Variation in promptness of presentation among 10,297 patients subsequently diagnosed with one of 18 cancers: Evidence from a National Audit of Cancer Diagnosis in Primary Care

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Cancer awareness public campaigns aim to shorten the interval between symptom onset and presentation to a doctor (the 'patient interval'). Appreciating variation in promptness of presentation can help to better target awareness campaigns. We explored variation in patient intervals recorded in consultations with general practitioners among 10,297 English patients subsequently diagnosed with one of 18 cancers (bladder, brain, breast, colorectal, endometrial, leukaemia, lung, lymphoma, melanoma, multiple myeloma, oesophageal, oro-pharyngeal, ovarian, pancreatic, prostate, renal, stomach, and unknown primary) using data from of the National Audit of Cancer Diagnosis in Primary Care (2009–2010). Proportions of patients with 'prompt'/non-prompt' presentation (0–14 or 15+ days from symptom onset, respectively) were described and respective odds ratios were calculated by multivariable logistic regression. The overall median recorded patient interval was 10 days (IQR 0–38). Of all patients, 56% presented promptly. Prompt presentation was more frequent among older or housebound patients (p < 0.001). Prompt presentation was most frequent for bladder and renal cancer (74% and 70%, respectively); and least frequent for oro-pharyngeal and oesophageal cancer (34% and 39%, respectively, p <.001). Using lung cancer as reference, the adjusted odds ratios of non-prompt presentation were 2.26 (95% confidence interval 1.57–3.25) and 0.42 (0.34–0.52) for oro-pharyngeal and bladder cancer, respectively. Sensitivity analyses produced similar findings. Routinely recorded patient interval data reveal considerable variation in the promptness of presentation. These findings can help to prioritise public awareness initiatives and research focusing on symptoms of cancers associated with greater risk of non-prompt presentation, such as oro-pharyngeal and oesophageal cancer.

Key words: cancer, patient interval, promptness, presentation, delay, oro-pharyngeal, oesophageal, bladder, renal, variation.

Diagnosing cancer promptly in symptomatic patients is a key aspect of contemporary cancer control policies in different countries.1–5 After symptom onset, delays in establishing the diagnosis may occur both before a patient presents to a doctor and post-presentation.6 In most cancer patients, initial symptoms have low specificity, as they are also associated with benign diseases.7 Appropriate appraisal and interpretation of symptoms that may be related to cancer by both patients (pre-presentation) and their doctor (post-presentation) are critical for timely diagnosis.6,8 There is large variation between different patient groups in the promptness with which general practitioners suspect the diagnosis of cancer and refer patients to specialists (i.e. in the 'primary care interval').9,10 It is also plausible that there is variation in the promptness with which cancer patients seek medical help (i.e. in the 'patient interval', defined as the period between first symptom onset and first relevant presentation to a doctor9). Variation in the patient interval may exist both between patients with different socio-demographic characteristics (since cancer awareness, beliefs and attitudes vary between socio-demographic groups or...
country populations; and between patients with different cancers (given wide variability in the nature of symptoms of different tumours). Understanding variation in the patient interval can help to identify patient groups at higher risk of different tumours. Understanding variation in the patient interval can help to identify patient groups at higher risk of non-prompt presentation, enabling better targeting of public health awareness interventions.

Evidence about patient interval variation is however limited, partly because accurate measurement is known to be challenging. Determining the date of onset of symptoms or bodily changes (the start of the patient interval) is difficult, given the potential for inaccurate or biased patient recall, and the gradual onset of many symptoms. The date of first presentation to a doctor with symptoms caused by cancer (the end of the patient interval) is often easy to identify, but there can be difficulties in determining the first relevant consultation in patients with multi-morbidity. Acknowledging these difficulties, broadly, patient interval information can be obtained either from the patients themselves (through interviews or questionnaire surveys) or from their medical consultation records. Either approach has advantages and disadvantages (Box). Although elicitation of symptom duration typically forms a key part of medical consultations, medical records studies assume accurate elicitation and recording of this information. On the other hand, patient interview or questionnaire studies can provide detailed information but may lack representativeness (as, by their nature, cancer patients who die early or are too sick soon after diagnosis are typically not included in such studies).

Appreciating both the strengths and the limitations of patient interval studies that are based on information from medical records, we conducted a secondary analysis of data from the National Audit of Cancer Diagnosis in Primary Care, 2009–2010. Our aim was to explore variation in the routinely recorded (i.e., during general practice consultations) patient interval of patients subsequently diagnosed with cancer. We were particularly interested in exploring likely variation by socio-demographic characteristic and cancer diagnosis.

### Material and Methods

#### Data

We analysed data from the (English) National Audit of Cancer Diagnosis in Primary Care (2009–2010). Information from patient records on different aspects of the diagnostic process was collected by general practitioners or other primary care professionals in an estimated total of 1,170 general practices (~14% of all practices in England). Audited patients were incident cases of cancer within the audit period and were representative of the age and diagnosis case-mix of English cancer patients. Although participation to the audit was voluntary, the organisational characteristics and care quality of participating and non-participating practices were similar. Screening-detected cases were excluded from the audit. The patient interval was defined as the number of days from first symptom onset to first presentation to a general practitioner with relevant symptoms based on information in the patients' records. Patients were categorised as housebound if primary care encounters usually occurred at home – we included information on housebound status in the analysis as a marker of severe co-morbidity, because of theoretical concerns that patients with higher levels of co-morbidity may be disadvantaged in respect of the timeliness of cancer diagnosis. The analysis was a priori restricted to patients who first presented to a general practitioner with any of 18 cancers for which there was data available.

### Box. Principal advantages and limitations of the two main approaches to measuring the patient interval

| Strengths | Limitations |
|-----------|-------------|
| Patient interview (or questionnaire) studies | Potentially highly accurate and detailed Can allow for detailed (‘in-depth’) appreciation of relevant symptoms and their time of onset. | Limited representativeness (generalisability) Patients dying soon after symptom onset/diagnosis and those ‘too ill to take part’ are unlikely to be included. |
| Studies of medical consultation records | High representativeness (generalisability) Information about all cancer patients can be included, even for those with poor prognosis/only short-term survival. | Potential limitations in completeness and accuracy Rely on doctors appropriately eliciting the timing of symptom onset as part of history taking and accurately interpreting and recording this information. Patient interval information may be missing. |
which variation in respect of the primary care interval was previously explored and were aged 15 or older.²⁵,²⁶ Analysis was restricted to records with patient interval values of up to two years, and complete information on outcome and exposure variables of interest (Fig. 1).

**Analysis**

We aimed to profile variation in promptness of presentation to a general practitioner after symptom onset. There is no uniform approach to analysing patient interval data, which tend to be zero-inflated and right-skewed. Therefore, we first described the key patient interval statistics (median and other relevant centile values) by patient group. Subsequently, we analysed variation in respect of a binary form of the patient interval (0–14 vs 15 or more days – hereafter, we use the terms prompt/non-prompt to denote either category, respectively). Our choice of binary cut-off was pragmatic – choosing a short-term period during which it could be reasonably assumed that most patients who did decide to see their doctor would have been able to do so. Additional short-term binary cut-off values were explored in sensitivity analysis (see below).

In univariable analysis, we examined crude differences between different patient groups in respect of the median patient interval, the proportion of non-prompt presenters and respective crude odds ratios. Subsequently, multivariable logistic regression was used to explore independent associations between patient characteristics or cancer diagnosis and prompt/non-prompt presentation. Further, interactions between cancer diagnosis and age and cancer diagnosis and gender were explored. Robust estimation of standard errors was used to account for potential clustering of observations.

**Sensitivity analysis**

We first repeated the multivariable regression model using alternative binary categories of the patient interval (0–7 vs 8+, 0–21 vs 22+ and 0–30 vs 31+ days, respectively). Complete case analysis pre-supposes that missing information is Missing Completely At Random which is a strong assumption. We, therefore, used extreme-case scenario analysis (assuming data are Missing Not At Random) by repeating the multivariable analysis assuming patients with missing interval values were either ‘all non-prompt’ or ‘all prompt’ presenters – these analyses do not intend to represent a real situation but are useful to illustrate the largest possible bias that could be introduced by missing patient interval information. We used further sensitivity analyses to explore potential confounding by ethnic group among patients with known ethnicity and the impact of only including patients with interval values of up to a year. Analysis was undertaken using Stata 11 (Stata Corporation, Texas).

**Results**

Of an initial 14,320 patients with one of the 18 cancers examined, 10,297 (72%) were included in complete case analysis (Fig. 1). The main single source of sample attrition was missing patient interval (3,004 or 21% of initially eligible patients). Patients with missing patient interval were more likely to be older and men ($p < 0.001$ for both) without evidence for an association with housebound status ($p = 0.342$). Missing patient interval also varied by cancer ($p < 0.001$), being most common among patients with leukaemia, prostate cancer, melanoma and multiple myeloma (41%, 40%, 36% and 28%, respectively, Supporting Information Appendix 1). Hereafter, results related to complete case analysis except were otherwise noted. Characteristics of included patients are shown in Table 1.

The overall median patient interval was 10 days (interquartile range 0–38 days); about half of all patients (5,789, or 56%) had an interval of up to 14 days, i.e. were prompt presenters by our definition (Table 1). There was substantial variation in promptness of presentation by age, housebound status and cancer diagnosis ($p < 0.001$ for all). Prompt presentation was more frequent among older patients; and those who were housebound (66% vs 56% among those non-housebound). These differences were also apparent when examining various centiles of the patient interval which tended to be shorter for older and housebound patients (Table 1). Prompt presentation was most frequent...
Table 1. Sample characteristics and descriptive statistics for patient interval by patient characteristic and cancer (n = 10,297)

| Age      | N   | 25th Centile | Median | 75th Centile | 90th Centile | 95th Centile | p-Value<sup>1</sup> | N   | %   | N   | %   | p-Value<sup>2</sup> |
|----------|-----|--------------|--------|--------------|--------------|--------------|----------------|-----|-----|-----|-----|-----------------|
| 15–44    | 784 | 1            | 13     | 42           | 120          | 242          | p < 0.0001 | 439 | 56.0 | 345 | 44.0 | p < 0.0001 |
| 45–54    | 1,220 | 1        | 14     | 45           | 108          | 187          |               | 669 | 53.2 | 571 | 46.8 |
| 55–64    | 2,170 | 0        | 12     | 41           | 102          | 191          |               | 1,186 | 54.7 | 984 | 45.3 |
| 65–74    | 2,807 | 0        | 11     | 43           | 112          | 185          |               | 1,526 | 54.4 | 1,281 | 45.6 |
| 75–84    | 2,459 | 0        | 7      | 31           | 92           | 183          |               | 1,463 | 59.5 | 996 | 40.5 |
| 85+      | 857  | 0        | 7      | 31           | 95           | 188          |               | 526 | 61.4 | 331 | 38.6 |

| Sex      | N   | 25th Centile | Median | 75th Centile | 90th Centile | 95th Centile | p-Value<sup>1</sup> | N   | %   | N   | %   | p-Value<sup>2</sup> |
|----------|-----|--------------|--------|--------------|--------------|--------------|----------------|-----|-----|-----|-----|-----------------|
| Male     | 5,028 | 0        | 11     | 43           | 116          | 200          | p = 0.37 | 2,742 | 54.5 | 2,286 | 45.5 | p = 0.0008 |
| Female   | 5,269 | 0        | 10     | 33           | 92           | 182          |               | 3,047 | 57.8 | 2,222 | 42.2 |

| Cancer   | N   | 25th Centile | Median | 75th Centile | 90th Centile | 95th Centile | p-Value<sup>1</sup> | N   | %   | N   | %   | p-Value<sup>2</sup> |
|----------|-----|--------------|--------|--------------|--------------|--------------|----------------|-----|-----|-----|-----|-----------------|
| Bladder  | 601  | 0            | 2      | 16           | 67           | 141          | p < 0.0001 | 446 | 74.2 | 155 | 25.8 | p < 0.0001 |
| Renal    | 209  | 0            | 3      | 19           | 74           | 184          |               | 146 | 69.9 | 63  | 30.1 |
| Brain    | 125  | 1            | 7      | 26           | 96           | 154          |               | 81  | 64.8 | 44 | 35.2 |
| Breast   | 2,124 | 1        | 7      | 27           | 77           | 164          |               | 1,371 | 64.5 | 753 | 35.5 |
| Unknown primary | 110 | 0        | 7      | 23           | 64.5         | 104          |               | 69 | 62.7 | 41 | 37.3 |

| Cancer   | N   | 25th Centile | Median | 75th Centile | 90th Centile | 95th Centile | p-Value<sup>1</sup> | N   | %   | N   | %   | p-Value<sup>2</sup> |
|----------|-----|--------------|--------|--------------|--------------|--------------|----------------|-----|-----|-----|-----|-----------------|
| Leukaemia| 239  | 0            | 7      | 30           | 86           | 140          |               | 144 | 60.3 | 95 | 39.7 |
| Prostate | 1,386 | 0        | 6      | 42           | 151          | 283          |               | 813 | 58.7 | 573 | 41.3 |
| Pancreatic | 272 | 1          | 9.5    | 31           | 73           | 97           |               | 162 | 59.6 | 110 | 40.4 |
| Stomach  | 187  | 0            | 9      | 33           | 125          | 205          |               | 104 | 55.6 | 83 | 44.4 |
| Lung     | 1,126 | 0        | 12     | 33           | 87           | 138          |               | 622 | 55.2 | 504 | 44.8 |
| Myeloma  | 127  | 0            | 14     | 40           | 95           | 193          |               | 69  | 54.3 | 58 | 45.7 |
| Endometrial | 311 | 1          | 14     | 57           | 152          | 259          |               | 165 | 53.1 | 146 | 46.9 |
| Ovarian  | 270  | 2            | 14     | 51           | 113.5        | 172          |               | 144 | 53.3 | 126 | 46.7 |
| Lymphoma | 482  | 1            | 14     | 43           | 92           | 183          |               | 243 | 50.4 | 239 | 49.6 |
| Melanoma | 477  | 0            | 20     | 69           | 241          | 366          |               | 216 | 45.3 | 261 | 54.7 |
| Colorectal | 1,697 | 1       | 19     | 60           | 131          | 203          |               | 786 | 46.3 | 911 | 53.7 |
| Oesophageal | 407 | 7          | 22     | 46           | 99           | 152          |               | 158 | 38.8 | 249 | 61.2 |
| Oro-pharyngeal | 147 | 7        | 30     | 62           | 122          | 212          |               | 50  | 34.0 | 97 | 66.0 |

Housebound status

| N   | 25th Centile | Median | 75th Centile | 90th Centile | 95th Centile | p-Value<sup>1</sup> | N   | %   | N   | %   | p-Value<sup>2</sup> |
|-----|--------------|--------|--------------|--------------|--------------|----------------|-----|-----|-----|-----|-----------------|
| No  | 9,707        | 0      | 11           | 39           | 103          | 188          | p < 0.0001 | 5,399 | 55.6 | 4,308 | 44.4 | p < 0.0001 |
| Yes | 590          | 0      | 5            | 28           | 91           | 200          |               | 390 | 66.1 | 200 | 33.9 |
| Total | 10,297     | 0      | 10           | 38           | 103          | 189          |               | 5,789 | 56.2 | 4,508 | 43.8 |

<sup>1</sup>Kruskal–Wallis test.
<sup>2</sup>Chi-squared test.

among patients with bladder and renal cancer (74% and 70%, respectively). Conversely, oro-pharyngeal and oesophageal cancer had the lowest proportions of prompt presenters (34% and 39%, respectively).

Table 2 and Figures 2 and 3 describe odds ratios of non-prompt presentation derived by both univariable and multivariable logistic regression. Except for gender for which there was no evidence of variation in the multivariable analysis (p = 0.17), these analyses produced similar findings, indicating only a limited degree of confounding between exposure variables. The largest degree of variation (>5-fold) in the odds of prompt presentation is seen between patients with different
cancers. Specifically, using patients with lung cancer as the reference group, the odds ratios of non-prompt presentation were 2.26 (95% confidence interval 1.57–3.25) and 0.42 (0.34–0.52) for patients with oro-pharyngeal and bladder cancer, respectively. There was no evidence of interaction between cancer diagnosis and either age or sex (p > 0.29 for both).

Sensitivity analysis
Using different binary categories of patient interval produced similar findings (Supporting Information Appendix 2). Assuming patients with missing data were either ‘all non-prompt’ or ‘all prompt’ presenters did either attenuate or accentuate patterns of variation observed in the main analysis, respectively, particularly by age and the four cancers with relatively high proportions of missing interval data (leukaemia, prostate, melanoma and myeloma) (Supporting Information Appendix 3). The degree of confounding by ethnicity was very limited (Supporting Information Appendix 4). Only including patients with interval values of up to a year produced highly concordant findings (results not shown).

Discussion
In this study, among patients with any of the 18 cancers prompt presentation was most frequent among those with

Table 2. Proportion of patients with non-prompt presentation and respective unadjusted and adjusted odds ratios (n = 10,297)

| Age             | % Non-prompt (15+ days) presentation | Unadjusted odds ratios for non-prompt (15+ days) presentation | Adjusted odds ratios for non-prompt presentation (15+ days) by patient characteristic and cancer diagnosis |
|-----------------|-------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| 15–44 (N = 784) | 44.0                                 | 0.94 (0.80–1.10)                                            | p = 0.0001                                                                                       |
| 45–54 (N = 1,220)| 46.8                                 | 1.05 (0.92–1.20)                                            | 1.12 (0.98–1.30)                                                                                 |
| 55–64 (N = 2,170)| 45.3                                 | 0.99 (0.88–1.11)                                            | 0.98 (0.87–1.10)                                                                                 |
| 65–74 (N = 2,807)| 45.6                                 | Baseline                                                   | Baseline                                                                                         |
| 75–84 (N = 2,459)| 40.5                                 | 0.81 (0.73–0.90)                                            | 0.83 (0.74–0.93)                                                                                 |
| 85+ (N = 857)   | 38.6                                 | 0.75 (0.64–0.88)                                            | 0.83 (0.70–0.98)                                                                                 |

| Gender          | % Non-prompt (15+ days) presentation | Unadjusted odds ratios for non-prompt (15+ days) presentation | Adjusted odds ratios for non-prompt presentation (15+ days) by patient characteristic and cancer diagnosis |
|-----------------|-------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Male (N = 5,028)| 45.5                                 | Baseline                                                   | p = 0.0008                                                                                       |
| Female (N = 5,269)| 42.2                                 | 0.87 (0.81–0.95)                                            | 0.93 (0.84–1.03)                                                                                 |

| Cancer type     | % Non-prompt (15+ days) presentation | Unadjusted odds ratios for non-prompt (15+ days) presentation | Adjusted odds ratios for non-prompt presentation (15+ days) by patient characteristic and cancer diagnosis |
|-----------------|-------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Bladder (N = 601)| 25.8                                 | 0.43 (0.35–0.53)                                            | p = 0.0001                                                                                       |
| Renal (N = 209)  | 30.1                                 | 0.53 (0.39–0.73)                                            | 0.51 (0.37–0.71)                                                                                 |
| Brain (N = 125)  | 35.2                                 | 0.67 (0.46–0.99)                                            | 0.66 (0.45–0.98)                                                                                 |
| Breast (N = 2,124)| 35.5                                 | 0.68 (0.58–0.79)                                            | 0.67 (0.57–0.78)                                                                                 |
| Unknown primary (N = 110) | 37.3                                 | 0.73 (0.49–1.10)                                            | 0.75 (0.50–1.12)                                                                                 |
| Leukaemia (N = 239)| 39.7                                 | 0.81 (0.61–1.08)                                            | 0.78 (0.58–1.03)                                                                                 |
| Prostate (N = 1,386)| 41.3                                 | 0.87 (0.74–1.02)                                            | 0.83 (0.70–0.98)                                                                                 |
| Pancreatic (N = 272)| 40.4                                 | 0.84 (0.64–1.10)                                            | 0.85 (0.65–1.11)                                                                                 |
| Stomach (N = 187) | 44.4                                 | 0.98 (0.72–1.34)                                            | 0.99 (0.73–1.35)                                                                                 |
| Lung (N = 1,126)  | 44.8                                 | Baseline                                                   | Baseline                                                                                         |
| Myeloma (N = 127) | 45.7                                 | 1.04 (0.72–1.50)                                            | 1.01 (0.70–1.47)                                                                                 |
| Endometrial (N = 311)| 46.9                                 | 1.09 (0.85–1.40)                                            | 1.08 (0.84–1.40)                                                                                 |
| Ovarian (N = 270) | 46.7                                 | 1.08 (0.83–1.41)                                            | 1.09 (0.83–1.43)                                                                                 |
| Lymphoma (N = 482)| 49.6                                 | 1.21 (0.98–1.50)                                            | 1.15 (0.93·1.43)                                                                                 |
| Melanoma (N = 477)| 54.7                                 | 1.49 (1.20–1.85)                                            | 1.41 (1.13–1.75)                                                                                 |
| Colorectal (N = 1,697)| 53.7                                 | 1.43 (1.23–1.66)                                            | 1.43 (1.23–1.67)                                                                                 |
| Oesophageal (N = 407)| 61.2                                 | 1.94 (1.54–2.45)                                            | 1.94 (1.54–2.45)                                                                                 |
| Oropharyngeal (N = 147)| 66.0                                 | 2.39 (1.67–3.43)                                            | 2.26 (1.57–3.25)                                                                                 |

| Housebound      | % Non-prompt (15+ days) presentation | Unadjusted odds ratios for non-prompt (15+ days) presentation | Adjusted odds ratios for non-prompt presentation (15+ days) by patient characteristic and cancer diagnosis |
|-----------------|-------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| No (N = 9,707)  | 44.4                                 | Baseline                                                   | p = 0.0001                                                                                       |
| Yes (N = 590)   | 33.9                                 | 0.64 (0.54–0.77)                                            | 0.67 (0.56–0.81)                                                                                 |

1This column repeats information presented in Table 1, for ease of reference regarding crude proportions.
bladder and renal cancer, and least frequent among patients
with oro-pharyngeal and oesophageal cancer. Prompt presen-
tation was also more frequent in older and housebound
patients.

Of the 18 cancers included in our study, 12 were also
examined previously by an audit (medical record) study of
Scottish patients23; and 10 by a similar Danish study. 24
Among Scottish cancer patients, those with ‘head and neck’
(including oro-pharyngeal) cancer presented least promptly,
whilst those with bladder and ‘other urological’ (including
renal) cancers did so most promptly. 23 In general, median
reported patient interval values for Scottish patients were
similar to those reported here; however, those reported for
Danish patients were longer – potentially reflecting differen-
ties in patient populations or in methods of data recording
and collection (Supporting Information Appendix 5).23,24
However, the Spearman rank correlation coefficient for pair-
wise comparisons of median patient interval values by cancer
is 0.87 (p = 0.0002) and 0.59 (p = 0.071) between the pres-
tent and the Scottish or the Danish study, respectively – indi-
cating an overall high degree of rank concordance. 23,24
Similarly, most Finnish patients with pharyngeal cancer have
patient intervals longer than a month.28

Prior evidence is inconsistent regarding the presence and
direction of associations between age and patient interval for
different cancers.22,28–32 We are unaware of previous descrip-
tions of variation in patient interval by housebound status.
Housebound patients may be more prone to seeking help
promptly, or are monitored more frequently and, therefore,
assessed more promptly. Disability may confer paradoxical
benefits in respect of stage at diagnosis of cancer.33

One of the strengths of our study is that it included
patients with many different cancers. The representativeness
of the patient population and of participating practices was
good.25,27 Because of continuous sampling, the study popula-
tion can be assumed to be a relatively unbiased sample of
incident cases first presenting to general practitioners, also
including patients with poor prognosis. The robustness of the
findings was explored by a range of sensitivity analyses,
which generally provided similar findings. Although patient
interval data were missing for between a fifth and a quarter
of patients, sensitivity analyses using extreme-case assump-
tions indicated that this factor might have biased the findings
regarding patients with four cancers with a relatively high
proportion of missing data (leukaemia, prostate cancer, mel-
oma and myeloma); in contrast, patterns of variation for
patients with all other cancers, and particularly for those
with bladder, renal, oesophageal and oro-pharyngeal cancer,
remained similar. Two of the cancers with higher than aver-
age proportion of missing patient interval data were prostate
cancer and leukaemia. For those cancers, diagnostic suspicion
is sometimes first raised at an asymptomatic stage or inciden-
tally, based on the findings of relatively simple-to-perform
blood tests (such as Prostate Specific Antigen testing or Full
Blood Count). In such circumstances, the diagnosis is not
symptom-driven and, therefore, measurement of the patient
interval is a priori not applicable. These factors may explain
the higher proportion of missing interval information for
those cancers.

There are several limitations. The validity of patient inter-
val data is contingent on several factors: patients need to
have been able to accurately appreciate the onset of their
symptoms and recall relevant dates; their doctors need to
have been able to elicit and appropriately interpret informa-
tion about the patient interval during consultations, and to
have accurately entered it in the patient records. Although
elicitation of information on symptom duration is a key
aspect of a medical consultation, inaccuracies and omissions
may occur in any of the above steps. However, previous
research indicates that inaccurate patient recall of diagnostic
intervals is unlikely to be systematic (e.g. biased towards
either over- or under-estimation of patient interval).34 It is
also unreasonable to assume that recall inaccuracies will be grossly differential between patients with different cancers – for example, between patients with bladder and oro-pharyngeal cancer, given the large size of the observed variation between these cancers (~5-fold difference in odds ratios). Although we believe this assertion to be reasonable, there is no direct evidence for it, and future evidence from relevant clinical psychology studies would be useful. It is important to also consider that non-systematic errors of this kind would result in under-estimation of true variation; therefore, our reported estimates of socio-demographic or cancer diagnosis differences may be conservative. We were not able to examine variation in the patient interval of patients with cancer whose first presentation did not involve previous contact with their general practitioner. Some patients have long or very long patient intervals, e.g. 90 or 180 days (Table 1) and the predictors of very long patient intervals may be different to the predictors of delay in respect of shorter intervals. We plan to explore variation in the patient interval amongst these patients in the future. Our findings relate to a population of English cancer patients, and extrapolations to other populations should therefore be cautious. Although at least some of the observed findings may be relevant, research questions about variation in the patient interval in other country populations are best addressed by new empirical evidence.

Promptness of presentation is a concept also applicable to a larger group of patients who experience symptoms but do not necessarily have cancer (or any other formal diagnosis). For example, even among patients with ‘alarm’ symptoms mandating specialist referral for investigation of suspected cancer, only one in nine are found to have cancer, whereas eight in nine patients with relevant symptoms will have another diagnosis.35 Therefore, future research should also explore variation in the timeliness of presentation among the broader population of patients with symptoms likely to be related to cancer, and not only among cancer cases. Although clearly important, exploring variation in patient interval among patients with symptoms (not simply among cancer patients) was impossible given our data.14

Measuring patient interval is challenging as it cannot be ‘objectively’ measured.6,18,36 Additional difficulties arise in the context of co-morbidity. Both patient interviews/surveys and medical record studies have strengths and limitations (Box). Patient interview/questionnaire studies can be subject to survivorship bias (differential attrition) as those who die early do not contribute information and their intervals may be different to those of survivors. In contrast, studies based on medical records information can provide for relatively large samples (including patients with rarer cancers) whilst limiting the potential for survivorship bias (as continuous sampling of all incident cases is possible). Ideally studies should encompass both approaches, and also measure patient intervals of patients with relevant symptoms who do not necessarily have cancer, as in the DISCOVERY programme’s SYMPTOM study, due to report 2014 (http://discovery-programme.org/symptom_study.php).

Variation in the promptness of presentation by cancer is likely to reflect differences in how patients appreciate and appraise typical symptoms of different cancers. Symptoms with abrupt and unexplained onset such as bleeding are associated with shorter patient intervals.22,29–31 As patients with bladder and renal cancer often present with haematuria, this may explain why patients with these two cancers seem to present more promptly than patients with any other examined cancer.23 Other factors, such as symptom frequency, duration and intensity may also matter. Familiarity with signs and symptoms in the context of previous self-limiting illness (e.g. oral ulcerations) has been judged responsible for non-prompt presentation of patients with oro-pharyngeal cancer.37,38

Whilst there is very strong evidence of variation in prompt presentation between patients with different cancers we cannot reliably distinguish between all individual cancers, particularly for cancers in the middle of the spectrum. We suggest that interpretation considers the general pattern of variation, particularly focusing on comparisons of the extremes (e.g. oro-pharyngeal or oesophageal vs bladder or renal cancer). We specifically draw attention to oro-pharyngeal and oesophageal cancer – the two cancers with the highest proportions of non-prompt presenters and longest median patient intervals. Oro-pharyngeal cancer has relatively poor 5-year relative survival (typically <50% for most sub-sites except lip). Together with our own findings, these considerations can support the development of awareness campaigns for oro-pharyngeal cancer.39 Oesophageal cancer also has poor prognosis (5-year relative survival <20%). Although dysphagia is a common cardinal symptom of oesophageal cancer (and one with relatively high specificity40, the findings indicate that patients with oesophageal cancer do not present promptly. These findings concord with prior evidence indicating that awareness of ‘difficulty swallowing’ as a potential sign of cancer is particularly poor among members of the British public (lowest compared with other eight cancer symptoms).11 Specifically, only about 1 in 20 respondents would immediately recall dysphagia as a symptom of cancer – in contrast lump/swelling (the symptom with the highest spontaneous recall) would be recalled by two thirds of respondents.11 These findings would therefore support the development of awareness campaigns about the importance of dysphagia. The clinical and population health outcomes of awareness campaigns nevertheless need to be evaluated, ideally using controlled designs.51

As the aim of public awareness interventions is to decrease patient intervals,17 we strongly advocate the conduct of regular surveys of patient interval in representative samples of cancer patients to help monitor the impact of such interventions and progress towards improving the timeliness of presentation in the population. Appreciating variation in promptness of presentation can help to better target and
tailor such interventions. Given the findings, prioritising public awareness interventions for symptoms of oro-pharyngeal and oesophageal cancer is particularly justified.

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Contributors
The study was initiated by SK and GL in the context of SK’s MPhil in Public Health studies (University of Cambridge) supervised by GL. Material and Methods were further developed and modified in discussions with GAA and all other authors. CLS and SK performed most analyses. GPR and SMcP led different aspects of the National Audit project and data collation. RDN and FMW commented on the methods and findings alongside all other authors. All authors commented on final drafts and saw and approved the final draft of the paper.

Ethical Approval
Not required. An integral part of the National Audit of Cancer Diagnosis in Primary Care project was that anonymous data may subsequently be used for purposes of early diagnosis research, and access to these data was granted by the Audit oversight group.

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