0.95, 1.08)		1.03 (0.94, 1.12)		1.27 (1.06, 1.53)	
80–84	0.73 (0.60, 0.89)		1.23 (1.10, 1.37)		1.02 (0.93,1.13)		1.04 (0.91, 1.19)		1.44 (1.09, 1.90)	
85+	0.66 (0.51, 0.86)		1.32 (1.13, 1.53)		1.03 (0.91, 1.17)		1.05 (0.88, 1.26)		1.62 (1.12, 2.35)	
	Renal*		Lung*		Melanoma*		Ovarian*		Prostate‡	
	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a	Odds ratio (95% CI)	P^a
Men	Reference	0.118	Reference	0.003	Reference	<0.001	n/a		n/a	
Women	0.89 (0.77, 1.03)		0.88 (0.81, 0.96)		0.68 (0.57, 0.81)					
Affluent	Reference	0.448	Reference		Reference		Reference		Reference	
2	1.02 (0.96, 1.09)		0.97 (0.94, 1.01)	0.109	1.22 (1.14, 1.32)	<0.001	0.93 (0.85, 1.01)	0.077	1.08 (1.05, 1.11)	<0.001
3	1.05 (0.93, 1.18)		0.95 (0.88, 1.01)		1.50 (1.29, 1.74)		0.86 (0.72, 1.02)		1.17 (1.11, 1.23)	
4	1.07 (0.90, 1.29)		0.92 (0.83, 1.02)		1.83 (1.46, 2.30)		0.79 (0.61, 1.03)		1.27 (1.17, 1.37)	
Deprived	1.10 (0.86, 1.40)		0.89 (0.78, 1.03)		2.24 (1.66, 3.03)		0.74 (0.52, 1.03)		1.37 (1.23, 1.52)	
30–49	0.68 (0.52, 0.88)	<0.001[b]	1.50 (1.20, 1.87)	<0.001[b]	0.46 (0.34, 0.63)	<0.001[b]	0.51 (0.36, 0.71)	<0.001[b]	0.93 (0.76, 1.15)	<0.001[b]
50–54	0.75 (0.61, 0.91)		1.35 (1.15, 1.60)		0.56 (0.45, 0.70)		0.60 (0.46, 0.78)		0.95 (0.81, 1.11)	
55–59	0.82 (0.72, 0.94)		1.22 (1.09, 1.37)		0.68 (0.58, 0.79)		0.71 (0.60, 0.84)		0.97 (0.87, 1.07)	
60–64	0.91 (0.85, 0.97)		1.11 (1.05, 1.17)		0.82 (0.76, 0.89)		0.84 (0.77, 0.92)		0.98 (0.93, 1.04)	
65–69	Reference		Reference		Reference		Reference		Reference	
70–74	0.92 (0.86, 0.98)	0.009[c]	0.91 (0.88, 0.94)	<0.001[c]	1.27 (1.17, 1.36)	<0.001[c]	1.00 (0.90, 1.11)	0.980[c]	1.02 (0.92, 1.13)	<0.001[c]
75–79	0.84 (0.74, 0.96)		0.83 (0.77, 0.89)		1.60 (1.38, 1.86)		1.00 (0.81, 1.23)		1.10 (0.99, 1.21)	
80–84	0.77 (0.63, 0.94)		0.76 (0.68, 0.84)		2.03 (1.62, 2.54)		1.00 (0.74, 1.37)		1.45 (1.30, 1.62)	
85+	0.71 (0.54, 0.92)		0.69 (0.60, 0.79)		2.57 (1.90, 3.46)		1.01 (0.66, 1.52)		2.30 (2.03, 2.60)	

[a]All testing is based on Wald tests with joint tests used where applicable.

[b]Test for overall variation between different age groups.

[c]Test for variation between age groups for patients 65 years or older.

*The models for these eight cancers (i.e. colon, rectal, lung, melanoma, female breast, ovarian, renal and bladder cancer) were adjusted for tumour type, gender and screening detection status (as applicable) and age and deprivation. Deprivation was treated as a continuous variable. Age was treated as two continuous variables (above and below the reference group) included together in the model (see also supplementary file S1, available at *Annals of Oncology* online).

†The model for endometrial cancer was adjusted for tumour type and linear terms for young and old age groups (see footnote * above). For deprivation, both a linear and a squared term were included, given evidence that such parameterisation improved model fit ($P = 0.023$). The presented odds ratio values for each deprivation group are derived by the combination of the linear and the squared terms [i.e. odds ratio = 1.48 (95% CI 1.12–1.95) and odds ratio = 0.92 (95% CI 0.86–0.99), respectively].

‡The model for prostate cancer was adjusted for tumour type and linear terms for deprivation category and young age group (see footnote * above). Old age group was treated as a categorical variable, because of strong evidence that such parameterisation improved model fit (<0.001). CI, Confidence Interval.

symptoms before specialist referral exist (with younger patients more likely to be referred to hospital less promptly)—such patterns also exist for patients with lung, renal and bladder cancer [13]. Another hypothesis is that these three cancers have more (and perhaps more specific) symptoms in older age.

Given that there is no robust evidence to explain the inverse age inequalities in the stage at diagnosis of lung, renal and bladder cancer, research to establish the causes of these patterns should be considered a priority. If the mechanisms responsible for these inequalities are better understood, interventions to reduce

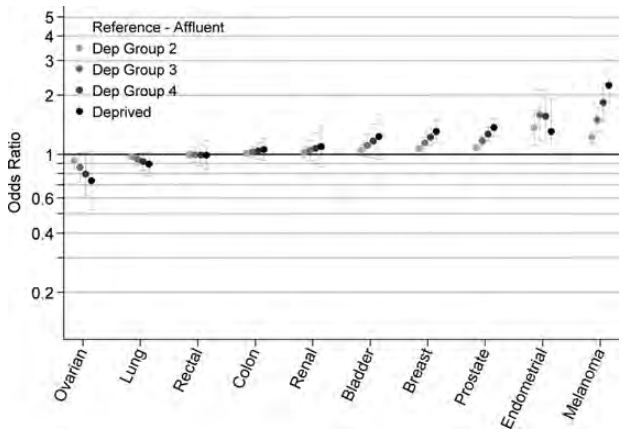

Figure 1. Deprivation inequalities in advanced stage at diagnosis by cancer (odds ratios and 95% confidence intervals for diagnosis in stage III/IV versus I/II).

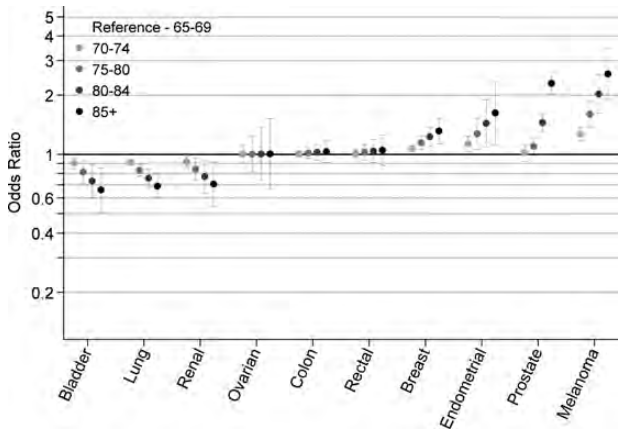

Figure 2. Age inequalities in advanced stage diagnosis in patients ≥65 by cancer (odds ratios and 95% confidence intervals for diagnosis in stage III/IV versus I/II).

Table 4. Estimated annual reduction in cancers diagnosed in stage III/IV as opposed to stage I/II in England that could be achievable if gender, deprivation and old age inequalities (2006–2010) were eliminated*

	Gender	Deprivation	Old age	Gender, deprivation and old age combined
Potential reduction in cancers diagnosed in advanced stage as a percentage of all new cancer diagnoses				
Melanoma	2.00 (1.10, 2.89)	3.06 (1.91, 4.22)	2.67 (1.86, 3.48)	6.78 (5.48, 8.09)
Prostate	n/a	2.62 (1.73, 3.51)	2.99 (2.07, 3.92)	5.45 (4.29, 6.62)
Endometrial	n/a	3.10 (1.25, 4.95)	1.51 (0.46, 2.57)	4.39 (2.52, 6.27)
Lung	1.21 (0.41, 2.01)		2.45 (1.45, 3.44)	3.75 (2.42, 5.08)
Renal			2.75 (0.66, 4.83)	2.75 (0.66, 4.83)
Breast (women)	n/a	1.45 (0.78, 2.13)	0.93 (0.47, 1.38)	2.32 (1.54, 3.11)
Bladder			1.87 (0.71, 3.03)	1.87 (0.71, 3.03)
Potential reduction in the number of cancers diagnosed in advanced stage				
Prostate	n/a	952 (628, 1277)	1089 (753, 1425)	1984 (1561, 2407)
Lung	423 (143, 703)		854 (507, 1202)	1310 (846, 1774)
Breast (women)	n/a	611 (328, 894)	390 (199, 580)	976 (646, 1306)
Melanoma	209 (115, 302)	320 (200, 440)	279 (194, 363)	708 (572, 844)
Endometrial	n/a	202 (82, 323)	99 (30, 167)	287 (164, 409)
Renal			186 (45, 328)	186 (45, 328)
Bladder			170 (64, 275)	170 (64, 275)

*Details are provided in Methods section. Note that the estimated potential combined impact of eliminating inequalities in stage at diagnosis by gender, deprivation and old age is not equal to the sum of the individual impacts because certain individuals may be subject to more than one inequality. No data shown for colon, rectal and ovarian cancer, because of no evidence of socio-demographic variation by gender (as applicable), deprivation or old age group (see Table 3).

advanced stage diagnosis in middle-aged patients with lung, renal and bladder cancer may be feasible.

The findings substantially amplify previous research [7, 23, 25–33]. Particular strengths of the present study are that it encompasses several common cancers; it examines old age alongside other socio-demographic inequalities; it takes into account potential confounding by tumour type, ethnicity and (for breast, colon and rectal cancer) screening detection status; it uses highly complete stage information and explores potential bias arising from missing information in sensitivity analysis; and it illustrates the population health impact of eliminating socio-demographic inequalities in stage at diagnosis. Adjustment for tumour type minimises the potential for confounding of socio-demographic differences in stage at diagnosis by socio-demographic differences in tumour morphology because of differential prior long-term exposure to risk factors.

An important limitation is that (unlike adjusting for breast and colorectal screening status), it was not possible to adjust for whether patients with prostate cancer were diagnosed with or without symptoms [e.g. because of prostate-specific antigen (PSA) testing in asymptomatic men]. There is ongoing uncertainty about the potential benefits of asymptomatic detection of prostate cancer [34]. Although the uptake of PSA testing in the UK is overall low, it is higher among older and least deprived patients [35]. Consequently, among symptomatic

patients, deprivation gradients in advanced stage of prostate cancer may be lower than those observed in our study; conversely, old age gradients may indeed be larger than those estimated by our study. Therefore, we urge caution against the potential for the prostate cancer findings to be dismissed as clinically unimportant. Melanoma, breast and prostate cancer in England have higher incidence among patients with higher socio-economic status [36], and it is likely that the observed higher frequency of advanced stage at diagnosis among more deprived patients partly reflects over-diagnosis of non-advanced stage disease among the more affluent patients.

A further limitation is the lack of availability of national data with similarly high complete information on stage for the studied cancers and period: this prevented expanding the analysis to a wider population. The relatively small number of patients for some rarer cancers may have prevented the detection of moderate or small inequalities in stage at diagnosis (e.g. this may apply to gender and deprivation differences in stage at diagnosis of bladder cancer, Table 3). Incidence patterns by age and gender between the study population and England are very similar. However, there are relative fewer patients with cancer in the most deprived group in the study population. For this reason, weights accounting for this difference were used in the estimation of the population health impact of eliminating socio-demographic inequalities in stage at diagnosis.

Among the seven cancers with substantial socio-demographic inequalities in stage at diagnosis, the size and direction of these associations varied widely. This complexity may signal a substantial potential for achieving earlier detection by targeting interventions to improve awareness and appraisal of cancer signs and symptoms on specific population groups [6, 8]. Policymakers could consider targeted approaches focusing either on a cancer or a specific population group. For example, given strong deprivation, old age and gender inequalities for this cancer, melanoma awareness interventions could particularly target more deprived old men. Among older people, interventions may specifically focus on improving awareness and appraisal of symptoms and signs of cancers associated with age inequality as a 'bundle' (e.g. 'breast and endometrial cancer' awareness interventions for older women, or 'melanoma and prostate' cancer awareness interventions for older men). National strategies can combine both cancer and population group approaches. Development and validation of new, tailored and more effective awareness interventions is likely to be required [6], given the persistence over time of some of these inequalities [21].

The absence of socio-demographic variation in stage at diagnosis of three cancers (colon, rectal and ovarian cancer) should not be interpreted as an indication that patient awareness interventions for those three cancers are not justified. Such interventions are currently being implemented for colorectal cancer [37], while evidence increasingly supports their consideration for ovarian cancer [38]. The findings need to be interpreted in relation to their temporal context (2006–2010). Evidence from breast cancer and melanoma which both benefited from long-standing awareness campaigns indicates that when such interventions are effective [39], they tend to also generate health inequalities (younger and more affluent people typically being able to benefit more so than older and less affluent people) [40]. Avoiding potential inequality that can be generated by future effective patient awareness campaigns about colorectal and ovarian cancer presents a challenge.

In conclusion, for most cancers, there are appreciable socio-demographic inequalities in stage at diagnosis, and this realisation can help motivate and support targeting of interventions on patients at higher risk.

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disclosure

The authors have declared no conflicts of interest.

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