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## **Abstract**

### **Background**

Diagnosis of cancer as an emergency is associated with poor outcomes but has a complex aetiology. Examining determinants and time trends in diagnostic routes can help to appreciate the critical and evolving role of general practice in diagnostic pathways for cancer patients.

### **Aim**

To examine socio-demographic, cancer site, and temporal associations with type of presentation among cancer patients diagnosed as emergencies.

### **Design and setting**

Analysis of Routes to Diagnosis data 2006-2015 for patients with cancer in England.

### **Method**

We estimated adjusted proportions of emergency presentation after emergency GP referral (GP-EP) or presentation to Accident & Emergency (AE-EP), by patient characteristic, cancer site, and year of diagnosis, using multivariable regression.

### **Results**

Among 554,621 emergency presenters, 24% presented as GP-EP and 62% as AE-EP (14% through Other-EP sub-routes). Emergency presenters were more likely to have been GP-referred if they lived in less deprived areas or were subsequently diagnosed with pancreatic, gallbladder or ovarian cancer, or acute leukaemia. During the study period the proportion and number of GP-EPs nearly halved (31%/17,364 in 2006; 17%/9,155 in 2015) whilst that of AE-EP increased (55%/31,049 to 68%/36,868).

### **Conclusion**

Emergency presenters with cancers characterised by symptoms/signs tolerable by patients but appropriately alarming to doctors (e.g. pancreatic cancer manifesting as painless jaundice) are over-represented among cases involving GP referral. Reductions in diagnoses of cancer through an emergency presentation likely reflect both the continually increasing use of two-week-wait GP referrals during the study period and reductions in emergency GP referrals.

**Keywords:** Early Diagnosis, Patients, Referral and Consultation, Emergencies, Population Groups

## **How this fits in**

Primary care has a crucial, though often misrepresented, role in the diagnosis of cancer in symptomatic patients. There have been welcome declines in the proportion of cancers diagnosed as emergencies but reasons are not well understood. We observed declining numbers of emergency presentations of a specific type, i.e. those generated after a GP has referred a patient to hospital as an emergency. Reductions in the number of emergency presentations likely reflect continually increasing two-week-wait GP referrals during the study period and reductions in presentations following an emergency GP referral.

## Introduction

Around one in five patients with cancer are diagnosed as emergencies, which are associated with worse clinical and patient experience outcomes compared with other diagnostic routes; these poorer outcomes are partially explained by later stage at diagnosis and disease-related complications.(1-5) Welcome reductions in the proportion of cancer patients who are diagnosed as emergencies have been reported,(6) but there is uncertainty about the responsible mechanisms involving tumour, patient and healthcare system factors, and how to achieve further reductions.(7, 8)

Diagnostic processes leading to emergency presentations can involve general practice in two different ways. First, about two-thirds of all patients with cancer who are diagnosed as emergencies would have had prior GP consultations with relevant symptoms, often leading to investigations or referrals.(9, 10) Second, GPs can be involved in the emergency presentation care episode itself. In England about a third of all emergency presentations involve an emergency referral to hospital by a GP.(1) In this paper we focus on the latter aspect of general practice involvement in emergency presentations.

In England, the frequency of emergency presentations (denoting diagnosis of cancer following an emergency hospital admission or outpatient appointment) is routinely monitored through the 'Routes to Diagnosis' programme of the National Cancer Registration and Analysis Service (NCRAS) of Public Health England.(2, 11) Emergency presentations comprise different pathways (hereafter termed 'sub-routes'), chiefly either emergency General Practitioner referral (GP-EP) or presentation to the Accident and Emergency department (AE-EP).(12, 13) As these two sub-routes reflect different patterns of healthcare utilisation before a cancer diagnosis, understanding associated factors can elucidate different mechanisms and pathways, particularly regarding the role of general practice.(9, 10, 14) Some of these pathways will represent appropriate care, e.g. an emergency GP referral following presentation with symptoms or signs highly suggestive of cancer in an unwell patient, but others may reflect patient factors, e.g. relatively late help-seeking, or healthcare factors, e.g. use of A&E departments due to difficulties in accessing primary care.(8)

We aimed to characterise socio-demographic, cancer site, and temporal associations with emergency presentation sub-route among cancer patients diagnosed as emergencies. Our objective was to examine patient groups that are either over- or under-represented in emergency presentations directly involving a GP emergency referral to hospital, and establish related temporal trends and their likely contribution to overall changes in how cancer patients are being diagnosed.

## Methods

### *Diagnostic routes data*

We studied Routes to Diagnosis data for 2006-15 on patients aged 25 years and over diagnosed with any of 35 common and rarer cancers, responsible for 95% of incident cases (Appendix 1). The 'diagnostic route' of each registered tumour is assigned by NCRAS using a rules-based (algorithmic) approach, that incorporates information from linked Hospital Episode Statistics, Cancer Waiting Times, and NHS Cancer Screening Programme data.(2) We focused on patients diagnosed with cancer through an emergency presentation, defined in Routes to Diagnosis data as diagnosis of cancer during/after an emergency hospital admission (including via GP, A&E, or bed bureau) or Accident & Emergency department attendance (including through direct presentation or after GP referral). The principal outcome of interest was emergency presentation sub-route, denoting different patterns of healthcare utilisation preceding the emergency cancer diagnosis. These included GP-EP (diagnosis during/after a hospital admission resulting from an emergency GP referral), AE-EP (diagnosis during/after a hospital admission following presentation to A&E) and Other-EP (diagnosis during a hospital admission not during/after an emergency GP referral, or presentation to A&E/dental casualty followed by hospital admission; e.g. diagnosis during admission via bed bureau).

### *Other variable data*

Exposure variables included sex, age (grouped as 25-49, 50-59, 60-69, 70-79 and 80+ years), deprivation (five categories from least to most deprived, using quintile cut-offs for England of Index of Multiple Deprivation [income domain] scores based on residential postcode), cancer (35 different sites as defined by ICD-10 codes shown in Appendix 1), and year of diagnosis.

### *Statistical analyses*

Our analysis had two objectives. First, to describe associations between exposure variables and each emergency presentation sub-route. We reported the number and proportions (both crude and adjusted) of emergency presenters (n=554,621) diagnosed via AE-EP, GP-EP and Other-EP by sex, age group, deprivation, cancer site, and year of diagnosis. Adjusted proportions were predicted from a multivariable multinomial logistic regression model where the outcome was AE-EP and Other-EP (baseline category: GP-EP) and including all of the exposure variables as independent variables (reference categories: male, 70-79 years old, least deprived, colon cancer, 2006).

Second, to describe temporal trends in each emergency presentation sub-route, also taking into account time-trends across all other diagnostic routes.(1, 6) We presented the numbers of all incident cases of the studied cancers (i.e. diagnosed through any route, including non-emergency presentation) over time, partitioned into adjusted numbers of each of the emergency presentation sub-routes and all other routes (using the same modelling technique as described above). These numbers were predicted from a second multinomial logistic regression model (this time including all cancer cases, as opposed to emergency presenters alone, n=2,619,067), where the outcome was AE-EP, Other-EP, Two Week Wait (TWW) referral, non-emergency GP referral, screening, and 'Other' (baseline category: GP-EP) and including the same independent variables as in the first multinomial logistic regression model.

## Results

Among the 554,621 emergency presenters during 2006-2015, 62% (n=346,192) had presented through AE-EP, 24% (n=130,372) through GP-EP (Table 1), and 14% through the Other-EP sub-route (Appendix 2).

### *Associations between socio-demographic characteristics and sub-route*

There was limited variation in emergency presentation sub-route by sex (Table 1; Appendix 2). Older emergency presenters were more likely to be diagnosed both via GP-EP and via AE-EP compared to younger patients, reflecting that younger emergency presenters were more likely to be diagnosed via the Other-EP sub-route (80+ vs 25-49: 11% vs 21%). The likelihood of GP-EP decreased with increasing levels of deprivation (e.g. adjusted proportions for least vs. most deprived: 25% vs. 19%), while in contrast, that of AE-EP increased (60% vs 67%). There was little variation in the likelihood of Other-EP by levels of deprivation (15% vs 14%). Confidence intervals and p-values for related model estimates are presented in Appendix 3.

### *Associations between cancer site and sub-route*

Emergency presenters with pancreatic, acute myeloid and acute lymphoblastic leukaemia, ovarian, and gallbladder cancers were most likely to be diagnosed via the GP-EP sub-route (adjusted proportions of GP-EP  $\geq 27\%$ ) (Table 1). In contrast, those diagnosed with oral, oropharyngeal, laryngeal, thyroid, melanoma, brain, and uterine cancers (adjusted proportions of GP-EP  $\leq 17.5\%$ ) were least likely to be diagnosed via the GP-EP sub-route (Table 1). Notably, most cancer sites with low proportions of GP-EP (i.e. oral, oropharyngeal, thyroid, melanoma, brain, and uterine cancers) had relatively high proportions of Other EP (Appendix 2).

### *Time trends*

The number of incident cases for the studied cancers increased each year (e.g. from 237,799 in 2006 to 284,660 in 2015, an increase of 20%), while the number of emergency presentations each year decreased slightly (from 56,104 to 54,102, a decrease of 4%; Table 1). Consequently, there was a progressive reduction in the number of cancers diagnosed as emergency presentations, and an expansion in the number of cancers diagnosed as non-emergency presentations, particularly via TWW referrals (Figure 1, left). Confidence intervals and p-values for related model estimates are presented in Appendix 4.

The changing proportion of emergency presentations overall was accompanied by a changing composition of EP sub-routes (Figure 1, right). GP-EP was less common among emergency presenters in more recent years of diagnosis (adjusted proportions down from 31% to 17% between 2006 and 2015), while the opposite was true for AE-EP (up from 56% to 68%; Table 1). The proportions of emergency presentation diagnosed through Other-EP slightly increased during this time (from 13% to 15%) (Appendix 2). Relatedly, against a slight overall decrease in the absolute numbers of emergency presentations of any type between 2006 and 2015 (Table 1), the absolute numbers of GP-EPs almost halved (17,364 to 9,155) and that of AE-EPs slightly increased (31,049 to 36,868).

## Discussion

### *Summary*

Over a recent decade, and against an overall continuous decrease in the percentage of patients diagnosed with cancer through an emergency presentation (from 24% in 2006 to 20% in 2015), the likelihood of emergency presentation via GP referral decreased, coupled with an increased likelihood of emergency presentation via A&E, even after accounting for socio-demographic and cancer site case-mix over time. Among emergency presenters, patients living in areas of greater deprivation were less likely to be diagnosed via the GP-EP sub-route, and more likely to be diagnosed via the AE-EP subroute. There was large heterogeneity in sub-route profile by cancer site.

### *Strengths and limitations*

We used a large population-based dataset covering a 10-year period and presented adjusted proportions of emergency presentation sub-routes by each patient characteristic, cancer site, and year of diagnosis, respectively. All variables included in this study come from high-quality cancer registration data. Diagnostic route, used to capture emergency presentation status and sub-route type, is derived via an algorithmic approach using linked routine population-based datasets.(2)

As common in observational studies, other variables (not available for inclusion in the analysis) could at least partially account for some of the reported socio-demographic, cancer site, and temporal variation in emergency presentation sub-routes. It could be revealing to examine the potential interplay between stage at diagnosis and emergency presentation, as advanced stage is associated with greater likelihood of emergency presentation,(3) but we could not address this question within the current study due to poor completeness of stage at diagnosis information during most of the study years 2006-2015.(15-17)

A limitation inherent to all research using routine data is that it does not allow for exact circumstances to be taken into account. For example, an emergency presenter may have attended A&E following verbal GP advice without a formal referral. This hypothetical patient would have likely been assigned an AE-EP sub-route (whilst GP-EP sub-route may have been more apt), which would introduce misclassification error. The magnitude of such a misclassification is difficult to quantify but is likely to be small.(9, 10)

### *Comparison with existing literature*

There are no other population-based studies of emergency presentation sub-routes for cancer cases in England covering both common and rarer cancers with which to compare our results.(8) Nonetheless, our study builds on previous reports of crude proportions of emergency presentation sub-route by age and cancer site,(12, 13) by presenting proportions adjusted for patient case-mix (age, sex, deprivation and cancer site). A previous study focusing on patients with lung cancer found that GP-EP sub-route was least likely in more deprived emergency presenters (and vice versa for AE-EP), concordant with our study, which covers a wider range of cancer sites.(18)

### *Implications for research and practice*

The findings overall indicate that certain cancers that can be associated with painless symptoms that may be tolerable to the patient but where GPs may appropriately request an urgent specialist assessment (e.g. pancreatic or gallbladder cancer presenting with painless jaundice; acute leukaemia

presenting with pallor; ovarian cancer presenting with abdominal distension) were associated with the highest likelihoods of GP-EP in this study. These findings underline the importance of tumour factors as a contributor to emergency presentations in some patients. As these symptoms have relatively high predictive values for cancer,(19) they can lead to appropriately accelerated assessment through 'same- or next-day' clinics, thus explaining the increased likelihood of diagnosis via GP-EPs that nevertheless represent good GP care. Some cancers had particularly high proportions of 'Other-EP', including oral, oropharyngeal, thyroid, melanoma and brain cancer. This likely denotes either the involvement of other clinical specialties (e.g. dental practitioners in the case of oral/oropharyngeal cancers) or greater than average involvement of hospital department clinics in the diagnosis of certain cancers. Younger emergency presenters were also more likely to be diagnosed through Other-EPs than older emergency presenters. As suspecting the diagnosis of cancer in younger patients is typically harder than in older patients, they may be more likely to be initially referred to specialist clinics, and escalated as emergency presentations through these clinics.(20, 21)

As more deprived emergency presenters were less likely to have been referred from their GP and more likely to have presented to A&E, help-seeking patterns among otherwise similar patients subsequently diagnosed with the same cancer seem to vary by socioeconomic status.

Against an overall decreasing proportion of cancer patients who are diagnosed through emergency presentations, the number of patients diagnosed through the GP-EP sub-route is decreasing, whilst that of patients diagnosed through AE-EP and non-emergency routes is increasing. This decreasing trend in emergency presentations overall has occurred in spite of other evidence for opposite (i.e. increasing) trends in both general A&E attendance and emergency hospital admissions.(22-27) Therefore, the overall trend cannot be accounted for by such general A&E/admission trends, and likely reflects a reciprocal rise in the use by GPs of two-week-wait referrals for suspected cancer in the same period (Figure 1).(28) Among emergency presenters, reductions in the GP-EP sub-route could reflect increasing difficulties in accessing in-hours primary care among patients with possible cancer symptoms,(26, 29, 30); and the progressive shrinkage (through the overall increase in two-week-wait referrals) of the pool of patients who would have otherwise been diagnosed with cancer as an emergency presentation.



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**Ethical approval**

Data used in this study was collected by the National Cancer Registration and Analysis Service under regulation 2 of the Health Service (Control of Patient Information) Regulation 2002.

**Competing interests**

None declared.

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**Figure 1. Adjusted numbers of cancer patients diagnosed via emergency presentation sub-route or any other diagnostic route (left)\*; adjusted proportions of emergency presentation type among emergency presenters, over time (right)\*\***

AE-EP = Emergency presentation through -presentation to Accident & Emergency; EP = Emergency presentation; GP-EP = Emergency presentation through a GP referral; GP ref = non-emergency GP referral; Other-EP = Emergency presentation through routes other than through the GP or Accident & Emergency (e.g. through referral during an inpatient admission); TWW = Two Week Wait referral

\*Estimated using a multivariable multinomial logistic regression, for AE-EP, GP-EP (reference outcome), Other-EP, TWW, non-emergency GP referral, Screening, and 'Other', fitted to all patients diagnosed with cancer (including non-EP) in 2006-15 (n=2,619,067), where independent variables were sex, age group, deprivation group, cancer, and year of diagnosis. Predicted numbers of AE-EPs, GP-EPs, Other-EPs, and non-EPs were derived by multiplying predicted proportions of these outcomes by the number of observed cancer cases (including non-EP), per year.

\*\*Estimated using a multivariable multinomial logistic regression, for AE-EP, GP-EP (reference outcome), and Other-EP, fitted to all patients diagnosed through EP in 2006-15 (n=554,621), where independent variables were sex, age group, deprivation group, cancer, and year of diagnosis.

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