Cancer Epidemiology 63 (2019) 101588

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Patient non-attendance at urgent referral appointments for suspected cancer and its links to cancer diagnosis and one year mortality: A cohort study of patients referred on the Two Week Wait pathway

Rebecca Sheridan[a], Steven E. Oliver[b], Geoff Hall[c], Victoria Allgar[b], Philip Melling[d], Edward Bolton[d], Karl Atkin[a], Denise Denton[e], Sarah Forbes[f], Trish Green[g], Una Macleod[g], Peter Knapp[b,*]

[a] Department of Health Sciences, University of York, United Kingdom
[b] Department of Health Sciences and the Hull York Medical School, University of York, United Kingdom
[c] Cancer Research UK Clinical Cancer Centre in Leeds, United Kingdom
[d] The Leeds Teaching Hospitals Trust NHS Trust, United Kingdom
[e] Patient and Public Involvement member, United Kingdom
[f] Associate Medical Director NHS Leeds CCG, United Kingdom
[g] Hull York Medical School, University of Hull, United Kingdom

ARTICLE INFO

Keywords:
Two week wait
Urgent referral
Cancer
Diagnosis
Early mortality
Non-attendance

ABSTRACT

Background: The 'Two Week Wait' policy aims to ensure patients with suspected cancer are seen within two weeks of referral. However, patient non-attendance can result in this target being missed. This study aimed to identify predictors of non-attendance; and analyse the relationship between attendance and outcomes including cancer diagnosis and early mortality.

Methods: A cohort study of 109,433 adults registered at 105 general practices, referred to a cancer centre within a large NHS hospital trust (April 2009 to December 2016) on the 'Two Week Wait' pathway.

Results: 5673 (5.2%) patients did not attend. Non-attendance was largely predicted by patient factors (younger and older age, male gender, greater deprivation, suspected cancer site, earlier year of referral, greater distance to the hospital) over practice factors (greater deprivation, lower Quality and Outcomes Framework score, lower cancer conversion rate, lower cancer detection rate). 10,360 (9.6%) patients were diagnosed with cancer within six months of referral (9.8% attending patients, 5.6% non-attending patients). Among these patients, 2029 (19.6%) died within 12 months of diagnosis: early mortality risk was 31.3% in non-attenders and 19.2% in attending patients.

Conclusions: Non-attendance at urgent referral appointments for suspected cancer involves a minority of patients but happens in predictable groups. Cancer diagnosis was less likely in non-attending patients but these patients had worse early mortality outcomes than attending patients. The study findings have implications for cancer services and policy.

1. Background

Short term cancer mortality rates are consistently higher in the UK than other comparable countries [1,2] in part due to rates of late stage diagnosis and emergency presentation [3–5]. The Two Week Wait (2WW) policy was introduced for all cancers in 2000 to address waiting list concerns. All NHS patients in England and Wales with suspected cancer should be seen within two weeks of general practitioner (GP) referral [2]. The policy was also expected to reduce geographical variation in referral patterns and waiting times, and reduce social inequalities in cancer diagnosis and outcomes [2]. as both later stage presentation and shorter survival times are associated with increased deprivation [3,6–8].

Earlier diagnosis of cancer is a priority in many developed countries, and in the UK [9] the relevant NICE guidance to GPs was last updated in 2015 [10]. Two Week Wait is a high volume referral pathway in England and Wales, now more than 1.9 million referrals annually [11], and an estimated 48.7% of cancers included in the policy

* Corresponding author.
E-mail address: peter.knapp@york.ac.uk (P. Knapp).

https://doi.org/10.1016/j.canep.2019.101588
Received 12 February 2019; Received in revised form 14 August 2019; Accepted 17 August 2019
Available online 11 September 2019

are identified through this route [12]. Referral results in a cancer diagnosis in 8.3% of patients [12]; i.e. for most patients referral will exclude cancer. One significant concern is patients not being seen by a specialist within two weeks of referral, and receiving hospital trusts may be penalised for breach of two-week target, classified as fewer than 93% of referred patients being seen within two weeks [13]. One common reason for breach is appointment postponement or non-attendance by the patient. This has been reported anecdotally as being problematic in several trusts but not previously researched. While cancer waiting times data indicate that the 93% standard is met nationally [11], these data do not take account of patients never seen as part of their 2WW referral.

Social and demographic patterning of patient non-attendance has been found in other health settings [14–16], with a focus on wasted resources and service costs, and has also been noted in cancer screening uptake [17–19]. In the 2WW setting, in which symptomatic patients are being referred by GPs to specialist services, concerns about non-attendance are not only about resource waste but also the potential for delayed diagnosis and treatment, and any impact on mortality. In this study there was an opportunity to analyse a data set at a large regional cancer centre in one NHS hospital Trust over seven years, to disaggregate non-attendance (including cancellation and did not attends) at urgent referral appointments for suspected cancer, to identify patient-level and practice-level predictors of non-attendance, and analyse patient outcomes including cancer diagnosis and mortality rates.

2. Method

2.1. Study setting and population

A cohort study was conducted based on routinely collected healthcare records from a single NHS hospital, The Leeds Teaching Hospitals Trust (LTHT), which provides comprehensive cancer services for a population of over 750,000 [20]. Information was derived from the LTHT electronic health record 'Patient Pathway Manager' (PPM) which integrates clinically relevant data (patient, appointment, diagnostic information, etc.) on all patients within the Trust including those referred or reviewed with a suspected cancer diagnosis [21]. The PPM database is used for generating mandatory reports for Cancer Waiting Times; for this study, data linkage to other Trust systems was also utilised to provide additional data. Over the study period healthcare in this predominantly urban area was organised at a population level across three Clinical Commissioning Groups (CCGs), jointly including 105 general practices.

In England and Wales, the 2WW pathway is operationalised via suspected cancer site, with the patient's GP determining which specialty to refer to, based on the signs and symptoms at presentation. Suspected cancer site specific referral forms are completed by the GP and received by the hospital Trust within 24 h (ideally), at which point suitable patients are accepted onto the 2WW pathway and the referral period begins. This referral period can normally be terminated in one of two ways: i) the patient is seen by the Trust or, ii) the Trust refers the patient back to the GP.

2.2. Study sample

The study sample comprised all adults currently registered with a general practice within the three Leeds CCGs, referred to LTHT between 1st April 2009 and 31st December 2016 on the 'urgent referral pathway for suspected cancer' (2WW) pathway for the following cancer sites: head and neck; upper gastrointestinal (GI); lower GI; hepato-pancreato-bilary (HPB); lung; skin; sarcoma; breast; gynaecology; urology; testicular; brain/central nervous system (CNS); thyroid; haematology. There were only small numbers of referrals for suspected haematological, brain/CNS, sarcoma and paediatric cancers; for analysis these cancer sites were combined into an 'other' category, alongside any referrals recorded by LTHT as 'other'. In the study area the pathway for the overwhelming majority of suspected lung cancer patients is via community-ordered chest X-ray and not through the 2WW pathway; it is not possible to distinguish the chest X-ray referrals in PPM. A small proportion of lung cancer referrals were recorded as 2WW, as a consequence either of referral without chest X-ray or a parallel referral and these were also categorised as 'other'. In accordance with Trust recording systems and relevant NICE guidelines [10], referrals with suspected HPB were included in upper GI and suspected thyroid cancer referrals were included with head and neck for analysis. Patients referred on the 2WW pathway are offered either an outpatient appointment or, if suitable, a straight-to-test (STT) appointment such as colonoscopy.

Patients were followed up for vital status until 5th July 2018 via PPM data extract on this date; cancer stage, where relevant and available, was identified by linkage to the National Cancer Registration and Analysis Service (NCRAS). Patients can be referred to the 2WW pathway more than once. Where multiple referrals were recorded, only the first referral period in the study window was taken as the index referral and formed the basis for analysis. Only patients with complete information on patient and general practice variables of interest were included in analysis (missing data were not imputed; see Fig. 1).

2.3. Individual and organisational variables

Patient demographics (age at index referral, sex); referral pathway characteristics (referral date, suspected cancer site, appointment type (outpatient or STT, where available), attendance date, and diagnostic outcomes (recorded referral outcome; recorded cancer diagnosis and date of diagnosis) were taken directly from PPM. We were unable to include patient ethnicity as a variable, given poor levels of recording and concerns about accuracy. An area-based measure of socio-economic deprivation (income domain of Index of Multiple Deprivation (IMD) 2015 at lower super output area, covering approximately 1500 people) [22] and straight-line distance to the hospital were derived from the patient's current recorded home postcode. In Leeds patients referred urgently for suspected cancer are seen at one of five LTHT hospitals, based on four sites throughout the city, depending on the suspected cancer site. Distance was therefore measured from the postcode centroid [23] to the hospital associated with the cancer site. Where patients could be seen at one of several hospitals (e.g. patients with suspected lower GI cancer), the hospital where the cancer centre is located and where the majority of referred patients are seen was used for analysis.

Only details of patients' current general practice were retained on hospital records and this was used to assign 'practice-level' characteristics; it was not possible to determine patients' general practice at referral or whether this had changed. The practice-level data included in the analysis were: 2015 list size [24]; 2015-16 UK Quality and Outcomes Framework (QOF) overall population achievement scores [25]; 2015-16 GP patient satisfaction survey overall domain scores [26]; average 2WW conversion rates between 2009 and 2016 (the proportion of 2WW referrals resulting in a diagnosis of cancer); and average 2WW detection rates between 2009 and 2016 (the proportion of cancer diagnoses identified via 2WW) [12]. We included both the conversion and detection rates of practices as a high conversion rate alone may not necessarily be a positive indicator; the two rates are important practice indicators when considered in tandem [27]. Practice-level deprivation was calculated using the income domain of the IMD (2015) averaging all practice-registered patients (not just the study sample).

2.4. Waiting list process and clinical outcomes

The outpatient appointment attendance date was taken from PPM along with recorded reasons for non-attendance ('cancelled by patient'; 'did not attend'; 'cancelled by the Trust', 'unknown'). In PPM 'cancelled

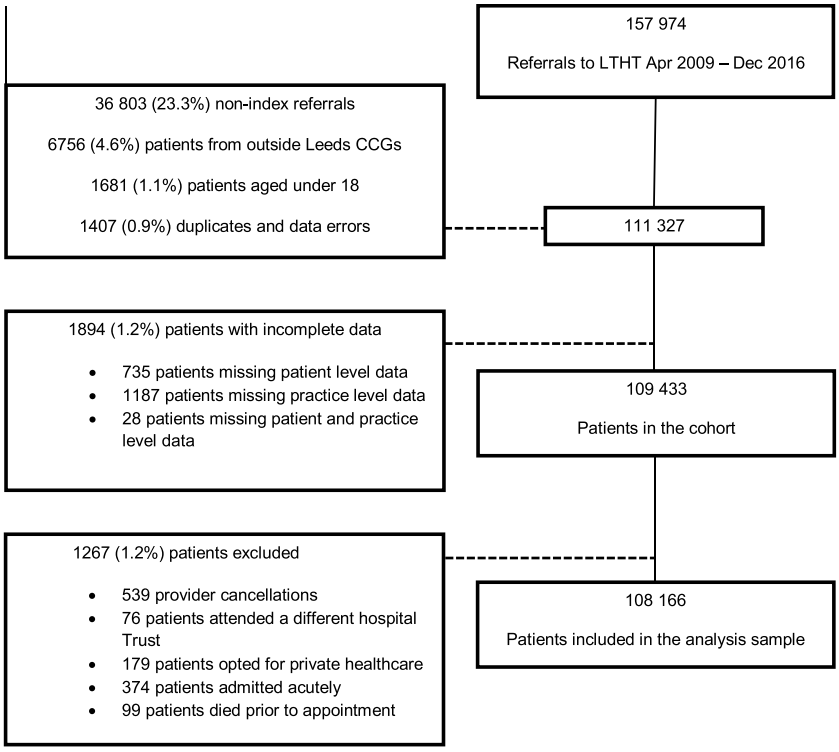

Fig. 1. Flow diagram showing identification of patients in the final sample (percent of full sample).

by patient', in combination with other data, can also be used to identify postponements; such patients will have both a 'cancelled by patient' appointment and a subsequent 'attended' appointment. In PPM patients with STT appointments can only be identified if they attended; non-attendance will generally result in the appointment type being 'unknown', however this is not exclusive to STT. When no information was available to distinguish the appointment type it was set to 'unknown'. For the 'unknown' appointment type free text was sometimes available, enabling categorisation of reasons for non-attendances (by RS, then cross-checked by SEO). For all appointment types, PPM records also identified if a patient had been admitted to hospital acutely prior to their appointment or if they had opted for a private healthcare provider.

Clinical outcomes included a classification of the 2WW referral outcome as recorded in PPM (e.g. 'on cancer pathway', 'on non-cancer pathway'). Data linkage within PPM also provided data on the first diagnosis of cancer in the six months following the conclusion of the index referral period. This allowed us to capture diagnoses which were not made at the referral (e.g. patients 'on non-cancer pathway'), but which were made within a timeframe such that the symptoms which led to referral may have been relevant to the diagnosis. For patients whose referral outcome was 'on cancer pathway', this diagnostic data would be the same as that identified via data linkage. ICD10 codes were used to identify cancer diagnoses. Diagnoses of basal cell carcinoma subsequent to 2WW referral were identified using text string searches and were not categorised as a cancer diagnosis for analysis. Data on cancer stage at diagnosis were available for only a small subset of those patients diagnosed between 2009 and 2013.

2.5. Statistical analysis

2.5.1. Clinic attendance

The primary outcome for analysis was 'non-attendance' *vs.* 'any attendance'. 'Non-attendance' included patients not seen at any appointment during their index 2WW referral period; 'attendance' included those seen at any point during this period, even if they were seen beyond the two week target. Associations between individual and 'practice-level' factors were explored using multilevel logistic regression, with patients' current practice as the higher level term. Individual characteristics included were: age at referral (18–29, 30–65, 66–84, 85+ years); sex; area-based measure of deprivation (lower super output area on basis of national quintiles: 1 = least deprived; 5 = most deprived); referral year; straight-line distance to hospital; and suspected cancer site (head and neck, lower GI, upper GI, skin, breast, gynaecological, urological, and 'other'). Practice-level factors included were: list size (study area-specific quintiles, 1 = smallest; 5 = largest); general practice deprivation (study area-specific national quintiles, 1 = least deprived; 5 = most deprived); QOF score (higher score indicating better performance); GP patient satisfaction score (proportion of patients rating the practice as 'good'); practice 2WW conversion rate (proportion of 2WW referrals resulting in cancer diagnosis) and practice 2WW detection rate (proportion of cancers diagnosed in patients at the practice via 2WW). Continuous practice level factors were normalised using z-scores prior to analysis. Whole data set analysis was conducted with subgroup analysis for suspected cancer site; referral year was added as an interaction term.

2.5.2. Diagnostic and early mortality outcomes

The diagnostic outcome was the first cancer diagnosed (excluding basal cell carcinoma) within six months of the index referral period concluding; diagnoses were included regardless of whether the cancer site matched the cancer suspected at referral. Six months was considered by clinical experts to be a reasonable threshold for cancers to be causally linked with the symptoms that triggered referral. One year overall mortality was calculated from the date of cancer diagnosis.

Associations between initial 2WW clinic attendance (attended *vs* non-attended) and diagnostic and mortality outcomes were examined using Cox's proportional hazard regression models, including individual terms for the suspected cancer site (where relevant), type of cancer diagnosed and those individual factors associated with attendance.

All variables discussed in the text and tables were included in the models simultaneously. Variable selection was consequent and

constrained on availability within a routine data source and informed by the research literature. Exact p-values are reported throughout and all analyses were carried out in SPSS (version 24).

2.5.3. Patient involvement

One patient was involved in the development of the research grant application and protocol. A Patient and Public Involvement Advisory Group (four members) met regularly throughout the study and offered advice on study plans and progress. The study results will not be disseminated to individual study participants due to the anonymised dataset.

3. Results

3.1. Characteristics of the sample

Data were extracted for 157,974 referrals to the Trust between April 2009 and December 2016; 36,803 of these were a subsequent referral and not the index referral, and so were removed from analyses. After data cleaning and the removal of non-index referral periods 109,433 patients registered at 105 general practices in Leeds were included in the final sample (Fig. 1).

The characteristics of participants and their current registered general practices are provided in Table 1. The mean age of included patients was 56.7 years (SD = 18.3) and the majority of referred patients were women (67,984, 62.1%), largely due to the high volume of referrals for suspected breast and gynaecological cancers. One quarter of referred patients lived in areas of high deprivation (27,994, 25.6%), but the proportions varied by suspected cancer site. For example, 26.8% patients (6561) referred with suspected skin cancer were in the least deprived quintile nationally. The number of referrals to LTHT increased each year over the study period. Most referrals led to outpatient appointments (77,075, 70.4%), but STT attendances were also common, particularly for suspected lower (9,447, 54.7%) and upper (7,055, 74.1%) gastrointestinal cancers. There was little patterning of referrals according to practice characteristics.

3.2. Factors associated with non-attendance

A total of 5673 (5.2%) patients did not attend their index 2WW referral (non-attended), of whom 3893 (68.6%) were scheduled to have an outpatient appointment. Outpatient non-attendance was largely due to cancellation (40.6%), did not attend (DNA) (31.4%) or a combination of the two (14.9%). An additional small proportion of patients (1,267, 1.2% of total sample) were not seen due to: provider cancellations; opting for private healthcare; being seen in another hospital Trust; admission to hospital, or dying prior to appointment. These patients were removed from all further analyses (Fig. 1).

Patients aged 18–29 and those aged over 85 years had the highest proportion of non-attendance at their index 2WW referral, 7.9% and 7.7% respectively (Table 2). Men were more likely to non-attend than women (5.8% versus 4.9%), and non-attendance was highest in the most deprived quintile (6.6%) and lowest in the least deprived quintile (4.4%). Non-attendance reduced over the study period (5.8% in 2009–2010; 4.9% in 2015–2016). Non-attendance also varied by the suspected cancer site; the highest proportions were seen in referral with suspected upper gastrointestinal cancer (8.1%) and lowest in those with suspected breast cancer (3.7%). A significant interaction was observed between referral year and suspected cancer site; non-attendance reduced over time for those referred on the following suspected cancer sites: head and neck (OR 0.95, p = 0.013, 95% CI = 0.91 to 0.99), skin (OR 0.93, p < 0.001, 95% CI = 0.89 to 0.96), gynaecological (OR 0.93, p = 0.007, 95% CI = 0.88 to 0.98), and urological (OR 0.95, p = 0.022, 95% CI = 0.90 to 0.99). Non-attendance increased with referral year for those categorised as 'other' for the suspected cancer site (OR 1.08, p = 0.021, 95% CI = 1.01–1.15). There was a small but statistically significant effect of distance to hospital on attendance; those who did not attend lived further away (mean = 8.1 km) than those who attended (mean = 7.7 km).

Regarding general practice characteristics, there was a trend for patients currently registered at general practices in the most deprived quintile to be most likely to non-attend (6.3%) compared to those in the least deprived quintile (4.7%) (Table 2). In the unadjusted model patients from general practices with higher QOF scores, higher 2WW conversion rates and higher 2WW detection rates were less likely to non-attend. These factors were largely attenuated in the adjusted model, with the exception of the association between 2WW detection rate and non-attendance.

We also examined patients classified as having breached the two-week target, either due to non-attendance or having attended after two weeks. A total of 13,446 (12.4%) patients were categorised as having breached for their index 2WW referral. Using this outcome variable rather than attendance versus non-attendance, did not modify the pattern of findings and therefore the results are not reported.

3.3. Non-attendance by suspected cancer site

The pattern of results observed in the whole dataset analysis remained when analysis was stratified by suspected cancer site; patients who did not attend their index 2WW referral were more likely in the youngest (18–29 years) or oldest (85+ years) age groups, males, living in an area of higher deprivation, and referred on the 2WW pathway earlier in the data collection period. Analyses are reported in Supplementary Table 1.

3.4. Outcomes following referral

3.4.1. Diagnosis of cancer

A total of 10,360 (9.6%) patients were diagnosed with cancer within six months of index 2WW referral (92.1% of these were diagnosed within three months). Of those 8644 (83.4%) were diagnosed with a cancer which matched the suspected cancer at referral, although this varied by cancer site: head and neck, 61.2%; upper gastrointestinal, 62.8%; lower gastrointestinal, 70.7%; skin, 92.5%; breast, 96.4%; gynaecological, 84.0%; urological, 91.9%; and 'other', 87.1%.

The rate of cancer diagnosis was higher among patients who attended their index 2WW referral (9.8%) than among non-attenders (5.6%) (Table 3). There was a small but statistically significant difference in the median time to diagnosis; 22 days (interquartile range 12–44 days) for attending patients and 34 days (interquartile range 14–70 days) for non-attending patients (p < 0.001). Other patient factors influencing the risk of cancer diagnosis included age, sex, referral year and suspected cancer site. Patients aged 85 years or older had the greatest risk of cancer diagnosis (19.5%) and those aged 18–29 years had the lowest risk (1.5%). Men were more likely to be diagnosed with cancer (13.3%) than women (7.3%), and the risk of diagnosis decreased with referral year (12.4% in 2009–2010 to 7.6% in 2015–2016). Finally, the proportion of patients diagnosed with cancer was greatest for those with 'other' suspected cancers (23.0%) and smallest for those with suspected skin cancer (5.8%). Patient deprivation did not influence risk of cancer diagnosis in the adjusted model, and only a small effect was observed in the unadjusted model.

Among the diagnosed patients who attended an appointment during their index referral period, 9100 (90.9%) of patients were placed on the 'cancer pathway' at the conclusion of the referral period, i.e. they were diagnosed at referral. The remaining 916 (9.1%) attending patients were placed on the 'non-cancer pathway' but were diagnosed within six months of referral; 309 (33.7%) of these patients had another 2WW referral prior to their diagnosis. The other 607 (66.3%) attending patients were diagnosed presumably through another route, e.g. emergency presentation. Among diagnosed patients not attending during their index 2WW referral period (n = 316), 128 (40.4%) had another

Table 1
Patient and practice characteristics of the sample by suspected cancer site.

	All suspected cancer n = 109433	Head & neck (suspected) n = 13666	Upper GI (suspected) n = 9524	Lower GI (suspected) n = 17278	Skin (suspected) n = 24493	Breast (suspected) n = 18528	Gynaecological (suspected) n = 8880	Urological (suspected) n = 11868	Other (including Lung)[a](suspected) n = 5196
Patient characteristics									
Age (mean [SD])	56.7 [18.3]	54.5 [17.4]	64.5 [14.6]	66.6 [13.4]	53.7 [20.6]	45.8 [16.3]	53.8 [15.6]	62.8 [15.9]	59.8 [18.3]
Sex (n [%])									
Male	41449 [37.9]	5947 [43.5]	4422 [46.4]	7983 [46.2]	10,413 [42.5]	987 [5.3]	–	8985 [75.7]	2712 [52.2]
Female	67984 [62.1]	7719 [56.5]	5102 [53.6]	9295 [53.8]	14,080 [57.5]	17,541 [94.7]	8880 [100]	2883 [24.3]	2484 [47.8]
Deprivation (n [%])									
Least deprived	23,916 [21.9]	2595 [19.0]	1657 [17.4]	3546 [20.5]	6561 [26.8]	3935 [21.2]	1922 [21.6]	2748 [23.2]	952 [18.3]
Second quintile	24,955 [22.8]	2814 [20.6]	2022 [21.2]	3970 [23.0]	6166 [25.2]	4084 [22.0]	2059 [23.2]	2798 [23.6]	1042 [20.1]
Third quintile	15,507 [14.2]	1901 [13.9]	1319 [13.8]	2385 [13.8]	3520 [14.4]	2682 [14.5]	1341 [15.1]	1672 [14.1]	687 [13.2]
Fourth quintile	17,061 [15.6]	2224 [16.3]	1559 [16.4]	2767 [16.0]	3582 [14.6]	2923 [15.8]	1296 [14.6]	1843 [15.5]	867 [16.7]
Most deprived	27994 [25.6]	4132 [30.2]	2967 [31.2]	4610 [26.7]	4664 [19.0]	4904 [26.5]	2262 [25.5]	2807 [23.7]	1648 [31.7]
Referral Year (n [%])									
2009-10[b]	19865 [18.2]	2361 [17.3]	1451 [15.2]	2886 [16.7]	4315 [17.6]	3998 [21.6]	1642 [18.5]	1996 [16.8]	1216 [23.4]
2011-12	25111 [23.0]	3160 [23.1]	2170 [22.8]	4082 [23.6]	5473 [22.4]	4140 [22.3]	1946 [21.9]	2683 [22.6]	1457 [28.0]
2013-14	30097 [27.5]	3781 [27.7]	2601 [27.3]	4907 [28.4]	6782 [27.7]	4846 [26.2]	2373 [26.7]	3554 [30.0]	1253 [24.1]
2015-16	34360 [31.4]	4364 [31.9]	3302 [34.7]	5403 [31.3]	7923 [32.4]	5544 [29.9]	2919 [32.9]	3635 [30.6]	1270 [24.4]
Distance home to hospital (km) mean [SD]	7.2 [12.9]	7.1 [12.4]	7.3 [11.1]	7.7 [12.6]	8.1 [15.0]	7.8 [12.6]	7.7 [10.1]	7.8 [13.2]	7.6 [14.4]
Appointment Type (n [%])									
Straight-to-test	29,325 [26.8]	0 [0.0]	7055 [74.1]	9447 [54.7]	0 [0.0]	0 [0.0]	0 [0.0]	9447 [54.7]	2810 [54.1]
Outpatient	77075 [70.4]	13,551 [99.2]	1434 [15.1]	6927 [40.1]	24,284 [99.1]	18,400 [99.3]	8787 [99.0]	6927 [40.1]	2072 [39.9]
Unknown	3033 [2.8]	115 [0.8]	1035 [10.9]	904 [5.2]	209 [0.9]	128 [0.7]	93 [1.0]	904 [5.2]	314 [6.0]
Practice characteristics									
Practice deprivation (n [%])									
First quintile - least deprived	20,926 [19.1]	2079 [15.2]	1681 [17.7]	3495 [20.2]	4928 [20.1]	3548 [19.1]	1785 [20.1]	2523 [21.3]	887 [17.1]
Second quintile	22,798 [20.8]	2682 [19.6]	1615 [17.0.]	3615 [20.9]	5751 [23.5]	3850 [20.8]	1825 [20.6]	2421 [20.4]	1039 [20.0]
Third quintile	22,068 [20.2]	2728 [20.0]	1835 [19.3]	3175 [18.4]	5317 [21.7]	3843 [20.7]	1755 [19.7]	2418 [20.4]	997 [19.2]
Fourth quintile	21,978 [20.1]	3045 [22.3]	2041 [21.4]	3290 [19.0]	4723 [19.3]	3741 [20.2]	1764 [19.8]	2233 [18.8]	1141 [22.0]
Fifth Quintile - most deprived	21,663 [19.8]	3132 [22.9]	2352 [24.7]	3703 [21.4]	3774 [15.4]	3546 [19.1]	1751 [19.8]	2273 [19.2]	1132 [21.8]
List size quintiles (n [%])									
Smallest (1515 to 6191)	21,511 [19.7]	2738 [20.0]	2006 [21.1]	3345 [19.4]	4481 [18.3]	3604 [19.5]	1741 [20.1]	2475 [20.9]	1121 [21.6]
Second (6247 to 8835)	21,914 [20.0]	2710 [19.8]	1858 [19.5]	3549 [20.5]	5092 [20.8]	3670 [19.8]	1746 [19.7]	2297 [19.4]	992 [19.1]
Third (8956 to 12,829)	21,768 [19.9]	2564 [18.8]	1927 [20.2]	3298 [19.1]	5180 [21.1]	3488 [18.8]	1823 [20.5]	2479 [20.9]	1009 [19.4]
Fourth (12,861 to 15,086)	22,915 [20.9]	2924 [21.4]	1987 [20.9]	3885 [22.5]	4668 [19.1]	3980 [21.5]	1849 [20.5]	2549 [21.5]	1073 [20.7]
Largest (15,861 to 35,319)	21,325 [19.5]	2730 [20.0]	1746 [18.3]	3201 [18.5]	5072 [20.7]	3786 [20.4]	1721 [19.2]	2068 [17.4]	1001 [19.3]
QoF[c] percentage score (mean [SD])	83.9 [3.1]	83.6 [3.4]	83.9 [2.8]	84.0 [2.7]	83.8 [3.5]	83.8 [3.0]	83.9 [2.9]	84.1 [2.8]	83.8 [3.2]
Patient satisfaction (mean [SD])	86.6 [7.9]	86.3 [7.8]	86.2 [8.0]	86.6 [7.8]	87.1 [8.1]	86.5 [7.9]	86.6 [7.7]	86.5 [8.1]	86.5 [7.7]
Conversion rate (mean [SD])	8.2 [2.0]	8.1 [2.0]	8.2 [1.9]	8.4 [1.9]	8.1 [2.1]	8.3 [2.0]	8.3 [1.9]	8.4 [1.9]	8.2 [2.0]
Detection rate (mean [SD])	43.7 [5.2]	43.5 [5.3]	43.7 [5.2]	43.6 [5.2]	43.9 [5.2]	43.6 [5.0]	43.7 [5.2]	43.8 [5.1]	43.6 [5.2]

[a] 'Other' category includes lung cancer (n = 2732), haematological cancer (n = 1171), paediatric cancers (n = 4), sarcomas (n = 369), brain/CNS cancer (n = 855) and other (n = 65).
[b] Incomplete year of data for 2009 (data included from April to December).
[c] QoF, Quality and Outcomes Framework.

Table 2
Patient and practice factors associated with patient non-attendance at index 2WW referral (n = 108,166).

Factors	Non-attended n = 5673 [5.2%]	Attended n = 102,493 [94.8%]	Unadjusted model		Adjusted model[a]	
			Odds Ratio [95% CI]	P diff	Odds Ratio [95% CI]	P diff
Patient factors						
Age Group						
18-29 years	783 [7.9]	9185 [92.1]	1.58 [1.45 to 1.72]	< 0.001	1.76 [1.61 to 1.92]	< 0.001
30-64 years	2887 [5.0]	54,787 [95.0]	(ref)		(ref)	
65-84 years	1583 [4.5]	33,417 [95.5]	0.92 [0.86 to 0.98]		0.80 [0.75 to 0.85]	
85+ years	420 [7.6]	5104 [92.4]	1.60 [1.44 to 1.78]		1.41 [1.26 to 1.57]	
Sex						
Male	2369 [5.8]	38,522 [94.2]	1.19 [1.13 to 1.26]	< 0.001	1.10 [1.03 to 1.17]	0.002
Female	3304 [4.9]	63,971 [95.1]	(ref)		(ref)	
Deprivation						
Least deprived	1047 [4.4]	22,566 [95.6]	(ref)	< 0.001	(ref)	< 0.001
Second quintile	1108 [4.5]	23,579 [95.5]	1.02 [0.93 to 1.11]		1.01 [0.92 to 1.10]	
Third quintile	752 [4.9]	14,576 [95.1]	1.12 [1.02 to 1.24]		1.10 [0.99 to 1.22]	
Fourth quintile	953 [5.7]	15,912 [94.3]	1.27 [1.15 to 1.40]		1.24 [1.12 to 1.37]	
Most deprived	1813 [6.6]	25,860 [93.4]	1.47 [1.35 to 1.61]		1.40 [1.28 to 1.54]	
Referral year						
2009-10	1141 [5.8]	18,559 [94.2]				
2011-12	1393 [5.6]	23,507 [94.4]				
2013-14	1487 [5.0]	28,221 [95.0]				
2015-16	1652 [4.9]	32,206 [95.1]				
Continuous	–	–	0.97 [0.96 to 0.98]	< 0.001	0.96 [0.95 to 0.97]	< 0.001
Distance home to hospital (km) mean [SE]	8.1 [0.2]	7.7 [0.0]	1.00 [1.00 to 1.00]	p trend 0.002	1.00 [1.00 to 1.00]	p trend 0.001
Suspected cancer site						
Head & neck	737 [5.4]	12,849 [94.6]	0.81 [0.74 to 0.90]	< 0.001	0.74 [0.67 to 0.83]	< 0.001
Upper GI	747 [8.1]	8464 [91.9]	1.27 [1.16 to 1.40]		1.25 [1.12 to 1.40]	
Lower GI	1094 [6.4]	15,935 [93.6]	(ref)		(ref)	
Skin	1309 [5.4]	23,109 [94.6]	0.83 [0.76 to 0.90]		0.72 [0.65 to 0.80]	
Breast	674 [3.7]	17,745 [96.3]	0.55 [0.50 to 0.60]		0.48 [0.42 to 0.54]	
Gynaecological	333 [3.8]	8496 [96.2]	0.57 [0.50 to 0.65]		0.54 [0.47 to 0.63]	
Urological	533 [4.5]	11,208 [95.5]	0.70 [0.62 to 0.77]		0.66 [0.58 to 0.74]	
Other (including Lung)[b]	246 [5.0]	4687 [95.0]	0.75 [0.65 to 0.87]		0.67 [0.58 to 0.79]	
Practice factors						
Practice deprivation						
Least deprived	978 [4.7]	19,586 [95.3]	(ref)	< 0.001	(ref)	0.058
Second quintile	982 [4.4]	21,435 [95.6]	0.90 [0.77 to 1.06]		0.81 [0.70 to 0.96]	
Third quintile	1107 [5.1]	20,520 [94.9]	1.03 [0.88 to 1.21]		0.83 [0.69 to 0.98]	
Fourth quintile	1266 [5.8]	20,388 [94.2]	1.19 [1.01 to 1.39]		0.91 [0.77 to 1.07]	
Most deprived	1340 [6.3]	20,001 [93.7]	1.32 [1.13 to 1.53]		0.93 [0.78 to 1.11]	
List size (quintiles)						
Smallest (1515 to 6191)	1158 [5.4]	20,098 [94.6]	(ref)	0.631	(ref)	0.868
Second (6247 to 8835)	1086 [5.0]	20,576 [95.0]	0.90 [0.78 to 1.05]		0.96 [0.83 to 1.10]	
Third (8956 to 12,829)	1088 [5.1]	20,427 [94.9]	0.95 [0.81 to 1.12]		0.97 [0.84 to 1.12]	
Fourth (12,861 to 15,086)	1280 [5.6]	21,385 [94.4]	1.03 [0.87 to 1.23]		0.99 [0.87 to 1.15]	
Largest (15,861 to 35,319)	1061 [5.0]	20,007 [95.0]	0.96 [0.79 to 1.15]		1.04 [0.87 to 1.23]	
QoF[c] percentage score (mean [SD])	83.5 [3.4]	83.9 [3.1]				
Per one SD change			0.89 [0.84 to 0.95]	p trend < 0.001	0.98 [0.92 to 1.05]	p trend 0.617
Patient satisfaction (mean [SD])	86.3 [7.8]	86.6 [7.9]				
Per one SD change			0.96 [0.90 to 1.02]	p trend 0.182	1.03 [0.97 to 1.09]	p trend 0.331
Conversion rate (proportion [SD])	8.1 [2.0]	8.2 [2.0]				

(*continued on next page*)

Table 2 (*continued*)

Factors	Non-attended n = 5673 [5.2%]	Attended n = 102,493 [94.8%]	Unadjusted model		Adjusted model[a]	
			Odds Ratio [95% CI]	P diff	Odds Ratio [95% CI]	P diff
Per one SD change			0.90 [0.84 to 0.97]	p trend 0.004	0.94 [0.88 to 1.01]	p trend 0.101
Detection rate (proportion [SD])	43.3 [5.3]	43.7 [5.2]				
Per one SD change			0.90 [0.84 to 0.96]	p trend 0.003	0.92 [0.86 to 0.99]	p trend 0.018

[a] Adjusted model : Adjusts for all patient factors (age, sex, deprivation, referral year and distance to the hospital) and practice factors (deprivation, list size, QoF percentage score, patient satisfaction, conversion rate, detection rate).

[b] 'Other' category includes lung cancer (n = 2705), haematological cancer (n = 1059), paediatric cancers (n = 4), sarcomas (n = 298), brain/CNS cancer (n = 808) and other cancers (n = 59).

[c] QoF, Quality and Outcomes Framework.

2WW referral before diagnosis.

3.4.2. Early mortality

Among patients diagnosed with cancer within 6 months of referral, 2029 (19.6%) died within 12 months of diagnosis (Table 4). The risk of dying within 12 months of diagnosis was greater for patients who did not attend their index 2WW referral (31.3%) than for those who attended (19.2%), although the rate varied by diagnosed cancer site. For example, the proportion of patients with breast cancer who died within 12 months was 14.3% for patients who did not attend their appointment and 5.0% for those who attended; this effect was somewhat attenuated in the adjusted model. Overall, there was a small difference in the median time to death; 128 days (interquartile range 54–236 days) for those who attended their index 2WW referral and 123 days (interquartile range 46–233 days) for those who did not attend (p = 0.480).

Data on cancer stage at diagnosis were available for a small proportion of patients (1,693, 16.3%). Patients who were not seen at 2WW had higher rates of advanced cancer (stage 4, 34.6%) compared to those who were seen (18.4%), as did patients who died within one year of cancer diagnosis (62.0% vs 12.2%). Stage at diagnosis also varied by cancer site; patients with upper gastrointestinal or 'other' cancers had the highest proportion of advanced cancer (46.8% and 50.9% respectively) and patients with skin cancer had the lowest proportion (3.3%).

4. Discussion

Our analysis of urgent referrals for suspected cancer showed that most patients attended and were seen by a specialist within the planned two-week target, with both number of referrals and attendance rates increasing year on year. However a minority of patients did not attend their index 2WW referral; this was more likely among the youngest and oldest patients, men, patients with certain suspected cancers, those living in more deprived areas and those living further from the hospital. Individual patient factors were more important predictors of non-attendance than factors associated with practices; only practice 2WW cancer detection rate influenced non-attendance after modelling adjustments. While non-attending patients had lower rates of cancer diagnosis, cancer outcomes were worse in non-attending patients. This effect was sustained after adjustment for other predictors of mortality, but it differed depending on the cancer type diagnosed.

The study was undertaken in a single NHS hospital Trust in Leeds, a large-sized city, including inner-city, suburban and semi-rural housing, a wide range of income levels and areas of the city with a multi-ethnic population. The context of the city and Trust, and the introduction of local initiatives to increase attendance, such as providing patients with enhanced information about 2WW referrals and highlighting the clinical concern for cancer, may reduce the generalisability to other settings. Nevertheless, the 2WW referral pathway is governed by nationwide guidelines [10] and Leeds is a typical tertiary cancer care setting. Leeds is nationally untypical in one respect: historically there has been a different referral pathway for respiratory problems in Leeds, meaning that relatively few patients with suspected lung cancer are referred on the urgent referral pathway.

Data were drawn from a single Trust but equivalent national data are not currently available and this study had access to a large, routinely collected historical dataset, augmented to enable research into cancer outcomes. Levels of missing data were low and data were well characterised, but some assumptions were needed and the origin of the data meant we had no control over data quality or completeness. For example, the way that non-attendance was recorded did not enable us to calculate separate rates or predictive analyses for patients referred for straight-to-test appointments. Furthermore, we could not explore the explanatory effects of 'ethnicity', a potentially important limitation given its known relationship in the UK with healthcare utilisation [28]. The use of routinely collected data meant that we could not assess the impact of such variables as patients' use of English, cultural

Table 3
Association of attendance and patient factors with diagnosis of cancer within six months.

	Diagnosis of cancer n = 10,360 [9.6%]	Unadjusted		Adjusted[a]	
		Hazard Ratio [95% CI]	p diff	Hazard Ratio [95% CI]	p diff
Attendance at index 2WW					
Non-attended	316 [5.6]	0.56 [0.50 to 0.62]	< 0.001	0.59 [0.53 to 0.66]	< 0.001
Attended	10,044 [9.8]	(ref)		(ref)	
Age					
18-29 years	153 [1.5]	0.24 [0.20 to 0.28]	< 0.001	0.25 [0.22 to 0.30]	< 0.001
30-65 years	3647 [6.3]	(ref)		(ref)	
65-84 years	5484 [15.7]	2.60 [2.49 to 2.71]		2.56 [2.45 to 2.67]	
85+ years	1076 [19.5]	3.35 [3.13 to 3.60]		3.60 [3.35 to 3.85]	
Sex					
Male	5452 [13.3]	1.88 [1.81 to 1.96]	< 0.001	1.62 [1.54 to 1.69]	< 0.001
Female	4908 [7.3]	(ref)		(ref)	
Deprivation					
Least deprived	2283 [9.7]	(ref)		(ref)	
Second quintile	2434 [9.9]	1.02 [0.96 to 1.08]	0.027	0.99 [0.93 to 1.05]	0.897
Third quintile	1503 [9.8]	1.01 [0.95 to 1.08]		1.01 [0.94 to 1.08]	
Fourth quintile	1620 [9.6]	0.99 [0.93 to 1.06]		1.01 [0.95 to 1.08]	
Most deprived	2520 [9.1]	0.94 [0.89 to 0.99]		0.99 [0.93 to 1.04]	
Referral Year					
2009-10	2452 [12.4]				
2011-12	2718 [10.9]				
2013-14	2601 [8.8]				
2015-16	2589 [7.6]				
Continuous		0.84 [0.82 to 0.85]	< 0.001	0.87 [0.85 to 0.88]	< 0.001
Distance home to hospital (km) mean [SE]					
Diagnosed/not diagnosed	7.7 [0.1] / 7.7 [0.0]	1.00 [1.00 to 1.00]	0.810	1.00 [0.99 to 1.00]	0.361
Suspected cancer site					
Head and Neck	963 [7.1]	0.86 [0.79 to 0.94]	< 0.001	1.84 [1.09 to 1.29]	< 0.001
Upper GI	882 [9.6]	1.19 [1.09 to 1.29]		1.29 [1.18 to 1.40]	
Lower GI	1402 [8.2]	(ref)		(ref)	
Skin	1426 [5.8]	0.71 [0.66 to 0.76]		0.94 [0.88 to 1.02]	
Breast	1533 [8.3]	1.04 [0.97 to 1.12]		2.25 [2.08 to 2.44]	
Gynaecological	636 [7.2]	0.88 [0.80 to 0.97]		1.65 [1.50 to 1.82]	
Urological	2391 [20.4]	2.70 [2.53 to 2.88]		2.62 [2.45 to 2.80]	
Other (including Lung)[b]	1127 [23.0]	3.00 [2.77 to 3.24]		3.30 [3.05 to 3.57]	

[a] Adjusted for age, sex, deprivation, referral year, distance to the hospital and suspected cancer site.
[b] 'Other' category includes lung cancer (n = 740), haematological cancer (n = 307), paediatric cancers (n = 0), sarcomas (n = 59), brain/CNS cancer (n = 18), and other cancers (n = 3).

understandings of health and disease, relationship status, co-morbidity, or continuity of GP care, all of which may influence patient reporting of symptoms and their navigation of the health system [29–32]. Ongoing developments within the PPM system mean that data such as these are becoming more accessible. The Two Week Wait policy has been subject to updated NICE guidance, which significantly increased numbers of GP referrals over the seven-year period of data collection on this study and produced changes in cancer detection and conversion rates, meaning that statistical relationships were being calculated in shifting ground and may have introduced measurement error.

The predictors of non-attendance (age, sex, area-level deprivation) were consistent with other settings; [14–16] although practice-level factors were not strongly associated with attendance in our analyses. However it is possible that relationships could be attenuated by some misclassification consequent on only current practice being identifiable in the dataset. However we have been unable to trace any published accounts of the proportion of UK patients who change their general practice registration annually, or whether patient moves tend to be towards or away from practices in more deprived areas. Other possible explanations for non-attendance specific to this setting, such as death or hospital admission in the period between GP and hospital appointments, or patients opting for private healthcare following GP appointment, affected a very small proportion. Studies investigating non-attendance for colonoscopy and colposcopy following screening have also observed age as a contributory factor, alongside procedure fear [33–35]. While not measured in this study, fear may be related to the high rates of non-attendance associated with certain suspected cancer sites, notably upper gastrointestinal. The conversion rate observed in this study (the proportion of patients diagnosed with cancer following referral) is similar to national figures [12] but does suggest systemic under-referral of patients, given that since 2015 2WW guidelines have recommended a referral threshold of 3% (5% prior to 2015), i.e. the positive predictive value for cancer [10].

Non-attendance in other clinical settings (i.e. primary care and hospital out-patient clinics) has been shown to be more common in patients living in more deprived areas, which tend to have poorer health outcomes [16] [31]. However, the relationship we observed of higher one-year mortality amongst patients diagnosed with cancer who were initially non-attenders following urgent referral is a novel finding and important. Death within 12 months of cancer diagnosis is strongly linked to advanced stage disease at diagnosis [7], and where staging data were available they confirmed that more advanced cases were present amongst initial non-attenders. There are a number of possible explanations why initial non-attendance could be related to advanced stage at diagnosis. A direct relationship between attendance behaviour and stage as a consequence of a long interval between referral and diagnosis is possible [36–38], but the delays identified were generally short (although highly variable) and seem unlikely to be sufficient to account for significant disease progression. The presence of advanced disease might contribute to initial non-attendance, as a consequence of symptomatic disease or heightened anxiety. Finally, clinic non-attendance may be acting as a marker for unmeasured patient characteristics and health behaviours that have cumulatively allowed disease progression to an advanced stage at the time of presentation. An alternate

Table 4
Patient characteristics by cancer type diagnosed within six months of referral and hazard ratio (HR) and confidence intervals (CI) predicting early mortality.

	All cancers n = 10,360	Head and neck n = 624	Upper GI n = 710	Lower GI n = 1126	Skin n = 1384	Breast n = 1562	Gynaecological n = 607	Urological n = 2456	Other (including Lung)[a] n = 1891
Age (mean [SD])	67.7 [14.4]	59.1 [13.7]	70.7 [11.0]	71.6 [11.2]	68.6 [17.7]	62.8 [16.7]	65.2 [13.3]	68.8 [12.6]	69.6 [13.0]
Sex (n [% male])									
Male/Female	5452/4908 [52.6]	367/257 [58.8]	452/258 [63.7]	651/475 [57.8]	766/618 [55.3]	14/1548 [0.9]	0/607 [0.0]	2181/275 [88.8]	1021/870 [54.0]
Deprivation (n [%])									
Least deprived	3812 [36.8]	168 [26.9]	217 [30.6]	426 [37.8]	627 [45.3]	574 [36.7]	223 [36.7]	977 [39.8]	600 [31.7]
Second quintile	2796 [27.0]	161 [25.8]	212 [29.9]	316 [28.1]	356 [25.7]	429 [27.5]	170 [28.0]	653 [26.6]	499 [26.4]
Most deprived	3752 [36.2]	295 [47.3]	281 [39.6]	384 [34.1]	401 [29.0]	559 [35.8]	214 [35.3]	826 [33.6]	792 [41.9]
Referral Year (n [%])									
2009-10	2452 [23.7]	134 [21.5]	148 [20.8]	246 [21.8]	297 [21.5]	397 [25.4]	130 [21.4]	588 [23.9]	512 [27.1]
2011-12	2718 [26.2]	156 [25.0]	215 [30.3]	265 [23.5]	342 [24.7]	394 [25.2]	165 [27.2]	627 [25.5]	554 [29.3]
2013-14	2601 [25.1]	144 [23.1]	187 [26.3]	283 [25.1]	351 [25.4]	408 [26.1]	171 [28.2]	619 [25.2]	438 [23.2]
2015-16	2589 [25.0]	190 [30.4]	160 [22.5]	332 [29.5]	394 [28.5]	363 [23.2]	141 [23.2]	622 [25.3]	387 [20.5]
Distance home to hospital (km) mean [SE]	7.7 [0.1]	7.1 [0.6]	7.1 [0.4]	7.8 [0.3]	8.5 [0.5]	7.7 [0.4]	7.4 [0.5]	7.8 [0.3]	7.6 [0.3]
Time to diagnosis (n [% diagnosed within one month])									
Within one month/After one month	6255/4105 [60.4]	329/295 [52.7]	487/223 [68.6]	448/678 [39.8]	742/642 [53.6]	1390/172 [89.0]	319/288 [52.6]	1654/802 [67.3]	886/1005 [46.9]
Attendance at index 2WW referral (n [% non-attended])									
Non-attended/attended	316/10,044 [3.1]	19/588 [3.1]	34/676 [4.8]	37/1089 [3.3]	37/1347 [2.7]	28/1534 [1.8]	19/588 [3.1]	66/2390 [2.7]	76/1815 [4.0]
Mortality (n [%])									
Attended	1930 [19.2]	93 [15.4]	402 [59.5]	208 [19.1]	81 [6.0]	76 [5.0]	64 [10.9]	235 [9.8]	771 [42.5]
Non-attended	99 [31.3]	5 [26.3]	22 [64.7]	13 [35.1]	2 [5.4]	4 [14.3]	4 [21.1]	8 [12.1]	41 [53.9]
HR [95% CI] Unadjusted	1.76 [1.44 to 2.15]	1.77 [0.72 to 4.35]	1.20 [0.78 to 1.84]	2.01 [1.15 to 3.52]	0.89 [0.22 to 3.60]	3.18 [1.16 to 8.69]	2.04 [0.74 to 5.61]	1.25 [0.62 to 2.53]	1.36 [0.99 to 1.86]
HR [95% CI] Adjusted[b]	1.76 [1.44 to 2.16]	3.14 [1.23 to 8.02]	1.34 [0.86 to 2.07]	1.81 [1.03 to 3.19]	0.90 [0.22 to 3.67]	2.69 [0.95 to 7.63]	2.43 [0.87 to 6.79]	1.17 [0.57 to 2.37]	1.38 [1.00 to 1.88]

[a] 'Other' category includes lung cancer (n = 950), haematological cancer (n = 646), paediatric cancers (n = 0), sarcomas (n = 125), brain/CNS cancer (n = 21), and other cancers (n = 149).
[b] Adjusted for age group, sex, deprivation, referral year, distance to the hospital and time to diagnosis.

explanation is that initial non-attendance is linked to factors that predispose to early disease progression and mortality regardless of initial stage, for example, non-compliance with therapy, frailty or co-morbidities. A linked qualitative study explores some of these possible explanations, and addresses the potential for improvement through changes within primary care and cancer services [39].

The study findings are important, with implications for primary care and cancer services. They show that the urgent referral process results in most patients being seen quickly by a specialist as intended, but that is not the case for more than five percent of patients. Further, there are worse health outcomes for those in the initial non-attending group who are diagnosed with cancer. A new standard to ensure all patients are informed whether they have cancer or not within 28 days is soon to be introduced [40], although it is unclear if this change will impact on patient non-attendance. The development of effective interventions both to ensure greater proportions of patients present to the GP with earlier stage disease and attend referral appointments, will depend on a clearer understanding of the phenomenon [39]. The reported association between patient deprivation and higher rates of diagnosis and early mortality is consistent with other cancer settings [6,8,41,42]. However, it is unclear the extent to which the effect reported here is mediated through increased rates of multi-morbidity, lower health literacy, or other factors. Replication, further investigation and clarification in other trust settings, and the identification of candidate interventions, are all warranted.

Supplementary information is available at the journal's website.

Ethics approval

The study was approved by the North East – Tyne and Wear South Research Ethics Committee (16/NE/0146), the Health Research Authority Confidentiality Advisory Group (16/CAG/0060), the Health Research Authority (HRA; 201,398) and the Department of Health Sciences Research Governance Committee at the University of York. The study was conducted in accordance with the Declaration of Helsinki.

Availability of data and materials

No additional data are available.

Details of contributors

PK conceived the study and led the development of the study design with specific input from SO, UM, GH and VA. Data extraction was completed by PM and EB, with guidance from RS and GH. RS analysed the data with guidance from SO, VA and PK. RS and PK drafted the manuscript with support from SO. All authors provided intellectual input to the design, conduct and/or analysis of the study, contributed to the revision of the manuscript and read and approved the final version. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. PK is the guarantor.

Funding

This work was funded by Yorkshire Cancer Research (grant Y390). The views expressed are those of the authors and not necessarily those of the funder. The funders had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

The authors wish to acknowledge The Leeds Teaching Hospitals Trust for their support in running the study. We also gratefully acknowledge the support of Ms Lisa Dyson, Ms Sandi Newby, Dr Adrian Rees and Mr Martin Waugh, as well as the 2WW study Patient and Public Involvement group (Mrs Denise Denton, Ms Alison Learwood, Mr David Lydall and Mrs Carol Miller) and the Study Steering Committee (Professor Robbie Foy, Professor Peter Bower and Dr Maureen Twiddy). We thank two anonymous reviewers for their helpful and constructive comments on a previous version of this paper.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.101588.

References

[1] M. Richards, The national awareness and early diagnosis initiative in England: assembling the evidence, Br. J. Cancer 101 (2009) S1–S4.
[2] NHS, The NHS Cancer Plan, Available at: (2000) https://www.thh.nhs.uk/documents/_Departments/Cancer/NHSCancerPlan.pdf.
[3] S. McPhail, L. Elliss-Brookes, J. Shelton, A. Ives, M. Greenslade, S. Vernon, et al., Emergency presentation of cancer and short-term mortality, Br. J. Cancer 109 (2013) 2027.
[4] L. Elliss-Brookes, S. McPhail, A. Ives, M. Greenslade, J. Shelton, S. Hiom, et al., Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets, Br. J. Cancer 107 (2012) 1220–1226.
[5] R. De Angelis, M. Sant, M.P. Coleman, S. Francisci, P. Baili, D. Pierannunzio, et al., Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5—a population-based study, Lancet Oncol. 15 (2014) 23–34.
[6] B. Rachet, L. Ellis, C. Maringe, T. Chu, U. Nur, M. Quaresma, et al., Socioeconomic inequalities in cancer survival in England after the NHS cancer plan, Br. J. Cancer 103 (2010) 446–453.
[7] S. McPhail, S. Johnson, D. Greenberg, M. Peake, B. Rous, Stage at diagnosis and early mortality from cancer in England, Br. J. Cancer 112 (2015) S108.
[8] E.D. Mitchell, B. Pickwell-Smith, U. Macleod, Risk factors for emergency presentation with lung and colorectal cancers: a systematic review, BMJ Open 5 (2015) e006965.
[9] NHS, Five Year Forward View, Available at: (2014) https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf.
[10] National Institute for Health and Care Excellence, Suspected Cancer: Recognition and Referral, Available at: (2015) https://www.nice.org.uk/guidance/ng12.
[11] NHS England, Waiting Times for Suspected and Diagnosed Cancer Patients: 2017-18 Annual Report, Available at: (2018) https://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2017/06/Cancer-Waiting-Times-Annual-Report-201617-1.pdf.
[12] Public Health England, Cancer Services: Two Week Wait Referrals, Available at: (2017) https://fingertips.phe.org.uk/profile/cancerservices/data#page/0/gid/1938133085/pat/46/par/E39000030/ati/153/are/E38000010.
[13] NHS, Delivering Cancer Waiting Times: a Good Practice Guide, Available at: (2015) https://www.england.nhs.uk/wp-content/uploads/2015/03/delivering-cancer-wait-times.pdf.
[14] D.A. Ellis, R. McQueenie, A. McConnachie, P. Wilson, A.E. Williamson, Demographic and practice factors predicting repeated non-attendance in primary care: a national retrospective cohort analysis, Lancet Public Health 2 (2017) e551–e559.
[15] A.E. Williamson, D.A. Ellis, P. Wilson, R. McQueenie, A. McConnachie, Understanding repeated non-attendance in health services: a pilot analysis of administrative data and full study protocol for a national retrospective cohort, BMJ Open 7 (2017) e014120.
[16] K. Campbell, A. Millard, G. McCartney, S. McCullough, Who Is Least Likely to Attend? An Analysis of Outpatient Appointment 'Did Not Attend'(DNA) Data in Scotland, NHS Health Scotland, 2015.
[17] J. Wardle, C. von Wagner, I. Kralj-Hans, S.P. Halloran, S.G. Smith, L.M. McGregor, et al., Effects of evidence-based strategies to reduce the socioeconomic gradient of uptake in the English NHS Bowel Cancer Screening Programme (ASCEND): four cluster-randomised controlled trials, Lancet 387 (2016) 751–759.
[18] J.Y. Bang, G. Yadegarfar, M. Soljak, A. Majeed, Primary care factors associated with cervical screening coverage in England, J. Public Health (Bangkok) 34 (2012) 532–538.
[19] R. Maheswaran, T. Pearson, H. Jordan, D. Black, Socioeconomic deprivation, travel distance, location of service, and uptake of breast cancer screening in North Derbyshire, UK, J. Epidemiol. Community Health 60 (2006) 208–212.
[20] Office for National Statistics, Population Estimates for UK, England and Wales, Scotland and Northern Ireland: mid-2016, Available at: (2017) https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland.

[21] A.C. Newsham, C. Johnston, G. Hall, M.G. Leahy, A.B. Smith, A. Vikram, et al., Development of an advanced database for clinical trials integrated with an electronic patient record system, Comput. Biol. Med. 41 (2011) 575–586.
[22] Department for Communities and Local Government, English Indices of Deprivation, Available at: (2015) http://imd-by-postcode.opendatacommunities.org/.
[23] R. Haynes, A.P. Jones, V. Sauerzapf, H. Zhao, Validation of travel times to hospital estimated by GIS, Int. J. Health Geogr. 51 (2006) 40.
[24] NHS Digital, Numbers of Patients Registered at a GP Practice (practice Level, 5 Year Age Groups), Available at: (2015) https://data.gov.uk/dataset/numbers_of_patients_registered_at_a_gp_practice.
[25] NHS Digital, Quality and Outcomes Framework (QOF) - 2015-16, Available at: (2016) https://digital.nhs.uk/catalogue/PUB22266.
[26] Ipsos MORI, Technical Annex for the GP Patient Survey. 2015-2016 Annual Report, Available at: (2016) https://www.gp-patient.co.uk/SurveysAndReportsV2.
[27] D. Meechan, C. Gildea, L. Hollingworth, M.A. Richards, D. Riley, G. Rubin, Variation in use of the 2-week referral pathway for suspected cancer: a cross-sectional analysis, Br. J. Gen. Pract. 62 (2012) e590–e597.
[28] S. Karlsen, M. Roth, L. Becares, Understanding the influence of ethnicity on health, in: S. Chattoo, K. Atkin, G. Craig, R. Flynn (Eds.), Understanding'Race'and Ethnicity: Theory, History, Policy, Practice, Policy Press, Bristol, 2018, p. 324.
[29] R.W. Batterham, M. Hawkins, P.A. Collins, R. Buchbinder, R.H. Osborne, Health literacy: applying current concepts to improve health services and reduce health inequalities, Public Health 132 (2016) 3–12.
[30] C.L. Bennett, M.R. Ferreira, T.C. Davis, J. Kaplan, M. Weinberger, T. Kuzel, et al., Relation between literacy, race, and stage of presentation among low-income patients with prostate cancer, J. Clin. Oncol. 16 (1998) 3101–3104.
[31] S.T. Lindau, C. Tomori, T. Lyons, L. Langseth, C.L. Bennett, P. Garcia, The association of health literacy with cervical cancer prevention knowledge and health behaviors in a multiethnic cohort of women, Am. J. Obstet. Gynecol. 186 (2002) 938–943.
[32] U. Macleod, E.D. Mitchell, C. Burgess, S. Macdonald, A.J. Ramirez, Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers, Br. J. Cancer 101 (Suppl 2) (2009) S92–s101.
[33] L. Sharp, S. Cotton, A. Thornton, N. Gray, M. Cruickshank, D. Whynes, et al., Who defaults from colposcopy? A multi-centre, population-based, prospective cohort study of predictors of non-attendance for follow-up among women with low-grade abnormal cervical cytology, Eur. J. Obstet. Gynecol. Reprod. Biol. 165 (2012) 318–325.
[34] A.A. Plumb, A. Ghanouni, S. Rainbow, N. Djedovic, S. Marshall, J. Stein, et al., Patient factors associated with non-attendance at colonoscopy after a positive screening faecal occult blood test, J. Med. Screen. 24 (2017) 12–19.
[35] E. Douglas, J. Wardle, N. Massat, J. Waller, Colposcopy attendance and deprivation: a retrospective analysis of 27 193 women in the NHS Cervical Screening Programme, Br. J. Cancer 113 (2015) 119–122.
[36] M.L. Tørring, M. Frydenberg, R.P. Hansen, F. Olesen, P. Vedsted, Evidence of increasing mortality with longer diagnostic intervals for five common cancers: a cohort study in primary care, Eur. J. Cancer 49 (2013) 2187–2198.
[37] R. Neal, P. Tharmanathan, B. France, N. Din, S. Cotton, J. Fallon-Ferguson, et al., Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review, Br. J. Cancer 112 (2015) S92–S107.
[38] M.L. Tørring, P. Murchie, W. Hamilton, P. Vedsted, M. Esteva, M. Lautrup, et al., Evidence of advanced stage colorectal cancer with longer diagnostic intervals: a pooled analysis of seven primary care cohorts comprising 11 720 patients in five countries, Br. J. Cancer 117 (2017) 888.
[39] L. Jefferson, K. Atkin, R. Sheridan, S.E. Oliver, U. Macleod, G. Hall, et al., Understanding non-attendance at urgent referral appointments for suspected cancer: a qualitative study of patients and medical General Practitioners, *Br. J. Gen. Pract.* (in press).
[40] NHS England, Diagnosing Cancer Earlier and Faster, Available at: www.england.nhsuk/cancer/early-diagnosis, 2018.
[41] L.X. Clegg, M.E. Reichman, B.A. Miller, B.F. Hankey, G.K. Singh, Y.D. Lin, et al., Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: national Longitudinal Mortality Study, Cancer Causes Control 20 (2009) 417–435.
[42] M. Quinn, P. Babb, A. Brock, L. Kirby, J. Jones, Cancer Trends in England and Wales, 1950-1999, Health Statistics Quarterly, 2000, pp. 5–19.