Time intervals and previous primary care consultations in the pathway to emergency cancer diagnosis

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Declarations of interests: none

Word counts:

Abstract 267
Total manuscript 3477
Highlights 64

Abstract

Background

Time intervals and number of prior consultations in primary care (PC) are recognised metrics of diagnostic timeliness of cancer and are interrelated. However, whether and how the two measures correlate with each other in the emergency diagnostic pathway is unknown. We investigated the association between the number of prereferral consultations and the length of intervals from PC presentation to cancer diagnosis following emergency referral to hospital.

Methods

Patients were eligible if they first consulted in PC and were diagnosed with cancer following emergency or nonemergency referral to hospital. We analysed for differences in PC and diagnostic intervals and number of consultations between emergency and nonemergency presenters and determined their associations by cancer type. Differences in presenting symptoms and stage at diagnosis between populations and according to number of consultations were also examined.

Results

There were 796 emergency and 865 nonemergency presenters with comparable sociodemographic and comorbidity data. Correlation analysis in emergency presenters revealed a strong positive association between number of consultations and intervals for seven of 13 different cancers, including cancers characterised by high proportions of ≥3 consultations and long intervals (pancreatic, lung, and colorectal cancer) and vice versa for others (e.g., endometrial, cervical, or oesophageal cancer). Additionally, emergency presenters with ≥3 consultations were more likely than those with 1-2 to report nonspecific symptoms (60 vs. 40%, respectively) and to be diagnosed at a later stage.

Conclusion

System level interventions are needed to reduce unnecessary delays in the emergency diagnostic pathway, particularly in cancer patients with multiple prereferral consultations. The findings also suggest opportunities to reduce the proportion of emergency diagnoses by targeting symptomatic individuals pre-presentation.

Keywords

Emergency cancer diagnosis; Emergency presentation; Time intervals; Prereferral consultations; Primary care

1. Introduction

Excluding incidentally and screen-detected cases, cancer is typically diagnosed following patient presentation to primary care (PC) with related symptoms [1]. More frequently, patients consult with a PC physician who refers them for hospital appointment, while others are referred to the emergency department (ED) and are diagnosed during emergency hospital admission (i.e., emergency presentation) or as outpatients [2]. Some patients diagnosed as an emergency do not seek medical help for their symptoms in PC but self-refer directly to the ED [3]. Given the incidence and adverse outcomes, diagnosis of cancer as an emergency is considered a serious health problem and reducing its frequency represents a priority for healthcare systems [3]. A recent study carried out in patients with eight cancer sites from six high-income countries showed that approximately 30% of them were diagnosed through an emergency presentation, which was associated with a considerably higher risk of 12-month mortality compared with diagnosis through nonemergency presentation [4].

The involvement of PC physicians in the lead up to an emergency presentation is unclear [5]. Data from the UK indicate that PC physicians are involved (via emergency referral) in about one-third of emergency presentations [2,6], whereas another third of patients have sought medical help for their symptoms in PC but were not referred as an emergency at the first opportunity [7,8]. A vignette-based survey administered to nearly 2800 PC physicians in 11 jurisdictions from six countries with similar PC-led health services demonstrated a correlation between readiness of PC physicians to investigate symptoms or refer patients for suspected cancer at the first consultation and cancer survival rates [9].

Time intervals from first-noticing symptoms to diagnosis and number of PC consultations before hospital referral are recognised metrics of diagnostic timeliness of cancer [10,11]. The number of prereferral consultations is strongly associated with the PC interval (i.e., from first PC presentation to hospital referral) and is used as a surrogate marker of this interval [12]. While the number of consultations is also used as a measure of quality of patient experience [11,13], prolonged intervals to diagnosis impact not only experience of care but also stage at diagnosis and survival [14–17].

As markers of diagnostic timeliness, intervals and prereferral consultations have been mostly investigated in patients diagnosed with cancer through nonemergency referral pathways such as fast-track patient pathways for suspected cancer [18–20]. Although we recently reported new interval definitions for the emergency diagnostic pathway [21], evidence about the association between the two measures is currently lacking. Because cancer diagnosis through emergency presentation is associated with more advanced stage and greater mortality than nonemergency diagnosis [4], clarifying whether and how intervals and prereferral consultations correlate with each other constitutes a relevant research question. The strength and direction of the association could help define targeted interventions to improve diagnostic timeliness and, eventually, cancer outcomes.

This study aims to address this evidential gap by analysing the association between number of prereferral consultations and time intervals in the pathway from PC presentation to cancer diagnosis following emergency referral to hospital.

2. Material and methods

2.1. Design, setting, and data sources

This was a retrospective observational study conducted at the Hospital Clinic of Barcelona, a large academic centre (760 adult beds) providing tertiary and quaternary care for 540,000 people. Patients with potential cancer symptoms are assessed at a specialised diagnostic centre at an ambulatory daycare facility following referral by emergency or PC physicians. Referrals to and appointments at the diagnostic centre must comply with prearranged evaluation criteria [22].

Data from eligible patients were obtained from e-health records of the hospital and PC centres. For each patient included in the study, information was prospectively collected in an anonymised database.

2.2. Population

Patients aged 18 years or older diagnosed with cancer between October 2021 and December 2022 following PC presentation were eligible. Cancer types included lung, colorectal, pancreatic, gastric, oesophageal, ovarian, liver, renal/bladder, breast, endometrial, head/neck (comprising oropharyngeal, laryngeal, and salivary gland tumors), prostate, and cervical cancer. Inclusion in the study required availability of all variables. Patients referred from or through other sources or pathways were excluded. Exclusion criteria also applied to patients not fulfilling evaluation criteria and cancers without histopathological confirmation.

2.3. Outcomes of interest

First, the sample of cancer patients was broken down into emergency presenters and nonemergency presenters. Emergency presenters were patients who presented to PC with symptoms and were referred at some time to ED. Patients who were diagnosed as emergencies without first accessing PC were not eligible. Upon ED attendance, emergency presenters were evaluated by emergency physicians and received any medical care before being appointed at the diagnostic centre. Nonemergency presenters were those who presented to PC and were referred at some point for an appointment at the diagnostic centre.

We then examined the number of prereferral consultations and the intervals (in days) from first PC presentation to cancer diagnosis. The number of consultations was categorised individually and as one or two and three or more. The PC interval went from presentation in PC to referral to emergency assessment (for emergency presenters) or referral to the diagnostic centre (for nonemergency presenters); the hospital interval, from referral to diagnosis; and the diagnostic interval, from PC presentation to diagnosis. Interval definitions relied on Aarhus statement recommendations and guidance from the Spanish Strategy on Cancer of the National Health System was observed [23,24].

Cancer stage at diagnosis was categorised according to the TNM Classification of Malignant Tumours (I-II, III, and IV or metastatic cancer) [25]. Sociodemographic variables included gender, age at diagnosis with 10-year age groups, ethnicity (white/other ethnic groups), and socioeconomic deprivation index (according to Catalan Health Surveillance System: five categories). Clinical variables included smoking habit (never/former/current), alcohol consumption (none/low/excessive), comorbidity (according to Charlson index score: 0, 1, 2, and $\geq$3) [26], and suspected symptoms. Information on presenting symptoms was retrieved from e-health records and referral forms submitted by emergency and PC physicians. Symptoms were also elicited before diagnosis during physician/patient encounters at the diagnostic centre. Symptoms were categorised according to their predictive value for cancer [27], as follows: bleeding (rectal bleeding, haematemesis, haemoptysis, metrorrhagia), abdominal symptoms (abdominal/rectal/anal mass, dysphagia, jaundice, ascites, abdominal pain, bowel habit change, nausea/vomiting), respiratory symptoms (dyspnoea, cough, hoarseness), pain (bone, chest, back pain), urological symptoms (haematuria, dysuria), lumps (breast lumps, peripheral lymphadenopathy), iron-deficiency anaemia, nonspecific symptoms (unintentional weight loss, fatigue, appetite loss, fever, night sweats, pruritus), and suspected abnormalities on imagining investigations.

2.4. Statistical analysis

Datasets were compared with the two-sample *t*-test or the nonparametric Wilcoxon rank-sum test for continuous variables (reported as means [SD] or medians [first and third interquartile range [IQR]], respectively) and χ^2 tests or the Fisher's exact test for categorical variables (reported as frequencies and proportions).

Intervals were analysed overall and for each cancer type. Given the skewed data distribution, intervals are reported as medians (50th) with 25th, 75th, and 90th centiles. Differences in the length of intervals were examined with the Kruskal-Wallis nonparametric analysis of variance test and the Wilcoxon rank-sum test. The effect size between groups was calculated with the Hodges-Lehmann nonparametric statistic and the difference between pseudomedians (with 95% confidence intervals [95% CI]) is reported [28,29].

The strength and direction of the association between intervals and number of prereferral consultations was assessed with the nonparametric rank-based correlation coefficients Spearman r_S and Kendall τ. This was done for all cancers and for each cancer type. Analyses were performed with OriginPro 2022 software (OriginLab, Northampton, MA, USA) and statistical significance was set at a *P*-value (two-sided) <0.05. Figures were generated with GraphPad Prism v9.3.0 (GraphPad Software, San Diego, CA, USA).

3. Results

Among 1783 potentially eligible patients, after applying the exclusion criteria of the study, a total of 1661 were included for final analysis, comprising 796 emergency presenters and 865 nonemergency presenters (see Fig. 1).

3.1. Cancer types and number of prereferral consultations

Lung, colorectal, and pancreatic cancer were the most common cancer diagnoses in emergency and nonemergency presenters. While the overall proportion of cancers in the two groups was not significantly different (P=0.07 on χ^2 test), emergency presenters were more likely than nonemergency presenters to be diagnosed with liver cancer (7.2 vs. 4.7%, respectively; P=0.038 on Fisher's exact test) and nonemergency presenters were more likely to be diagnosed with head/neck cancer (8 vs. 5%, respectively; P=0.017) (Table 1).

The number of prereferral consultations in emergency and nonemergency presenters was virtually the same (2 [IQR 1–3] [range 1–12] vs. 2 [1–3] [range 1–9], respectively). Of all emergency presenters, 41.3% reported three or more consultations and 10.8% five or more. Emergency presenters with gastric, pancreatic, and lung cancer had the highest proportions of three or more consultations, whereas those with breast, endometrial, and cervical cancer had the lowest. Although the overall number of nonemergency presenters with three or more consultations (31.3%) was significantly lower than that of emergency presenters (P<0.0001), differences by cancer type were not significant (Table 1).

Table 1. Cancer diagnoses in emergency and nonemergency presenters and distribution according to number of prereferral consultations.

Cancer diagnosis	Emergency presenters					Nonemergency presenters				
	All	One or two		Three or more		All	One or two		Three or more	
	N (%)	n	%	n	%	N (%)	n	%	n	%
Lung	101 (12.7)	56	55.4	45	44.6	96 (11.1)	61	63.5	35	36.5
Colorectal	98 (12.3)	59	60.2	39	39.8	91 (10.5)	63	69.2	28	30.8
Pancreatic	87 (10.9)	41	47.1	46	52.9	84 (9.7)	47	56.0	37	44.1
Gastric	70 (8.8)	32	45.7	38	54.3	65 (7.5)	33	50.8	32	49.2
Oesophageal	65 (8.2)	43	66.2	22	33.8	75 (8.7)	57	76.0	18	24.0
Ovarian	59 (7.4)	33	55.9	26	44.1	52 (6.0)	32	61.5	20	38.5
Liver	57 (7.2)	33	57.9	24	42.1	41 (4.7)	27	65.9	14	34.1
Renal/bladder	54 (6.8)	34	63.0	20	37.0	72 (8.3)	54	75.0	18	25.0
Breast	54 (6.8)	37	68.5	17	31.5	67 (7.7)	53	79.1	14	20.9
Endometrial	41 (5.2)	28	68.3	13	31.7	56 (6.5)	44	78.6	12	21.4
Head/neck	40 (5.0)	26	65.0	14	35.0	69 (8.0)	51	73.9	18	26.1
Prostate	37 (4.6)	23	62.2	14	37.8	51 (5.9)	37	72.5	14	27.5
Cervical	33 (4.1)	22	66.7	11	33.3	46 (5.3)	35	76.1	11	23.9
All	796	467	58.7	329	41.3	865	594	68.7	271	31.3

3.2. General characteristics of study patients

Sociodemographic variables and comorbidity burden in emergency and nonemergency presenters were not significantly different nor were they in emergency presenters with one or two vs. three or more consultations (see detailed results in Table S1).

Symptoms reported most frequently by emergency and nonemergency presenters were abdominal (57.5 vs. 51.3%, respectively; P=0.012) and nonspecific symptoms (48.5 vs. 40.3%, respectively; P=0.0009). Among emergency presenters, 37.9% of those with one or two vs. 24% with three or more consultations had one single symptom of high predictive value for cancer, including rectal bleeding, haemoptysis, metrorrhagia, haematuria, dysphagia, and lumps (P<0.0001). In contrast, 40.3% with one or two vs. 59.6% with three or more consultations reported symptoms of low predictive value, including abdominal pain, unintentional weight loss, and fever (P<0.0001) (Table S1).

3.3. Cancer stage

There were significant differences in stage at diagnosis between emergency and nonemergency presenters, overall and for most cancer types. Emergency presenters were more likely to be diagnosed at stage III-IV (72.9 vs. 51.2%, respectively), with pancreatic, gastric, and lung cancer showing the highest proportions of metastatic disease and renal/bladder, endometrial, and ovarian cancer the lowest (Table S2). By number of consultations, emergency presenters with three or more were more likely than those with one or two to be diagnosed at stage III-IV (81.5 vs. 66.8%, respectively; P<0.0001) (Table S3, Fig. S1).

3.4. Time intervals

Overall, the median PC interval in emergency presenters (24 [14–37] days [range 1–70]) was 10 days shorter (95% CI -12 to -8) than in nonemergency presenters. While varying by cancer type, emergency presenters with pancreatic, gastric, and ovarian cancer had the longest PC intervals which were, however, significantly shorter than those seen in nonemergency presenters with these cancers (Figs. 2 and 3, Table S4). Tables S5 and S6 show the PC interval by number of consultations considered individually and as one or two vs. three or more. Among emergency presenters, the PC interval in those with three or more consultations (34 [24–47] days) was 16 days longer (95% CI 14 to 18) than in those with one or two, but it was 19 days shorter (95% CI -22 to -17) than in nonemergency presenters (Table S6). When considering the subgroup of emergency presenters with highest proportions of three or more consultations, PC intervals ranged from 42.5 (29–48) days in gastric cancer to 55 (36–65) days in pancreatic cancer. Conversely, in the subgroup with lowest proportions, PC intervals ranged from 26 (21–33) days in cervical cancer to 28 (19.5–37.5) days in endometrial cancer.

Hospital intervals in emergency and nonemergency presenters were similar (Fig. S2). Differences in diagnostic intervals in both populations were consistent with those seen for the PC interval, though more pronounced. Overall, the median diagnostic interval in emergency presenters (38 [27–54] days [range 5–98]) was 11 days shorter (95% CI -13 to -8) than in nonemergency presenters (Table S4). Among emergency presenters, the diagnostic interval in those with three or more consultations was 20 days shorter (95% CI -23 to -17) than in nonemergency presenters with three or more (Table S7, Fig. S3).

3.5. Correlation analysis

The association between PC intervals and number of prereferral consultations was moderately strong for the entire population of emergency presenters (Spearman r_S 0.586; P<0.0001; Kendall τ 0.457; P<0.0001) (Fig. 4). However, levels of rank agreement varied by cancer type. There was a strong positive association for seven cancers (Spearman r_S range 0.662 [cervical]−0.783 [lung]; P<0.0001), a moderate association for breast cancer (Spearman r_S 0.577; P<0.0001), and a weak association for other cancers (Spearman r_S range 0.211 [ovarian]−0.286 [gastric]; P=0.017 for gastric cancer and not significant for others) (Table 2). Assessment with Kendall test yielded similar results (Kendall τ range 0.165 [ovarian; P=0.09]–0.634 [lung; P<0.0001]). Patterns of association between diagnostic intervals and number of consultations were consistent with those seen for the PC interval (Table S8, Fig. S4).

Table 2. Association between primary care intervals and number of prereferral consultations in emergency and nonemergency presenters.

Cancer diagnosis	Emergency presenters					Nonemergency presenters				
	Spearman			Kendall		Spearman			Kendall	
	r_S	95% CI	*P*	τ	*P*	r_S	95% CI	*P*	τ	*P*
Lung	0.783	0.691–0.850	<0.0001	0.634	0	0.690	0.563–0.784	<0.0001	0.533	<0.0001
Colorectal	0.781	0.686–0.850	<0.0001	0.632	<0.0001	0.611	0.459–0.729	<0.0001	0.483	<0.0001
Pancreatic	0.740	0.623–0.824	<0.0001	0.595	<0.0001	0.678	0.537–0.781	<0.0001	0.533	<0.0001
Gastric	0.286	0.047–0.493	0.017	0.192	0.031	0.180	-0.074–0.412	0.15	0.129	0.16
Oesophageal	0.757	0.624–0.847	<0.0001	0.632	<0.0001	0.606	0.434–0.735	<0.0001	0.483	<0.0001
Ovarian	0.211	-0.055–0.449	0.11	0.165	0.09	0.212	-0.073–0.465	0.13	0.157	0.14
Liver	0.221	-0.050–0.461	0.10	0.190	0.06	0.227	-0.096–0.507	0.15	0.168	0.16
Renal/bladder	0.701	0.528–0.819	<0.0001	0.570	<0.0001	0.643	0.479–0.765	<0.0001	0.540	<0.0001
Breast	0.577	0.359–0.736	<0.0001	0.473	<0.0001	0.613	0.432–0.747	<0.0001	0.508	<0.0001
Endometrial	0.704	0.499–0.834	<0.0001	0.584	<0.0001	0.650	0.460–0.783	<0.0001	0.535	<0.0001
Head/neck	0.252	-0.074–0.530	0.12	0.185	0.13	0.158	-0.089–0.386	0.20	0.116	0.21

Prostate	0.274	-0.064–0.556	0.10	0.202	0.11	0.263	-0.022–0.508	0.06	0.199	0.07
Cervical	0.663	0.404–0.823	<0.0001	0.548	<0.0001	0.572	0.329–0.743	<0.0001	0.472	<0.0001
Overall	0.586	0.537–0.631	<0.0001	0.457	0	0.521	0.470–0.570	<0.0001	0.404	0

4. Discussion

The PC interval and the number of prereferral consultations are important measures of diagnostic timeliness of cancer and are interrelated. Yet, no study has so far investigated their precise association in the emergency diagnostic pathway. Our research expands on earlier findings in several ways. First, we examined individual-level differences in intervals and number of consultations within and between emergency and nonemergency presenters and determined their correlation for each cancer type. Second, we analysed for differences in stage at diagnosis between emergency and nonemergency presenters and according to number of consultations in emergency presenters. Cancers in emergency presenters were significantly more advanced than in nonemergency presenters as were cancers in those emergency presenters with three or more consultations compared with those with one or two. Last, we analysed for differences in presenting symptoms between emergency and nonemergency presenters and according to number of consultations in emergency presenters to shed light on how different symptoms were associated with the length of intervals, which is considered a priority for research on early cancer diagnosis [30]. Emergency presenters with higher proportions of three or more consultations were more likely to be diagnosed with cancers characterised by low-specificity symptoms, whereas those with lower proportions were more likely to report site-specific symptoms.

Available evidence shows that the number of prereferral consultations reflects the symptom signature of cancer, defined as 'the nature and relative frequency of symptoms (or symptom combinations) reported at presentation by patients later diagnosed with a particular cancer' [30]. In short, cancers with a broad symptom signature may be harder to suspect and diagnose than those characterised by a narrow symptomatic presentation and vice versa, explaining the reported differences in number of consultations by cancer type. Analysing data from 41,300 patients with 24 different cancers, Lyratzopoulos *et al* reported in 2012 that patients diagnosed with harder-to-suspect cancers (e.g., pancreatic, gastric, or lung cancer) were more likely to visit their PC physician three or more times before hospital referral, whereas those with easy-to-suspect cancers (e.g., breast, endometrial, or cervical cancer) were more commonly referred after only one or two visits [13]. The authors identified tumour site as the strongest predictor of three or more consultations and found that women, younger patients, and patients from ethnic minorities were more likely to consult three or more times before referral. In an additional study published one year later, Lyratzopoulos *et al* demonstrated that the PC interval was moderately or highly correlated with the number of prereferral consultations across 18 cancer types [12]. Interestingly, the patterns of variation in the number of consultations in relation to the level of diagnostic difficulty described by Lyratzopoulos *et al* are similar to those observed in our emergency presenters and in those reported by Abel *et al* from England [8] and Murchie *et al* from Scotland [7]. In Abel *et al* study, for example, emergency presenters with lung and ovarian cancer were more likely to report multiple consultations, reflecting the challenges of suspecting cancer when symptoms are nonspecific or the baseline risk of cancer is low (as suggested by the younger age of these patients). Inversely, emergency presenters with bladder, oesophageal, and breast cancer had higher proportions of one or two consultations [8]. To the best of our knowledge, our study is the first to examine the association between time intervals and number of prereferral consultations in the pathway from first PC presentation to emergency referral and diagnosis.

It should be emphasised that the study was limited to emergency presenters with relevant PC consultations and that those taken directly to ED as first presenters (i.e., no prior contact with PC) were not eligible. We have previously documented that 35% of emergency presenters have no history of prereferral consultations [21]. Research has also shown that these patients constitute a subgroup of emergency presenters different from those who do have such consultations. For instance, Abel *et al* reported that first presenters (29% of total) were more likely than others to be older, males, more deprived, and more commonly diagnosed with brain, renal, endometrial, or breast cancer [8].

A salient finding of our study was that emergency presenters were significantly more likely than nonemergency-diagnosed patients to present with nonlocalising symptoms (P=0.0009). This observation has some similarities to previously reported data from England. By comparing emergency vs. nonemergency presenters with colorectal cancer, Renzi *et al* found that the risk of emergency presentation was significantly lower among patients presenting with alarm symptoms such as rectal bleeding [31]. Further, in their

investigation of cancer patients diagnosed following presentation with nonspecific vs. more specific symptoms, Pearson *et al* reported that those with nonspecific symptoms were more likely to be diagnosed via emergency presentation [32].

Research data suggest that patients diagnosed with cancer following presentation in PC with related symptoms may turn into emergency presenters due to cancer progression as a result of delayed help-seeking or system delays with prolonged PC and diagnostic intervals [3,33]. Since early recognition of cancer symptoms by physicians will influence clinical decision-making and therefore PC and diagnostic intervals and prereferral consultations are potentially modifiable, our results could guide the design, delivery, and evaluation of public health and healthcare approaches to improve diagnostic timeliness in cancer patients diagnosed as an emergency. Our results also suggest opportunities to reduce the number of such occurrences by targeting symptomatic individuals before first presentation. Patients diagnosed as an emergency after PC contact had significantly shorter PC and diagnostic intervals than nonemergency-diagnosed cancers, indicating accelerated disease process and increased symptom burden leading to a quicker diagnostic journey. This suggests that at least some emergency diagnoses might be preventable through educational programmes raising public awareness of potential cancer symptoms, such as the 'Be Clear on Cancer' campaigns in the UK [34], and even intensifying the participation in population-based screening (where available), as reported for colorectal and lung cancer [35,36].

Several limitations must be noted. First, a single-site design represents an important limitation precluding generalisability of the reported findings to other healthcare settings unless a multicentre approach comparing data between different jurisdictions is done. Second, the contextual detail of patient interactions with PC physicians before emergency referral was not explored. In their study of patients with an emergency cancer diagnosis, Murchie *et al* identified a subgroup (nearly 20%) who had consulted previously with a PC physician, often multiple times, but were not referred according to the Scottish Referral Guidelines for Suspected Cancer [7]. Third, information about the patient interval (i.e., from symptom onset to first healthcare contact) was not available. However, the long delays experienced by some emergency presenters were more likely to be the result of system delays than delayed help-seeking. Fourth, the prognosis of emergency-diagnosed patients was not investigated. Given the substantially greater risk of mortality in the shorter term in this population, which prevails even after adjustment for stage [4], the question about prognosis of emergency vs. nonemergency presenters should be addressed by a subsequent study. Finally, we cannot exclude the contribution of other unmeasured confounders to the delays reported.

5. Conclusion

Our research in patients who had first consulted in PC with relevant symptoms and were diagnosed with 13 different cancers following emergency referral showed that the association between the number of prereferral consultations and the length of the PC and diagnostic interval was strong for seven cancer types. These included cancers characterised by high proportions of three or more consultations and long intervals (e.g., pancreatic or lung cancer) and vice versa for other cancers (e.g., endometrial or oesophageal cancer). Cancers in emergency presenters with three or more consultations were more advanced than in those with one or two and presenting symptoms were more likely to be nonspecific.

Taken together, the findings provide insights that can be used to inform system level interventions aimed at reducing unnecessary delays in the emergency diagnostic route, particularly in cancer patients with multiple (i.e., three or more) consultations in PC, and also provide pointers for future research. Furthermore, our results offer possible windows of opportunity for reducing the proportion of emergency diagnoses by targeting individuals with more severe symptoms pre-presentation who were diagnosed faster (i.e., those with shorter PC and diagnostic intervals).

CRediT author statement

Xavier Bosch: Conceptualisation, Formal analysis, Investigation, Writing–original draft, Writing–review & editing, Supervision. Elisabet Montori-Palacin: Methodology, Investigation, Visualisation. José Naval-Álvarez: Investigation, Data curation. Ana Matas: Investigation, Data curation. Pedro Moreno: Methodology, Formal analysis, Visualisation. Alfonso López-Soto: Conceptualisation, Writing–review & editing, Supervision.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper**.**

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

The study was approved by the Ethical Research Committee of the Hospital Clínic of Barcelona. Patient consent was waived due to the anonymisation of data and the retrospective design of the study.

References

[1] J.D. Emery, K. Shaw, B. Williams, et al., The role of primary care in early detection and follow-up of cancer, Nat. Rev. Clin. Oncol. 11 (2014) 38–48, https://doi.org/10.1038/nrclinonc.2013.212
[2] A. Herbert, G.A. Abel, S. Winters, S. McPhail, L. Elliss-Brookes, G. Lyratzopoulos, Cancer diagnoses after emergency GP referral or A&E attendance in England: determinants and time trends in Routes to Diagnosis data, 2006-2015, Br. J. Gen. Pract. 69 (2019) e724–e730, https://doi.org/10.3399/bjgp19X705473
[3] G. Lyratzopoulos, C.L. Saunders, G.A. Abel, Are emergency diagnoses of cancer avoidable? A proposed taxonomy to motivate study design and support service improvement, Future Oncol. 10 (2014) 1329–1333, https://doi.org/10.2217/fon.14.80
[4] S. McPhail, R. Swann, S.A. Johnson, et al., Risk factors and prognostic implications of diagnosis of cancer within 30 days after an emergency hospital admission (emergency presentation): an International Cancer Benchmarking Partnership (ICBP) population-based study, Lancet Oncol. 23 (2022) 587–600, https://doi.org/10.1016/S1470-2045(22)00127-9
[5] D. Coxon, C. Campbell, F.M. Walter, et al., The Aarhus statement on cancer diagnostic research: turning recommendations into new survey instruments, BMC Health Serv. Res. 18 (2018) 677, https://doi.org/10.1186/s12913-018-3476-0
[6] T.M. Pham, M. Gomez-Cano, T. Salika, D. Jardel, G.A. Abel, G. Lyratzopoulos, Diagnostic route is associated with care satisfaction independently of tumour stage: evidence from linked English Cancer Patient Experience Survey and cancer registration data, Cancer Epidemiol. 61 (2019) 70–78, https://doi.org/10.1016/j.canep.2019.04.011
[7] P. Murchie, S.M. Smith, M.S. Yule, et al., Does emergency presentation of cancer represent poor performance in primary care? Insights from a novel analysis of linked primary and secondary care data, Br. J. Cancer 116 (2017) 1148–1158, https://doi.org/10.1038/bjc.2017.71
[8] G.A. Abel, S.C. Mendonca, S. McPhail, Y. Zhou, L. Elliss-Brookes, G. Lyratzopoulos, Emergency diagnosis of cancer and previous general practice consultations: insights from linked patient survey data, Br. J. Gen. Pract. 67 (2017) e377–e387, https://doi.org/10.3399/bjgp17X690869
[9] P.W. Rose, G. Rubin, R. Perera-Salazar, et al., Explaining variation in cancer survival between 11 jurisdictions in the International Cancer Benchmarking Partnership: a primary care vignette survey, BMJ Open 5 (2015) e007212, https://doi.org/10.1136/bmjopen-2014-007212
[10] G. Lyratzopoulos, Markers and measures of timeliness of cancer diagnosis after symptom onset: a conceptual framework and its implications, Cancer Epidemiol. 38 (2014) 211–213, https://doi.org/10.1016/j.canep.2014.03.009
[11] G. Lyratzopoulos, J. Wardle, G. Rubin, Rethinking diagnostic delay in cancer: how difficult is the diagnosis? BMJ 349 (2014) g7400, https://doi.org/10.1136/bmj.g7400
[12] G. Lyratzopoulos, GA. Abel, S. McPhail, R.D. Neal, G.P. Rubin, Measures of promptness of cancer diagnosis in primary care: secondary analysis of national audit data on patients with 18 common and rarer cancers, Br. J. Cancer 108 (2013) 686– 690, https://doi.org/10.1038/bjc.2013.1
[13] G. Lyratzopoulos, R.D. Neal, J.M. Barbiere, G.P. Rubin, G.A. Abel, Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England, Lancet Oncol. 13 (2012) 353–365, https://doi.org/10.1016/S1470-2045(12)70041-4
[14] M.L. Tørring, M. Frydenberg, R.P. Hansen, F. Olesen, W. Hamilton, P Vedsted, Time to diagnosis and mortality in colorectal cancer: a cohort study in primary care, Br. J. Cancer 104 (2011) 934–940. Erratum in: Br. J. Cancer 104 (2011) 1930, https://doi.org/10.1038/bjc.2011.60
[15] R.D. Neal, P. Tharmanathan, B. France, et al., Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review, Br. J. Cancer 112 (Suppl 1) (2015) S92–S107, https://doi.org/10.1038/bjc.2015.48

[16] M.L. Tørring, A.Z. Falborg, H. Jensen, et al., Advanced-stage cancer and time to diagnosis: an International Cancer Benchmarking Partnership (ICBP) cross-sectional study, Eur. J. Cancer Care (Engl) 28 (2019) e13100, https://doi.org/10.1111/ecc.13100
[17] H. Jensen, M.L. Tørring, F. Olesen, J. Overgaard, P. Vedsted, Cancer suspicion in general practice, urgent referral and time to diagnosis: a population-based GP survey and registry study, BMC Cancer 14 (2014) 636, https://doi.org/10.1186/1471-2407-14-636
[18] R. Swann, S. McPhail, J. Witt, et al., Diagnosing cancer in primary care: results from the National Cancer Diagnosis Audit, Br. J. Gen. Pract. 68 (2018) e63–e72, https://doi.org/10.3399/bjgp17X694169
[19] N.F. van Erp, C.W. Helsper, P. Slottje, et al., Time to diagnosis of symptomatic gastric and oesophageal cancer in the Netherlands: where is the room for improvement? United European Gastroenterol. J. 8 (2020) 607–620, https://doi.org/10.1177/2050640620917804
[20] P. Murchie, R. Adam, E. McNair, et al., Cancer diagnosis in Scottish primary care: results from the National Cancer Diagnosis Audit, Eur. J. Cancer Care (Engl) 29 (2020) e13234, https://doi.org/10.1111/ecc.13234
[21] X. Bosch, E. Montori-Palacin, J. Naval-Álvarez, A. Matas, P. Moreno, A. López-Soto, Time intervals in the pathway to emergency cancer diagnosis, Future Oncol. 19 (2023) 829–843, https://doi.org/10.2217/fon-2023-0062
[22] X. Bosch, J. Aibar, S. Capell, A. Coca, A. López-Soto, Quick diagnosis units: a potentially useful alternative to conventional hospitalisation, Med. J. Aust. 191 (2009) 496–498, https://doi.org/10.5694/j.1326-5377.2009.tb02912.x
[23] D. Weller, P. Vedsted, G. Rubin, et al., The Aarhus statement: improving design and reporting of studies on early cancer diagnosis, Br. J. Cancer 106 (2012) 1262–1267, https://doi.org/10.1038/bjc.2012.68
[24] Ministerio de Sanidad, Estrategia en Cáncer del Sistema Nacional de Salud (2021). https://www.sanidad.gob.es/organizacion/sns/planCalidadSNS/pdf/ESTRATEGIA_EN_CANCER_DEL_SNS.pdf (accessed 3 August 2023).
[25] J.D. Brierley, M.K. Gospodarowicz, C. Wittekind, TNM Classification of Malignant Tumours, eight ed., Wiley-Blackwell, Hoboken, 2016.
[26] M.E. Charlson, P. Pompei, K.L. Ales, C.R. MacKenzie, A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, J. Chronic Dis. 40 (1987) 373–383, https://doi.org/10.1016/0021-9681(87)90171-8
[27] National Institute for Health and Care Excellence, Suspected Cancer: Recognition and Referral (2015). https://www.nice.org.uk/guidance/ng12 (accessed 3 August 2023).
[28] J.L. Hodges, E.L. Lehmann, Estimates of location based on rank tests, Annals of Mathematical Statistics 34 (1963) 598–611.
[29] E.L. Lehmann, Nonparametric confidence intervals for a shift parameter, Annals of Mathematical Statistics 34 (1963) 1507–1512.
[30] M.M. Koo, W. Hamilton, F.M. Walter, G.P. Rubin, G. Lyratzopoulos, Symptom signatures and diagnostic timeliness in cancer patients: a review of current evidence, Neoplasia 20 (2018) 165–174, https://doi.org/10.1016/j.neo.2017.11.005
[31] C. Renzi, G. Lyratzopoulos, T. Card, T.P. Chu, U. Macleod, B. Rachet, Do colorectal cancer patients diagnosed as an emergency differ from non-emergency patients in their consultation patterns and symptoms? A longitudinal data-linkage study in England, Br. J. Cancer 115 (2016) 866–875, https://doi.org/10.1038/bjc.2016.250
[32] C. Pearson, V. Poirier, K. Fitzgerald, G. Rubin, W. Hamilton, Cross-sectional study using primary care and cancer registration data to investigate patients with cancer presenting with non-specific symptoms, BMJ Open 10 (2020) e033008, https://doi.org/10.1136/bmjopen-2019-033008
[33] Y. Zhou, G.A. Abel, W. Hamilton, et al., Diagnosis of cancer as an emergency: a critical review of current evidence, Nat. Rev. Clin. Oncol. 14 (2017) 45–56, https://doi.org/10.1038/nrclinonc.2016.155
[34] Public Health England, Be Clear on Cancer. https://www.cancerresearchuk.org/health-professional/awareness-and-prevention/be-clear-on-cancer (accessed 3 August 2023).
[35] K.M. Decker, P. Lambert, Z. Nugent, N. Biswanger, J. Samadder, H. Singh, Time trends in the diagnosis of colorectal cancer with obstruction, perforation, and emergency admission after the introduction of population-based organized screening, JAMA Netw. Open 3 (2020) e205741, https://doi.org/10.1001/jamanetworkopen.2020.5741
[36] J.R. Walder, S.A. Faiz, M. Sandoval, Lung cancer in the emergency department, Emerg. Cancer Care 2 (2023) 3, https://doi.org/10.1186/s44201-023-00018-9

Figure captions

Fig. S1. Flowchart of study population

Fig. 2. Bar graphs illustrating the overall median primary care and diagnostics interval (days) in emergency and nonemergency presenters. Medians are the height of the bars and the horizontal lines in each bar denote the interquartile range. The aligned symbols in each data set represent the values of single patients. The first pair of bars on the graph (red and blue) correspond to primary care intervals and the second pair (light washed yellow and green) to diagnostics intervals.

Fig. 3. Representation of the median primary care interval (days) for each cancer type in emergency and nonemergency presenters. Medians are the height of the bars and the symbols in each dataset indicate the values of individual patients.

Fig. 4. Correlation plot depicting the relationship between the primary care interval (days) and the number of prereferral consultations for all cancers in emergency and nonemergency presenters. Assessment with nonparametric correlation coefficients revealed a moderately strong association.

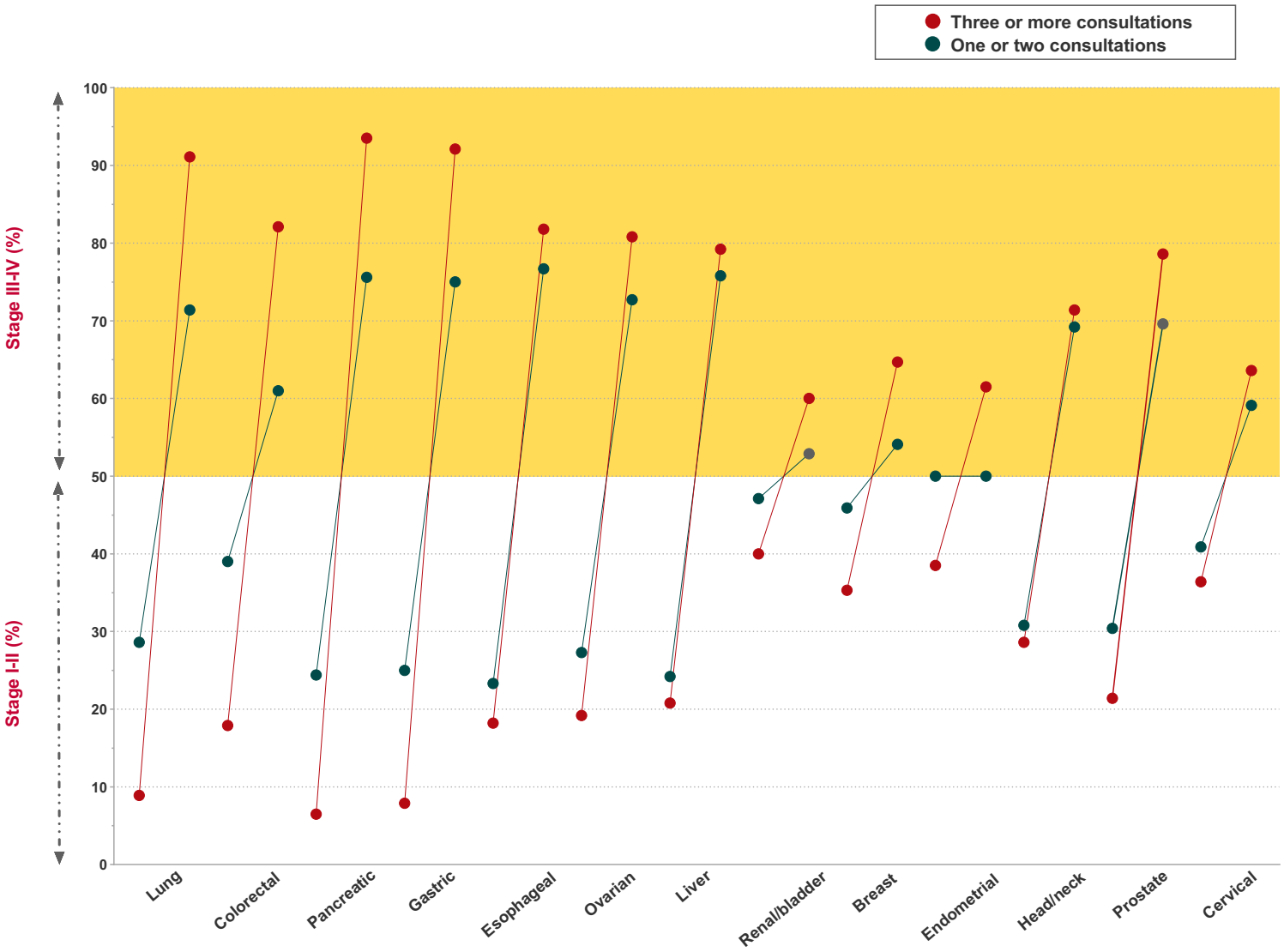
Three or more consultations
One or two consultations
Stage III-IV (%)
Stage I-II (%)
100
90
80
70
60
50
40
30
20
10
0
Lung
Colorectal
Pancreatic
Gastric
Esophageal
Ovarian
Liver
Renal/bladder
Breast
Endometrial
Head/neck
Prostate
Cervical

Fig.1

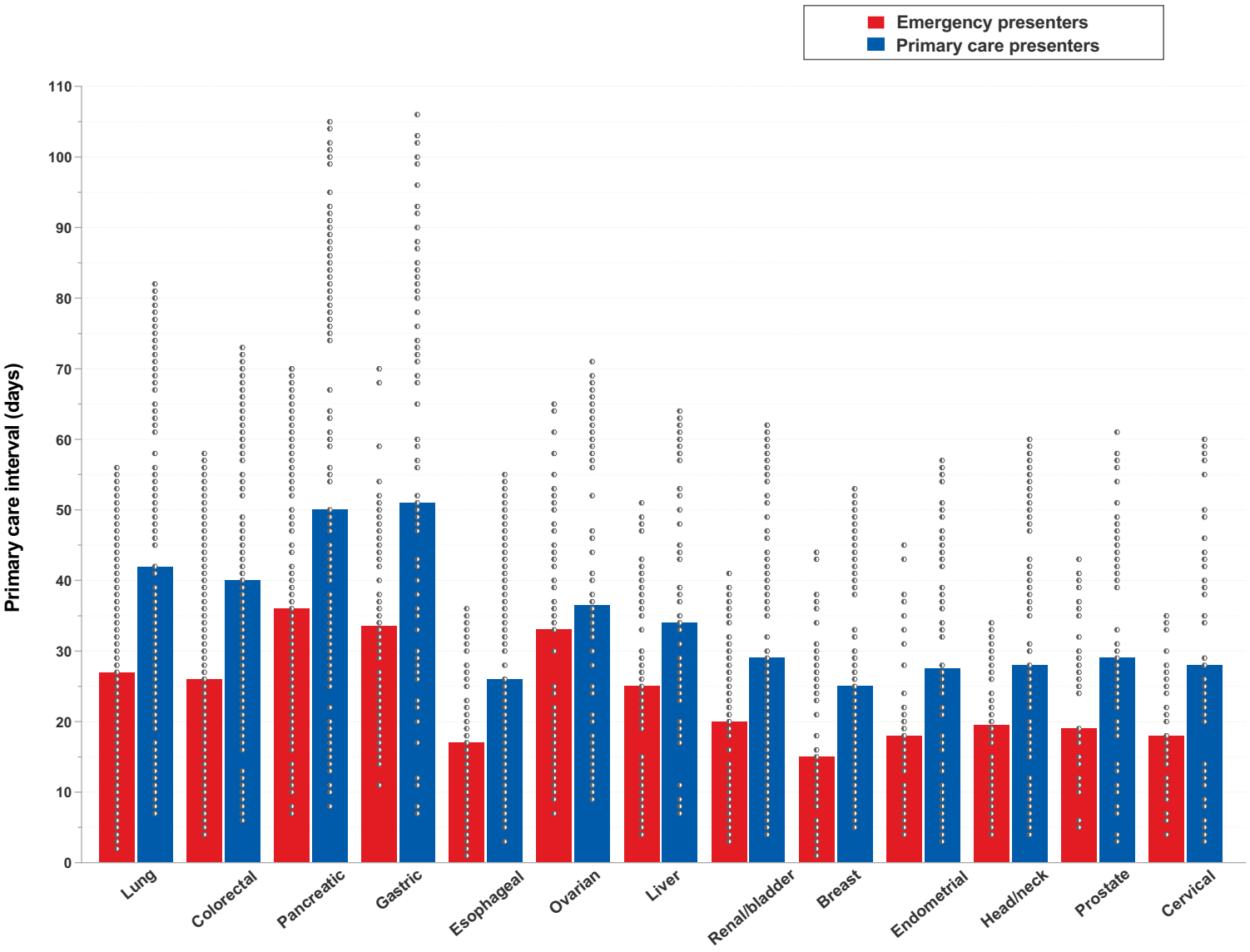
Emergency presenters
Primary care presenters
Primary care interval (days)
110
100
90
80
70
60
50
40
30
20
10
0
Lung
Colorectal
Pancreatic
Gastric
Esophageal
Ovarian
Liver
Renal/bladder
Breast
Endometrial
Head/neck
Prostate
Cervical

Fig. 2

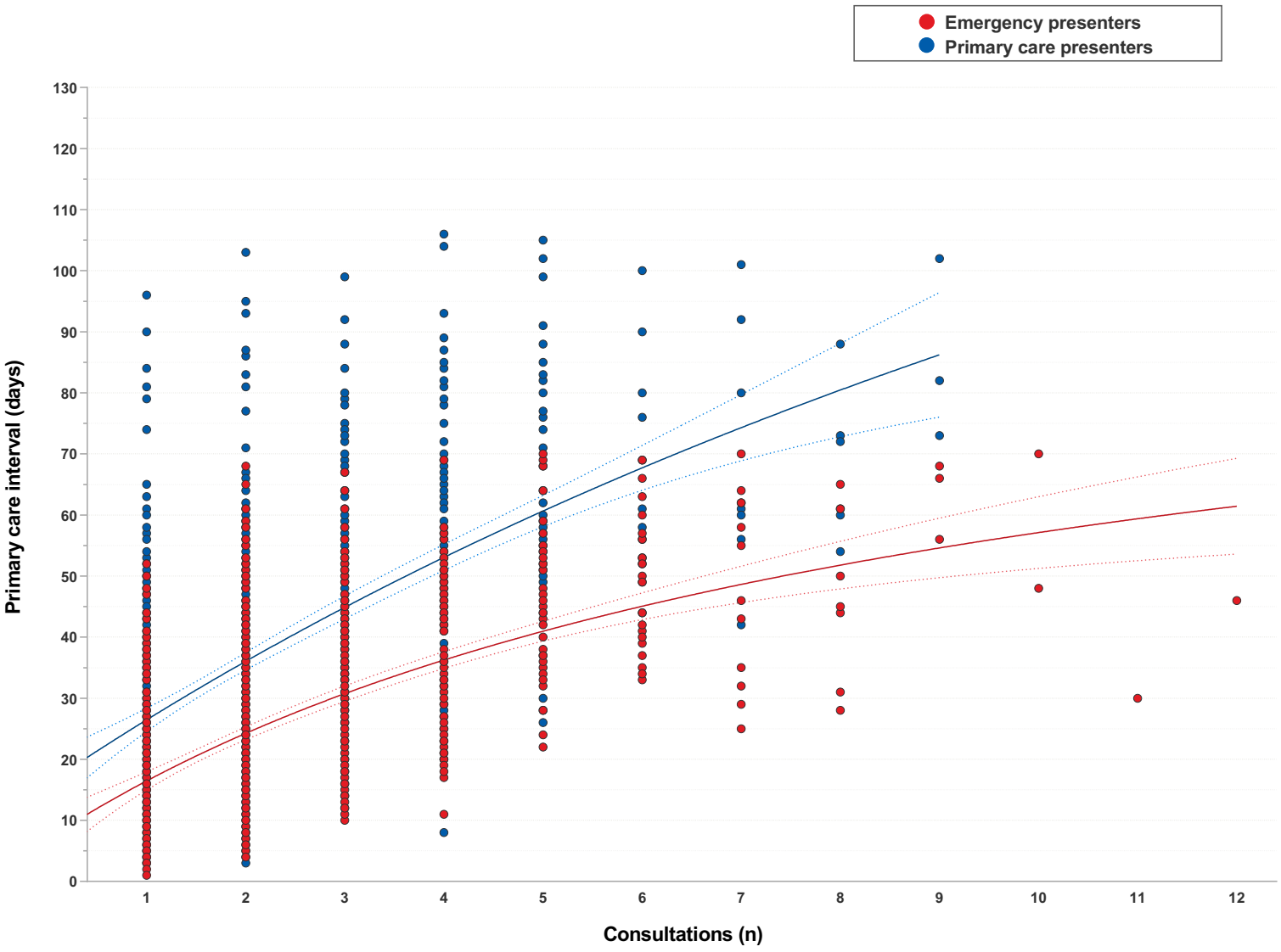
Emergency presenters
Primary care presenters
Primary care interval (days)
Consultations (n)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
1
2
3
4
5
6
7
8
9
10
11
12

Fig.3

Supplementary material

Table S1. General characteristics of study patients.

	Emergency presenters	Nonemergency presenters	*P*	Emergency presenters		*P*
				One or two	Three or more	
Gender			0.55			0.52
Men	430 (54.0)	454 (52.5)		257 (59.8)	173 (40.2)	
Women	366 (46.0)	411 (47.5)		210 (57.4)	156 (42.6)	
Age at diagnosis, years						
Mean (SD)	65.8 (14.1)	64.2 (14.6)	0.36	66.1 (14.2)	65.5 (13.9)	0.66
Median (IQR)	65 (54–77)	64 (52–77)		66 (54–77)	64 (55–77)	
18–49	132 (16.6)	177 (20.5)		78 (59.1)	54 (40.9)	0.36
50–59	161 (20.2)	180 (20.8)		87 (54.0)	74 (46.0)	
60–69	170 (21.4)	172 (19.9)		96 (56.5)	74 (43.5)	
70–79	170 (21.4)	167 (19.3)		110 (64.7)	60 (35.3)	
≥80	163 (20.5)	169 (19.5)		96 (58.9)	67 (41.1)	
Ethnicity			0.33			0.28
White	736 (92.5)	811 (93.8)		436 (59.2)	300 (40.8)	
Other ethnic groups	60 (7.5)	54 (6.2)		31 (51.7)	29 (48.3)	
Deprivation			0.46			0.53
1 Most deprived	28 (3.5)	23 (2.7)		13 (46.4)	15 (53.6)	
2	199 (25.0)	190 (22.0)		111 (55.8)	88 (44.2)	
3	280 (35.2)	318 (36.8)		167 (59.6)	113 (40.4)	
4	267 (33.5)	306 (35.4)		162 (60.7)	105 (39.3)	
5 Least deprived	22 (2.8)	28 (3.2)		14 (63.6)	8 (36.4)	
Smoking			0.18			0.32
Never	199 (25.0)	250 (28.9)		108 (54.3)	91 (45.7)	
Former	338 (42.5)	356 (41.2)		201 (59.5)	137 (40.5)	
Current	259 (32.5)	259 (29.9)		158 (61.0)	101 (39.0)	
Alcohol consumption			0.28			0.29
None	502 (63.1)	562 (65.0)		286 (57.0)	216 (43.0)	
Low	220 (27.6)	241 (27.9)		132 (60.0)	88 (40.0)	
Excessive	74 (9.3)	62 (7.2)		49 (66.2)	25 (33.8)	
Comorbidity score			0.48			0.60
0	270 (33.9)	324 (37.5)		150 (32.1)	120 (36.5)	
1	259 (32.5)	272 (31.4)		154 (33.0)	105 (31.9)	
2	179 (22.5)	184 (21.3)		108 (23.1)	71 (21.6)	
≥ 3	88 (11.1)	85 (9.8)		55 (11.8)	33 (10.0)	
Symptoms at presentation						
Bleeding	117 (14.7)	148 (17.1)		73 (62.4)	44 (37.6)	
Abdominal symptoms	458 (57.5)	444 (51.3)		256 (55.9)	202 (44.1)	
Respiratory symptoms	82 (10.3)	82 (9.5)		49 (59.8)	33 (40.2)	
Pain	75 (9.4)	76 (8.8)		46 (61.3)	29 (38.7)	
Urological symptoms	57 (7.2)	80 (9.2)		34 (59.6)	23 (40.4)	
Lumps or masses	69 (8.7)	106 (12.3)		45 (65.2)	24 (34.8)	

Nonspecific symptoms	386 (48.5)	349 (40.3)	201 (52.1)	185 (47.9)
Iron-deficiency anaemia	41 (5.2)	48 (5.5)	26 (63.4)	15 (36.6)
Suspicion of cancer in imaging test	37 (4.6)	56 (6.5)	22 (59.5)	15 (40.5)
Total	796	865	467	329

Continuous variables are presented as means (SD) or medians (IQR) and categorical variables as n (%)

Table S2. Distribution of cancers in emergency and nonemergency presenters according to stage at diagnosis.

Cancer diagnosis	Emergency presenters					Nonemergency presenters					
	No.	I-II	III	IV	III-IV	No.	I-II	III	IV	III-IV	*P* *
Lung	101	20 (19.8)	17 (16.8)	64 (63.4)	81 (80.2)	96	37 (38.5)	17 (17.7)	42 (43.8)	59 (61.5)	0.0046
Colorectal	98	30 (30.6)	27 (27.6)	41 (41.8)	68 (69.4)	91	42 (46.2)	24 (26.4)	25 (27.5)	49 (53.8)	0.036
Pancreatic	87	13 (14.9)	16 (18.4)	58 (66.7)	74 (85.1)	84	24 (28.6)	13 (15.5)	47 (56.0)	60 (71.4)	0.041
Gastric	70	11 (15.7)	13 (18.6)	46 (65.7)	59 (84.3)	65	21 (32.3)	10 (15.4)	34 (52.3)	44 (67.7)	0.027
Oesophageal	65	14 (21.5)	15 (23.1)	36 (55.4)	51 (78.5)	75	34 (45.3)	11 (14.7)	30 (40.0)	41 (54.7)	0.0041
Ovarian	59	14 (23.7)	22 (37.3)	23 (39.0)	45 (76.3)	52	23 (44.2)	15 (28.8)	14 (26.9)	29 (55.8)	0.027
Liver	57	13 (22.8)	12 (21.1)	32 (56.1)	44 (77.2)	41	12 (29.3)	8 (19.5)	21 (51.2)	29 (70.7)	0.49
Renal/bladder	54	24 (44.4)	11 (20.4)	19 (35.2)	30 (55.6)	72	48 (66.7)	11 (15.3)	13 (18.1)	24 (33.3)	0.018
Breast	54	23 (42.6)	6 (11.1)	25 (46.3)	31 (57.4)	67	48 (71.6)	6 (9.0)	13 (19.4)	19 (28.4)	0.0016
Endometrial	41	19 (46.3)	7 (17.1)	15 (36.6)	22 (53.7)	56	41 (73.2)	7 (12.5)	8 (14.3)	15 (26.8)	0.011
Head/neck	40	12 (25.0)	4 (10.0)	24 (60.0)	28 (70.0)	69	34 (49.3)	7 (10.1)	28 (40.6)	35 (50.7)	0.07
Prostate	37	10 (27.0)	4 (10.8)	23 (62.2)	27 (73.0)	51	27 (52.9)	13 (25.5)	11 (21.6)	24 (47.1)	0.018
Cervical	33	13 (39.4)	7 (21.2)	13 (39.4)	20 (60.6)	46	31 (67.4)	6 (13.0)	9 (19.6)	15 (32.6)	0.021
All	796	216 (27.1)	161 (20.4)	419 (52.6)	580 (72.9)	865	422 (48.8)	148 (17.1)	295 (34.1)	443 (51.2)	<0.0001

* Stage I-II and III-IV in emergency and nonemergency presenters were compared with the Fisher's exact test.

Table S3. Stage at diagnosis in emergency presenters according to number of prereferral consultations.

Cancer diagnosis	Emergency presenters						
	One or two			Three or more			
	No.	I-II	III-IV	No.	I-II	III-IV	*P* *
Lung	56	16 (28.6)	40 (71.4)	45	4 (8.9)	41 (91.1)	0.022
Colorectal	59	23 (39.0)	36 (61.0)	39	7 (17.9)	32 (82.1)	0.043
Pancreatic	41	10 (24.4)	31 (75.6)	46	3 (6.5)	43 (93.5)	0.033
Gastric	32	8 (25.0)	24 (75.0)	38	3 (7.9)	35 (92.1)	0.10
Oesophageal	43	10 (23.3)	33 (76.7)	22	4 (18.2)	18 (81.8)	0.76
Ovarian	33	9 (27.3)	24 (72.7)	26	5 (19.2)	21 (80.8)	0.55
Liver	33	8 (24.2)	25 (75.8)	24	5 (20.8)	19 (79.2)	1
Renal/bladder	34	16 (47.1)	18 (52.9)	20	8 (40.0)	12 (60.0)	0.78
Breast	37	17 (45.9)	20 (54.1)	17	6 (35.3)	11 (64.7)	0.56
Endometrial	28	14 (50.0)	14 (50.0)	13	5 (38.5)	8 (61.5)	0.52
Head/neck	26	8 (30.8)	18 (69.2)	14	4 (28.6)	10 (71.4)	1
Prostate	23	7 (30.4)	16 (69.6)	14	3 (21.4)	11 (78.6)	0.71
Cervical	22	9 (40.9)	13 (59.1)	11	4 (36.4)	7 (63.6)	1
All	467	155 (33.2)	312 (66.8)	329	61 (18.5)	268 (81.5)	<0.0001

* The Fisher's exact test was used to compare stage I-II and III-IV in emergency presenters with one or two vs. three or more prereferral consultations.

Table S4. Primary care and diagnostic intervals by cancer type in emergency and nonemergency presenters.

Cancer diagnosis	Primary care interval (days)								Diagnostic interval (days)							
	Emergency presenters				Nonemergency presenters				Emergency presenters				Nonemergency presenters			
	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th
Lung	16.5	27	43.5	50	22	42	62	76	31	44	57.5	69	41	61.5	80	95
Colorectal	16	26	44	53	26	40	62	68	32	41.5	58	66	37	59	75	83
Pancreatic	23	36	58	67	32	50	83	92.5	41	56	79	85	50	75.5	100.5	117
Gastric	24	33.5	46	52	29	51	81.5	94	41	52.5	63	75	47	79	100.5	116.5
Oesophageal	9.5	17	26	32	17	26	40	50	23	32	38	45.5	28	38	54	62
Ovarian	16	33	47	58	24	36.5	59	66	32	46	64	73	42	55	73	83
Liver	11.5	25	36.5	42	23	34	52.5	61	26	41	51	59	36	51	70.5	80
Renal/bladder	11	20	28	37	18	29	45.5	58	24.5	32	41.5	54.5	30.5	44	59	72
Breast	9	15	27	37	17	25	43	49	15	25	40	46	27	38	55	62.5
Endometrial	12	18	28	37	14.5	27.5	44	52	18	27	37	49	23	37.5	53	66
Head/neck	11	19.5	27	32	18	28	49.5	56	25	29	39	43	30	43	60.5	74
Prostate	14.5	19	31	39	23	29	44	54	25.5	33	48	57	33	47	59	69
Cervical	11.5	18	25.5	32	13	28	43	55.5	21.5	30	35.5	40.5	26	43.5	57	64
Overall	14	24	37	50	21	36	52	68	27	38	54	68	34	49	69	86.5

Table S5. Overall primary care intervals (days) in emergency and nonemergency presenters with 1, 2, 3, 4, and ≥5 prereferral consultations.

Consultations	Emergency presenters (N=796)				Nonemergency presenters (N=865)			
	Primary care interval (days)				Primary care interval (days)			
	No. (%)	50th	IQR	90th	No. (%)	50th	IQR	90th
1	247 (31.0)	14	8–22	37	312 (36.1)	25.5	15–38	50
2	220 (27.6)	21.5	13–31	44	282 (32.6)	29.5	18–44	58
3	159 (20.0)	27	20–38	51	107 (12.4)	47	38–58	72
4	84 (10.6)	34.5	26–46	52.5	92 (10.6)	54.5	44–66	82
≥5	86 (10.8)	46	37–56	66	72 (8.3)	61.5	54–80	97

Table S6. Primary care intervals (days) by cancer type in emergency and nonemergency presenters with 1-2 vs. ≥3 prereferral consultations.

Cancer diagnosis	Primary care interval (days)															
	Emergency presenters								Nonemergency presenters							
	One or two				Three or more				One or two				Three or more			
	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th
Lung	8	18	26	37	31.5	43	48	53.5	15	27	43	52	52	68	77	80
Colorectal	12	18	25	39	35	46	53	56	20	32	44	59	55.5	65	69	71
Pancreatic	17.5	25	36.5	54.5	36	55	65	69	25	36	50	79.5	59.5	82	90.5	101
Gastric	22	28	38	51.5	29	42.5	48	52	26.5	47	77.5	92	42.5	64	84	100
Oesophageal	6	13	17	27	20	26	32	35	14	23	32.5	39	40.5	47.5	51	54
Ovarian	14	30	44.5	52.5	19.5	33.5	49	59	18	36	58.5	64.5	32	41	61	68
Liver	7.5	15	37.5	41.5	20	25.5	36	48	19	33	48	59	24.5	40.5	59	62.5
Renal/bladder	7	13.5	20.5	28.5	23.5	28.5	37	39	15	23.5	35	44	44	54.5	59	61
Breast	6	12	17	29.5	19.5	27	37	43	14.5	22	31	43.5	43.5	48.5	50.5	52.5
Endometrial	8	15.5	20	31.5	19.5	28	37.5	44	10.5	24	36	44.5	44	50.5	55	56.5
Head/neck	7.5	14.5	25	31.5	16	21.5	29.5	32.5	15	27	43	55	25.5	42.5	54	57
Prostate	11	18	29	38	19	24.5	36	40.5	19.5	28	41.5	49.5	27.5	43.5	52	56
Cervical	9	15.5	20.5	25.5	21	26	33	35	11	24	34	44	40	50	58	60
Overall	10	17	28	39	24	34	47	56	16	27	41	54	43	54	68	82

Table S7. Median diagnostic intervals by cancer type in emergency and nonemergency presenters according to number of prereferral consultations**.**

Cancer diagnosis	Diagnostic interval (days)											
	Emergency presenters						Nonemergency presenters					
	One or two			Three or more			One or two			Three or more		
	50th	IQR	90th	50th	IQR	90th	50th	IQR	90th	50th	IQR	90th
Lung	33.5	26–44	54.5	57	48–68	71	44	35–63.5	73	87	70–95	103
Colorectal	34	25–42	55	58	51–66	76	44	34–60	80.5	75.5	72–83	84.5
Pancreatic	45	35–57	76	74.5	56–82	90	58	42–75	97.5	99	83–112	120
Gastric	43.5	36.5–60.5	74	56	50–65	77.5	60	45.5–99	106	83.5	58–104	122.5
Oesophageal	25	19–34	38	39	32–45	51	32	26–43	53.5	59.5	53.5–67	73
Ovarian	44	31–61	71	48	32.5–65	75	55.5	40.5–69	82.5	55	42.5–74	89
Liver	33	19.5–48.5	54.5	42.5	31–54	60	48	33–70	78	55	44–74	82
Renal/bladder	26	15–37	49.5	40.5	33.5–53	56	37.5	27–47	56	67.5	58.5–74	78.5
Breast	21	14–29	45	37	31.5–46	52	33	22.5–42.5	55.5	59.5	54–67	72
Endometrial	22.5	17–35.5	38	36	26.5–50.5	53	35.5	18–48	53	60	52.5–71.5	73.5
Head/neck	27.5	23–40	43	30	27–38	42	40	28–59	73.5	55.5	44.5–67	75.5
Prostate	30	22–48	57	40	32–49	56	41	30–56.5	67	56	45–64.5	74.5
Cervical	23	20–31	36	36	31–37	49	33	21–45	58	64	50–65	69
Overall	32	22–43	56	50	37–62	76	42	30–57	73	70	57–83	103

Table S8. Analysis of correlation between diagnostic intervals and number of prereferral consultations in emergency and nonemergency presenters.

Cancer diagnosis	Emergency presenters					Nonemergency presenters				
	Spearman			Kendall		Spearman			Kendall	
	r_S	95% CI	*P*	τ	*P*	r_S	95% CI	*P*	τ	*P*
Lung	0.743	0.637–0.821	<0.0001	0.587	<0.0001	0.666	0.533–0.767	<0.0001	0.519	<0.0001
Colorectal	0.736	0.626–0.817	<0.0001	0.596	<0.0001	0.528	0.356–0.666	<0.0001	0.416	<0.0001
Pancreatic	0.685	0.550–0.785	<0.0001	0.539	<0.0001	0.652	0.504–0.763	<0.0001	0.507	<0.0001
Gastric	0.213	-0.031–0.432	0.08	0.155	0.08	0.168	-0.086–0.402	0.18	0.119	0.20
Oesophageal	0.640	0.464–0.768	<0.0001	0.511	<0.0001	0.529	0.338–0.679	<0.0001	0.410	<0.0001
Ovarian	0.221	-0.045–0.457	0.09	0.156	0.11	0.074	-0.211–0.348	0.60	0.059	0.58
Liver	0.325	0.062–0.545	0.014	0.254	0.011	0.257	-0.065–0.530	0.11	0.196	0.10
Renal/bladder	0.646	0.451–0.782	<0.0001	0.510	<0.0001	0.627	0.458–0.753	<0.0001	0.523	<0.0001
Breast	0.572	0.352–0.732	<0.0001	0.454	<0.0001	0.578	0.386–0.722	<0.0001	0.469	<0.0001
Endometrial	0.621	0.380–0.784	<0.0001	0.500	<0.0001	0.623	0.424–0.765	<0.0001	0.501	<0.0001
Head/neck	0.142	-0.187–0.442	0.38	0.100	0.42	0.145	-0.102–0.375	0.24	0.100	0.28
Prostate	0.308	-0.028–0.581	0.064	0.239	0.06	0.283	-0.0004–0.524	0.044	0.215	0.048
Cervical	0.552	0.248–0.757	0.0009	0.443	0.0011	0.576	0.336–0.746	<0.0001	0.468	<0.0001
Overall	0.534	0.481–0.584	<0.0001	0.410	0	0.500	0.447–0.550	<0.0001	0.385	0

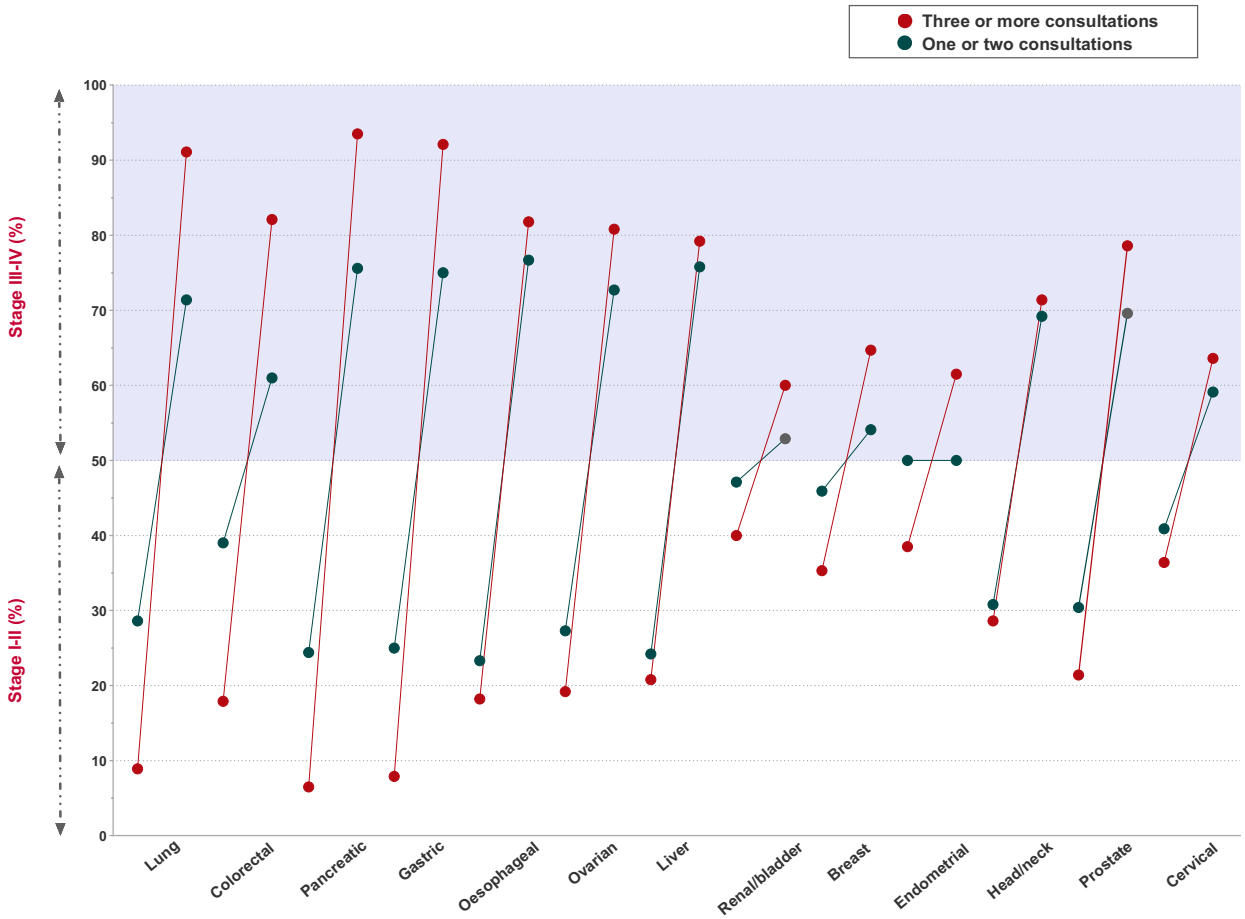

Fig. S1. Visualisation of stage at diagnosis in emergency presenters according to number of prereferral consultations (one or two vs. three or more). For each cancer type, the proportion of stage I-II (white area) and III-IV (bluish area) diagnoses is shown.

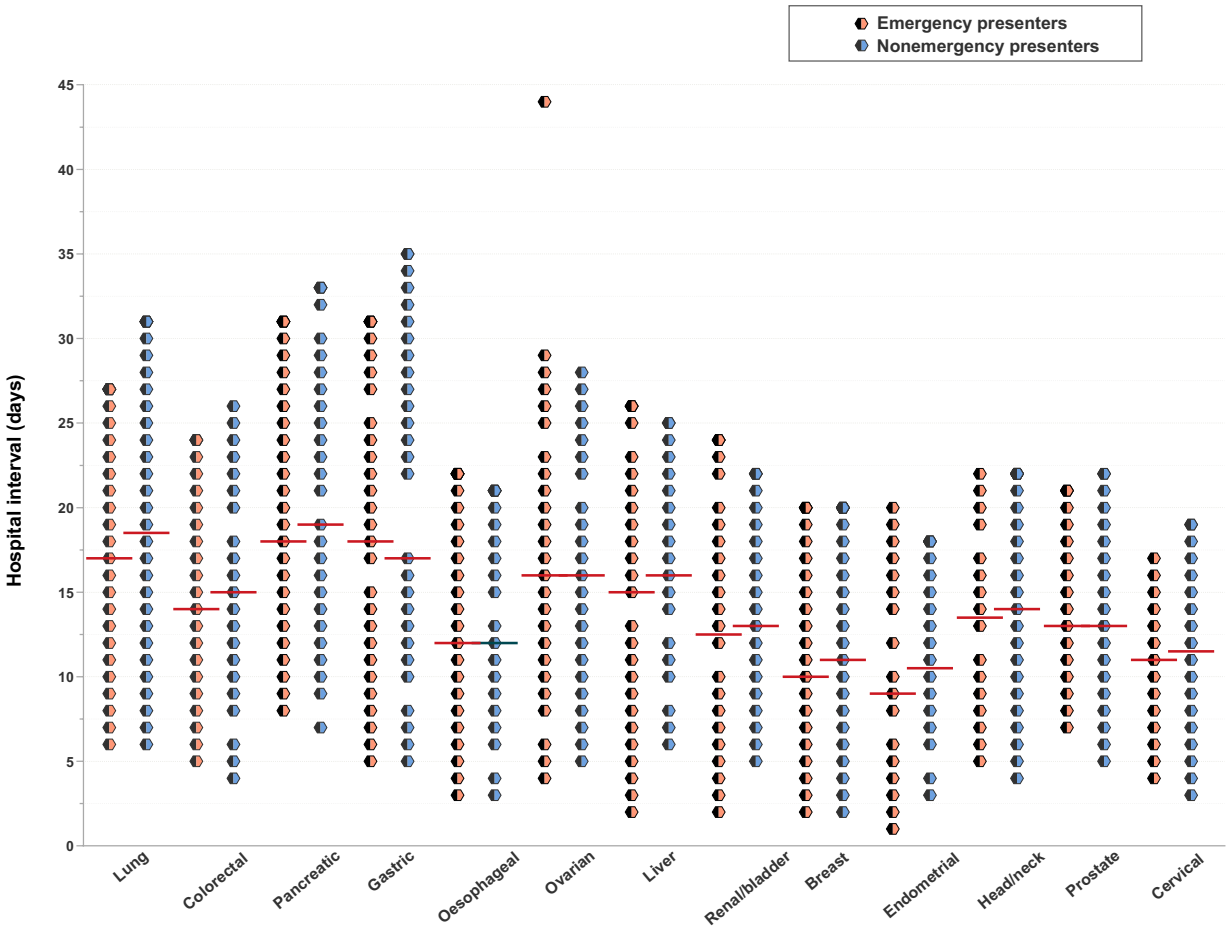

Fig. S2. Aligned dot plots portraying the median hospital interval (days) by cancer type in emergency and nonemergency presenters. Horizontal red lines in each data set represent the median.

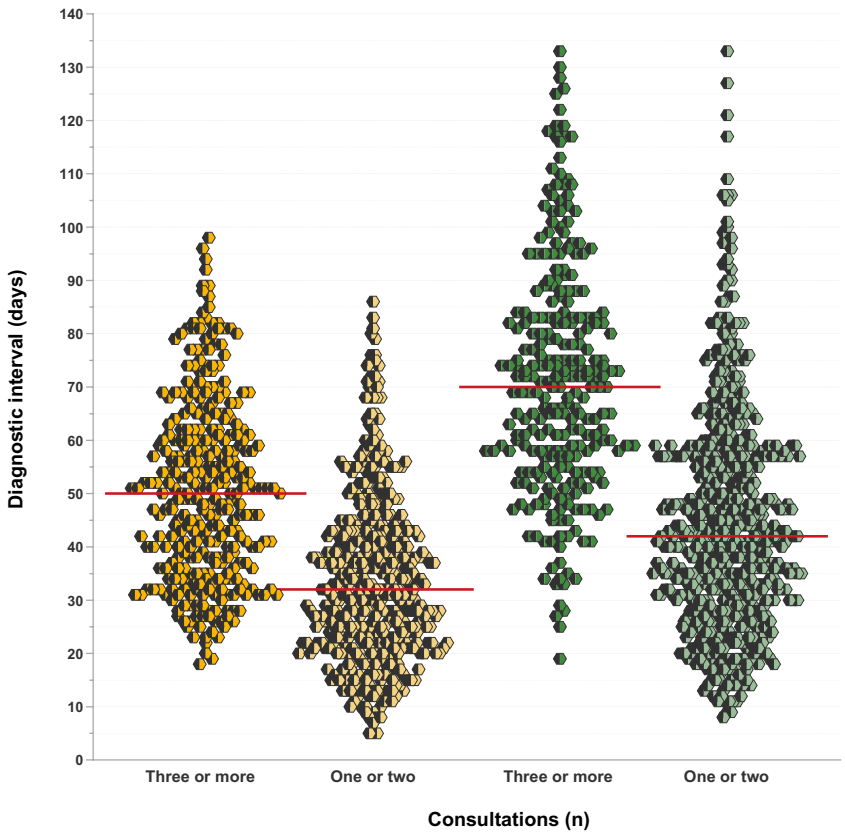

Fig. S3. Scatter dot plots representing the overall median diagnostic interval (days) in emergency and nonemergency presenters according to number of prereferral consultations. Emergency presenters with three or more vs. one or two consultations are illustrated with dark orange and lighter orange symbols, respectively. Nonemergency presenters are represented by dark green symbols (three or more consultations) and lighter green symbols (one or two consultations). Horizontal red lines in each data set indicate the median.

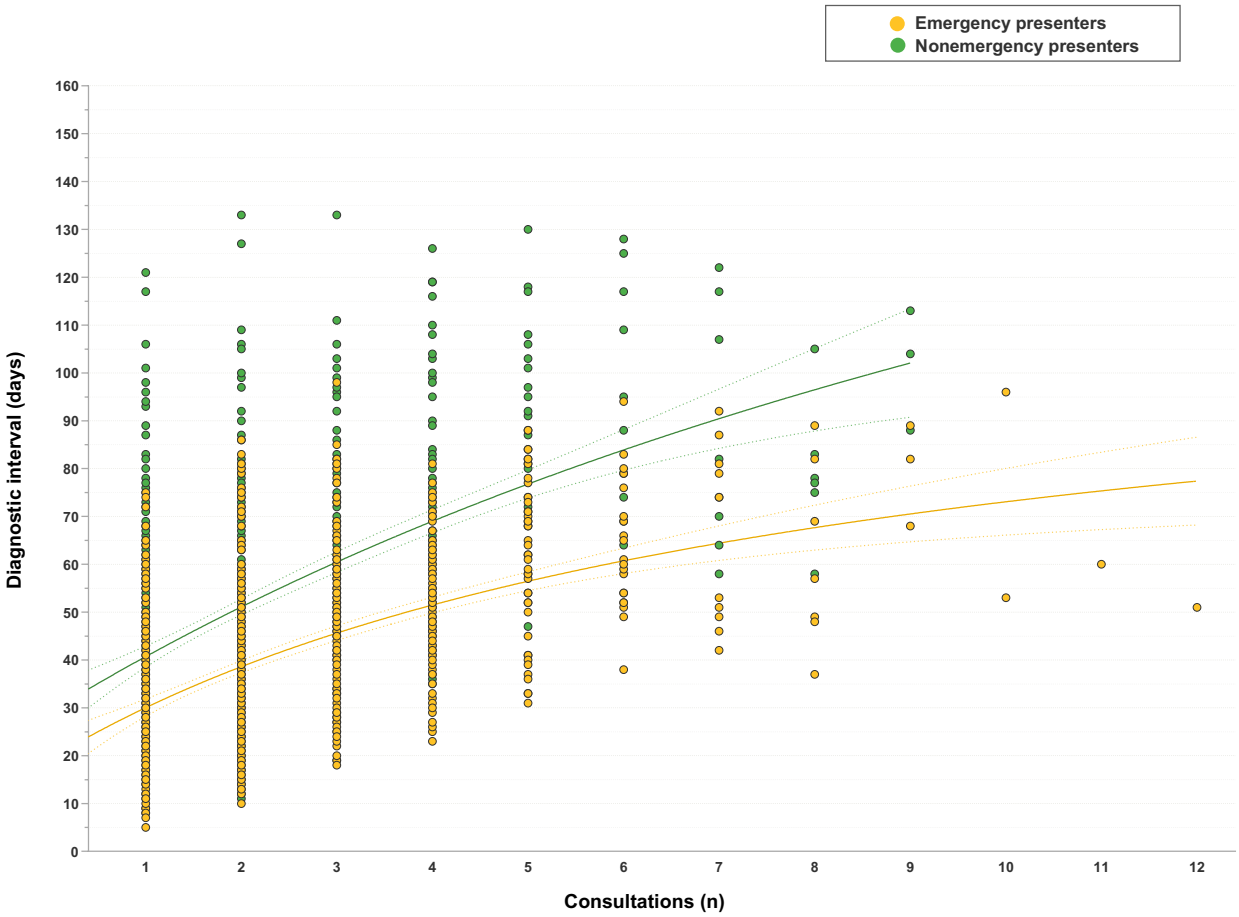

Fig. S4. Correlation plot portraying the association between the diagnostic interval (days) and the number of prereferral consultations for all emergency and nonemergency presenters. Correlation analysis showed a moderately strong positive association.

Table S1. General characteristics of study patients.

	Emergency presenters	Nonemergency presenters	*P*	Emergency presenters		*P*
				One or two	Three or more	
Gender			0.55			0.52
Men	430 (54.0)	454 (52.5)		257 (59.8)	173 (40.2)	
Women	366 (46.0)	411 (47.5)		210 (57.4)	156 (42.6)	
Age at diagnosis, years						
Mean (SD)	65.8 (14.1)	64.2 (14.6)	0.36	66.1 (14.2)	65.5 (13.9)	0.66
Median (IQR)	65 (54–77)	64 (52–77)		66 (54–77)	64 (55–77)	
18–49	132 (16.6)	177 (20.5)		78 (59.1)	54 (40.9)	0.36
50–59	161 (20.2)	180 (20.8)		87 (54.0)	74 (46.0)	
60–69	170 (21.4)	172 (19.9)		96 (56.5)	74 (43.5)	
70–79	170 (21.4)	167 (19.3)		110 (64.7)	60 (35.3)	
≥80	163 (20.5)	169 (19.5)		96 (58.9)	67 (41.1)	
Ethnicity			0.33			0.28
White	736 (92.5)	811 (93.8)		436 (59.2)	300 (40.8)	
Other ethnic groups	60 (7.5)	54 (6.2)		31 (51.7)	29 (48.3)	
Deprivation			0.46			0.53
1 Most deprived	28 (3.5)	23 (2.7)		13 (46.4)	15 (53.6)	
2	199 (25.0)	190 (22.0)		111 (55.8)	88 (44.2)	
3	280 (35.2)	318 (36.8)		167 (59.6)	113 (40.4)	
4	267 (33.5)	306 (35.4)		162 (60.7)	105 (39.3)	
5 Least deprived	22 (2.8)	28 (3.2)		14 (63.6)	8 (36.4)	
Smoking			0.18			0.32
Never	199 (25.0)	250 (28.9)		108 (54.3)	91 (45.7)	
Former	338 (42.5)	356 (41.2)		201 (59.5)	137 (40.5)	
Current	259 (32.5)	259 (29.9)		158 (61.0)	101 (39.0)	
Alcohol consumption			0.28			0.29
None	502 (63.1)	562 (65.0)		286 (57.0)	216 (43.0)	
Low	220 (27.6)	241 (27.9)		132 (60.0)	88 (40.0)	
Excessive	74 (9.3)	62 (7.2)		49 (66.2)	25 (33.8)	
Comorbidity score			0.48			0.60
0	270 (33.9)	324 (37.5)		150 (32.1)	120 (36.5)	
1	259 (32.5)	272 (31.4)		154 (33.0)	105 (31.9)	
2	179 (22.5)	184 (21.3)		108 (23.1)	71 (21.6)	
≥ 3	88 (11.1)	85 (9.8)		55 (11.8)	33 (10.0)	
Symptoms at presentation						
Bleeding	117 (14.7)	148 (17.1)		73 (62.4)	44 (37.6)	
Abdominal symptoms	458 (57.5)	444 (51.3)		256 (55.9)	202 (44.1)	
Respiratory symptoms	82 (10.3)	82 (9.5)		49 (59.8)	33 (40.2)	
Pain	75 (9.4)	76 (8.8)		46 (61.3)	29 (38.7)	
Urological symptoms	57 (7.2)	80 (9.2)		34 (59.6)	23 (40.4)	
Lumps or masses	69 (8.7)	106 (12.3)		45 (65.2)	24 (34.8)	
Nonspecific symptoms	386 (48.5)	349 (40.3)		201 (52.1)	185 (47.9)	

Iron-deficiency anaemia	41 (5.2)	48 (5.5)	26 (63.4)	15 (36.6)
Suspicion of cancer in imaging test	37 (4.6)	56 (6.5)	22 (59.5)	15 (40.5)
Total	796	865	467	329

Continuous variables are presented as means (SD) or medians (IQR) and categorical variables as n (%)

Table S2. Distribution of cancers in emergency and nonemergency presenters according to stage at diagnosis.

Cancer diagnosis	Emergency presenters					Nonemergency presenters					
	No.	I-II	III	IV	III-IV	No.	I-II	III	IV	III-IV	*P* *
Lung	101	20 (19.8)	17 (16.8)	64 (63.4)	81 (80.2)	96	37 (38.5)	17 (17.7)	42 (43.8)	59 (61.5)	0.0046
Colorectal	98	30 (30.6)	27 (27.6)	41 (41.8)	68 (69.4)	91	42 (46.2)	24 (26.4)	25 (27.5)	49 (53.8)	0.036
Pancreatic	87	13 (14.9)	16 (18.4)	58 (66.7)	74 (85.1)	84	24 (28.6)	13 (15.5)	47 (56.0)	60 (71.4)	0.041
Gastric	70	11 (15.7)	13 (18.6)	46 (65.7)	59 (84.3)	65	21 (32.3)	10 (15.4)	34 (52.3)	44 (67.7)	0.027
Oesophageal	65	14 (21.5)	15 (23.1)	36 (55.4)	51 (78.5)	75	34 (45.3)	11 (14.7)	30 (40.0)	41 (54.7)	0.0041
Ovarian	59	14 (23.7)	22 (37.3)	23 (39.0)	45 (76.3)	52	23 (44.2)	15 (28.8)	14 (26.9)	29 (55.8)	0.027
Liver	57	13 (22.8)	12 (21.1)	32 (56.1)	44 (77.2)	41	12 (29.3)	8 (19.5)	21 (51.2)	29 (70.7)	0.49
Renal/bladder	54	24 (44.4)	11 (20.4)	19 (35.2)	30 (55.6)	72	48 (66.7)	11 (15.3)	13 (18.1)	24 (33.3)	0.018
Breast	54	23 (42.6)	6 (11.1)	25 (46.3)	31 (57.4)	67	48 (71.6)	6 (9.0)	13 (19.4)	19 (28.4)	0.0016
Endometrial	41	19 (46.3)	7 (17.1)	15 (36.6)	22 (53.7)	56	41 (73.2)	7 (12.5)	8 (14.3)	15 (26.8)	0.011
Head/neck	40	12 (25.0)	4 (10.0)	24 (60.0)	28 (70.0)	69	34 (49.3)	7 (10.1)	28 (40.6)	35 (50.7)	0.07
Prostate	37	10 (27.0)	4 (10.8)	23 (62.2)	27 (73.0)	51	27 (52.9)	13 (25.5)	11 (21.6)	24 (47.1)	0.018
Cervical	33	13 (39.4)	7 (21.2)	13 (39.4)	20 (60.6)	46	31 (67.4)	6 (13.0)	9 (19.6)	15 (32.6)	0.021
All	796	216 (27.1)	161 (20.4)	419 (52.6)	580 (72.9)	865	422 (48.8)	148 (17.1)	295 (34.1)	443 (51.2)	<0.0001

* Stage I-II and III-IV in emergency and nonemergency presenters were compared with the Fisher's exact test.

Table S3. Stage at diagnosis in emergency presenters according to number of prereferral consultations.

Cancer diagnosis	Emergency presenters						
	One or two			Three or more			
	No.	I-II	III-IV	No.	I-II	III-IV	*P* *
Lung	56	16 (28.6)	40 (71.4)	45	4 (8.9)	41 (91.1)	0.022
Colorectal	59	23 (39.0)	36 (61.0)	39	7 (17.9)	32 (82.1)	0.043
Pancreatic	41	10 (24.4)	31 (75.6)	46	3 (6.5)	43 (93.5)	0.033
Gastric	32	8 (25.0)	24 (75.0)	38	3 (7.9)	35 (92.1)	0.10
Oesophageal	43	10 (23.3)	33 (76.7)	22	4 (18.2)	18 (81.8)	0.76
Ovarian	33	9 (27.3)	24 (72.7)	26	5 (19.2)	21 (80.8)	0.55
Liver	33	8 (24.2)	25 (75.8)	24	5 (20.8)	19 (79.2)	1
Renal/bladder	34	16 (47.1)	18 (52.9)	20	8 (40.0)	12 (60.0)	0.78
Breast	37	17 (45.9)	20 (54.1)	17	6 (35.3)	11 (64.7)	0.56
Endometrial	28	14 (50.0)	14 (50.0)	13	5 (38.5)	8 (61.5)	0.52
Head/neck	26	8 (30.8)	18 (69.2)	14	4 (28.6)	10 (71.4)	1
Prostate	23	7 (30.4)	16 (69.6)	14	3 (21.4)	11 (78.6)	0.71
Cervical	22	9 (40.9)	13 (59.1)	11	4 (36.4)	7 (63.6)	1
All	467	155 (33.2)	312 (66.8)	329	61 (18.5)	268 (81.5)	<0.0001

* The Fisher's exact test was used to compare stage I-II and III-IV in emergency presenters with one or two vs. three or more prereferral consultations.

Table S4. Primary care and diagnostic intervals by cancer type in emergency and nonemergency presenters.

Cancer diagnosis	Primary care interval (days)								Diagnostic interval (days)							
	Emergency presenters				Nonemergency presenters				Emergency presenters				Nonemergency presenters			
	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th
Lung	16.5	27	43.5	50	22	42	62	76	31	44	57.5	69	41	61.5	80	95
Colorectal	16	26	44	53	26	40	62	68	32	41.5	58	66	37	59	75	83
Pancreatic	23	36	58	67	32	50	83	92.5	41	56	79	85	50	75.5	100.5	117
Gastric	24	33.5	46	52	29	51	81.5	94	41	52.5	63	75	47	79	100.5	116.5
Oesophageal	9.5	17	26	32	17	26	40	50	23	32	38	45.5	28	38	54	62
Ovarian	16	33	47	58	24	36.5	59	66	32	46	64	73	42	55	73	83
Liver	11.5	25	36.5	42	23	34	52.5	61	26	41	51	59	36	51	70.5	80
Renal/bladder	11	20	28	37	18	29	45.5	58	24.5	32	41.5	54.5	30.5	44	59	72
Breast	9	15	27	37	17	25	43	49	15	25	40	46	27	38	55	62.5
Endometrial	12	18	28	37	14.5	27.5	44	52	18	27	37	49	23	37.5	53	66
Head/neck	11	19.5	27	32	18	28	49.5	56	25	29	39	43	30	43	60.5	74
Prostate	14.5	19	31	39	23	29	44	54	25.5	33	48	57	33	47	59	69
Cervical	11.5	18	25.5	32	13	28	43	55.5	21.5	30	35.5	40.5	26	43.5	57	64
Overall	14	24	37	50	21	36	52	68	27	38	54	68	34	49	69	86.5

Table S5. Overall primary care intervals (days) in emergency and nonemergency presenters with 1, 2, 3, 4, and ≥5 prereferral consultations.

Consultations	Emergency presenters (N=796)				Nonemergency presenters (N=865)			
	Primary care interval (days)				Primary care interval (days)			
	No. (%)	50th	IQR	90th	No. (%)	50th	IQR	90th
1	247 (31.0)	14	8–22	37	312 (36.1)	25.5	15–38	50
2	220 (27.6)	21.5	13–31	44	282 (32.6)	29.5	18–44	58
3	159 (20.0)	27	20–38	51	107 (12.4)	47	38–58	72
4	84 (10.6)	34.5	26–46	52.5	92 (10.6)	54.5	44–66	82
≥5	86 (10.8)	46	37–56	66	72 (8.3)	61.5	54–80	97

Table S6. Primary care intervals (days) by cancer type in emergency and nonemergency presenters with 1-2 vs. ≥3 prereferral consultations.

Cancer diagnosis	Primary care interval (days)															
	Emergency presenters								Nonemergency presenters							
	One or two				Three or more				One or two				Three or more			
	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th	25th	50th	75th	90th
Lung	8	18	26	37	31.5	43	48	53.5	15	27	43	52	52	68	77	80
Colorectal	12	18	25	39	35	46	53	56	20	32	44	59	55.5	65	69	71
Pancreatic	17.5	25	36.5	54.5	36	55	65	69	25	36	50	79.5	59.5	82	90.5	101
Gastric	22	28	38	51.5	29	42.5	48	52	26.5	47	77.5	92	42.5	64	84	100
Oesophageal	6	13	17	27	20	26	32	35	14	23	32.5	39	40.5	47.5	51	54
Ovarian	14	30	44.5	52.5	19.5	33.5	49	59	18	36	58.5	64.5	32	41	61	68
Liver	7.5	15	37.5	41.5	20	25.5	36	48	19	33	48	59	24.5	40.5	59	62.5
Renal/bladder	7	13.5	20.5	28.5	23.5	28.5	37	39	15	23.5	35	44	44	54.5	59	61
Breast	6	12	17	29.5	19.5	27	37	43	14.5	22	31	43.5	43.5	48.5	50.5	52.5
Endometrial	8	15.5	20	31.5	19.5	28	37.5	44	10.5	24	36	44.5	44	50.5	55	56.5
Head/neck	7.5	14.5	25	31.5	16	21.5	29.5	32.5	15	27	43	55	25.5	42.5	54	57
Prostate	11	18	29	38	19	24.5	36	40.5	19.5	28	41.5	49.5	27.5	43.5	52	56
Cervical	9	15.5	20.5	25.5	21	26	33	35	11	24	34	44	40	50	58	60
Overall	10	17	28	39	24	34	47	56	16	27	41	54	43	54	68	82

Table S7. Median diagnostic intervals by cancer type in emergency and nonemergency presenters according to number of prereferral consultations**.**

Cancer diagnosis	Diagnostic interval (days)											
	Emergency presenters						Nonemergency presenters					
	One or two			Three or more			One or two			Three or more		
	50th	IQR	90th	50th	IQR	90th	50th	IQR	90th	50th	IQR	90th
Lung	33.5	26–44	54.5	57	48–68	71	44	35–63.5	73	87	70–95	103
Colorectal	34	25–42	55	58	51–66	76	44	34–60	80.5	75.5	72–83	84.5
Pancreatic	45	35–57	76	74.5	56–82	90	58	42–75	97.5	99	83–112	120
Gastric	43.5	36.5–60.5	74	56	50–65	77.5	60	45.5–99	106	83.5	58–104	122.5
Oesophageal	25	19–34	38	39	32–45	51	32	26–43	53.5	59.5	53.5–67	73
Ovarian	44	31–61	71	48	32.5–65	75	55.5	40.5–69	82.5	55	42.5–74	89
Liver	33	19.5–48.5	54.5	42.5	31–54	60	48	33–70	78	55	44–74	82
Renal/bladder	26	15–37	49.5	40.5	33.5–53	56	37.5	27–47	56	67.5	58.5–74	78.5
Breast	21	14–29	45	37	31.5–46	52	33	22.5–42.5	55.5	59.5	54–67	72
Endometrial	22.5	17–35.5	38	36	26.5–50.5	53	35.5	18–48	53	60	52.5–71.5	73.5
Head/neck	27.5	23–40	43	30	27–38	42	40	28–59	73.5	55.5	44.5–67	75.5
Prostate	30	22–48	57	40	32–49	56	41	30–56.5	67	56	45–64.5	74.5
Cervical	23	20–31	36	36	31–37	49	33	21–45	58	64	50–65	69
Overall	32	22–43	56	50	37–62	76	42	30–57	73	70	57–83	103

Table S8. Analysis of correlation between diagnostic intervals and number of prereferral consultations in emergency and nonemergency presenters.

Cancer diagnosis	Emergency presenters					Nonemergency presenters				
	Spearman			Kendall		Spearman			Kendall	
	r_S	95% CI	*P*	τ	*P*	r_S	95% CI	*P*	τ	*P*
Lung	0.743	0.637–0.821	<0.0001	0.587	<0.0001	0.666	0.533–0.767	<0.0001	0.519	<0.0001
Colorectal	0.736	0.626–0.817	<0.0001	0.596	<0.0001	0.528	0.356–0.666	<0.0001	0.416	<0.0001
Pancreatic	0.685	0.550–0.785	<0.0001	0.539	<0.0001	0.652	0.504–0.763	<0.0001	0.507	<0.0001
Gastric	0.213	-0.031–0.432	0.08	0.155	0.08	0.168	-0.086–0.402	0.18	0.119	0.20
Oesophageal	0.640	0.464–0.768	<0.0001	0.511	<0.0001	0.529	0.338–0.679	<0.0001	0.410	<0.0001
Ovarian	0.221	-0.045–0.457	0.09	0.156	0.11	0.074	-0.211–0.348	0.60	0.059	0.58
Liver	0.325	0.062–0.545	0.014	0.254	0.011	0.257	-0.065–0.530	0.11	0.196	0.10
Renal/bladder	0.646	0.451–0.782	<0.0001	0.510	<0.0001	0.627	0.458–0.753	<0.0001	0.523	<0.0001
Breast	0.572	0.352–0.732	<0.0001	0.454	<0.0001	0.578	0.386–0.722	<0.0001	0.469	<0.0001
Endometrial	0.621	0.380–0.784	<0.0001	0.500	<0.0001	0.623	0.424–0.765	<0.0001	0.501	<0.0001
Head/neck	0.142	-0.187–0.442	0.38	0.100	0.42	0.145	-0.102–0.375	0.24	0.100	0.28
Prostate	0.308	-0.028–0.581	0.064	0.239	0.06	0.283	-0.0004–0.524	0.044	0.215	0.048
Cervical	0.552	0.248–0.757	0.0009	0.443	0.0011	0.576	0.336–0.746	<0.0001	0.468	<0.0001
Overall	0.534	0.481–0.584	<0.0001	0.410	0	0.500	0.447–0.550	<0.0001	0.385	0

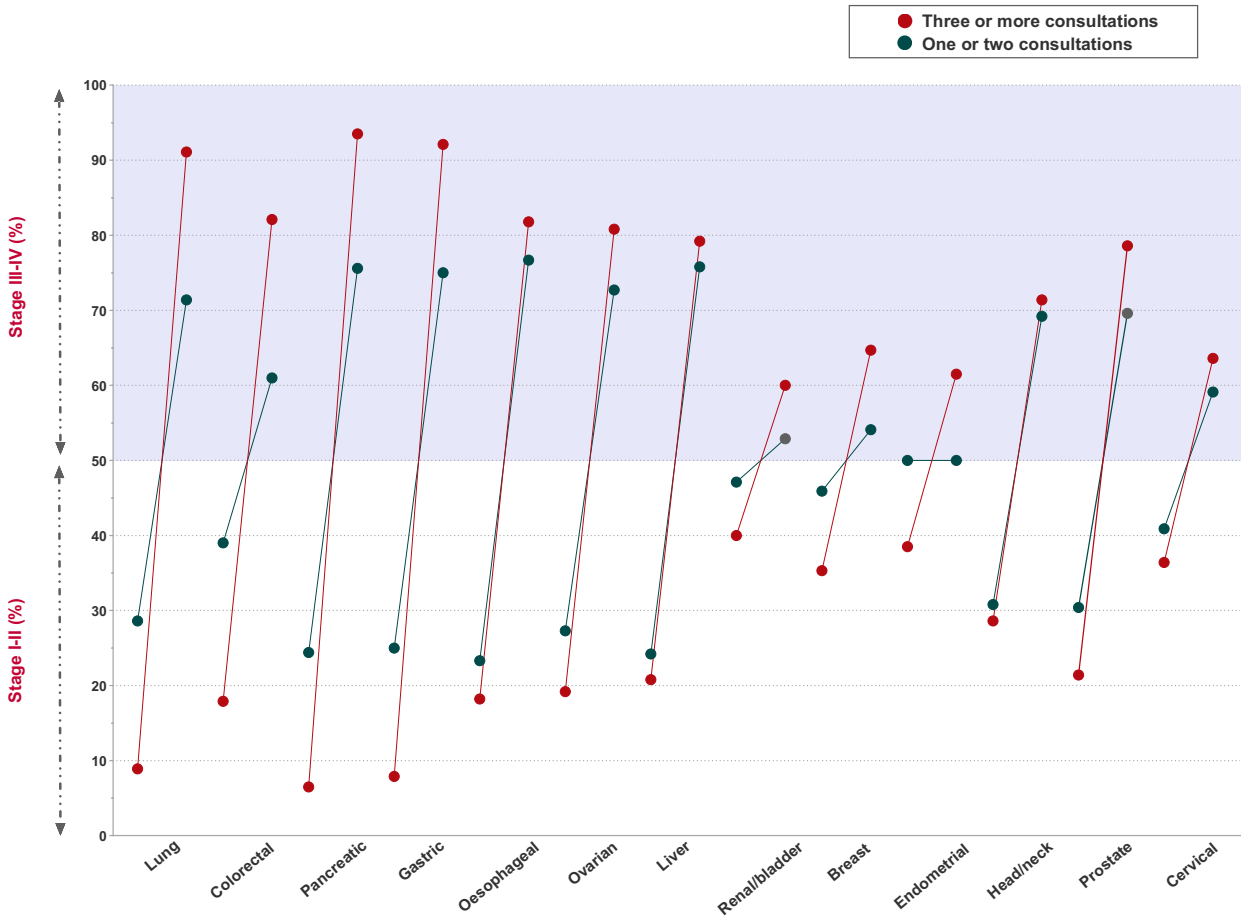

Fig. S1. Visualisation of stage at diagnosis in emergency presenters according to number of prereferral consultations (one or two vs. three or more). For each cancer type, the proportion of stage I-II (white area) and III-IV (bluish area) diagnoses is shown.

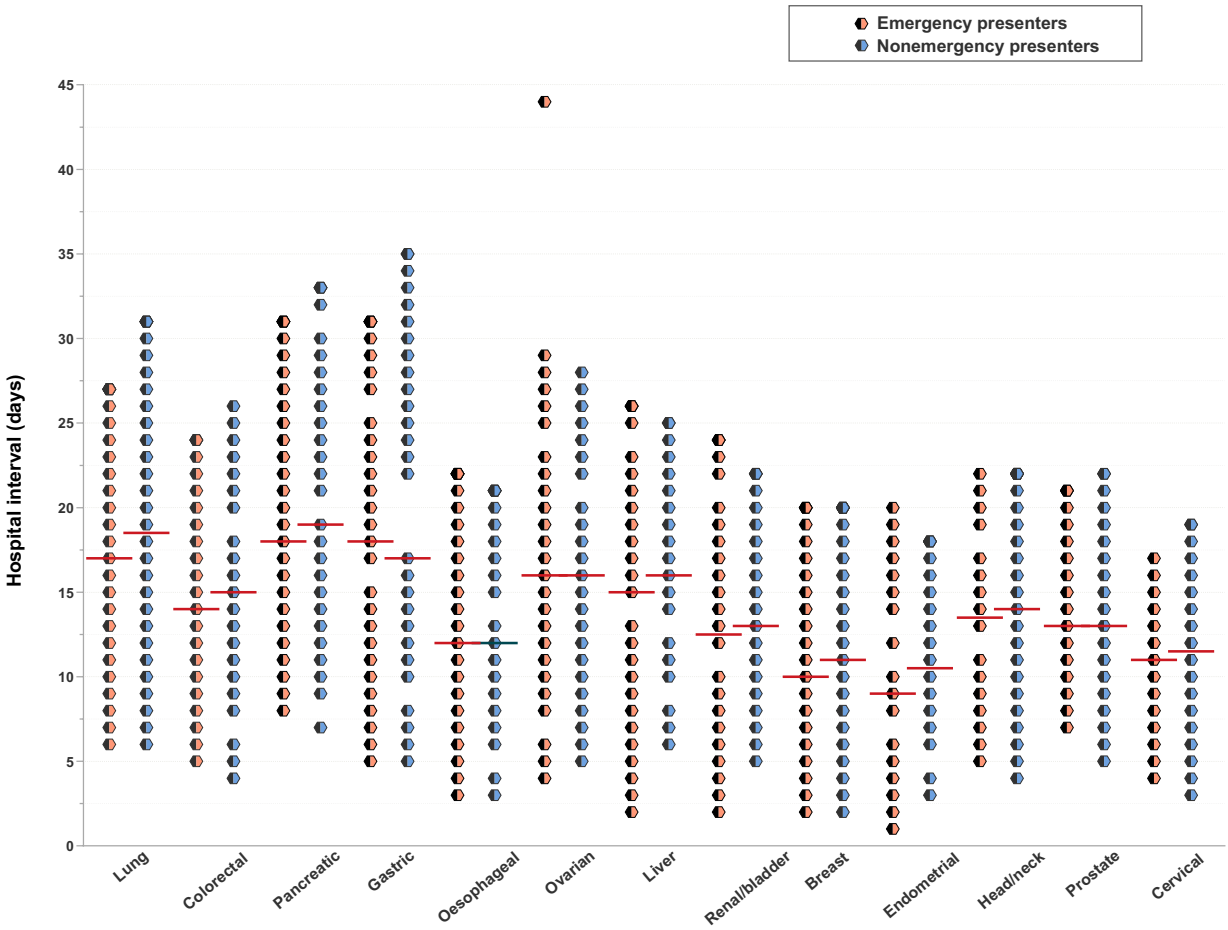

Fig. S2. Aligned dot plots portraying the median hospital interval (days) by cancer type in emergency and nonemergency presenters. Horizontal red lines in each data set represent the median.

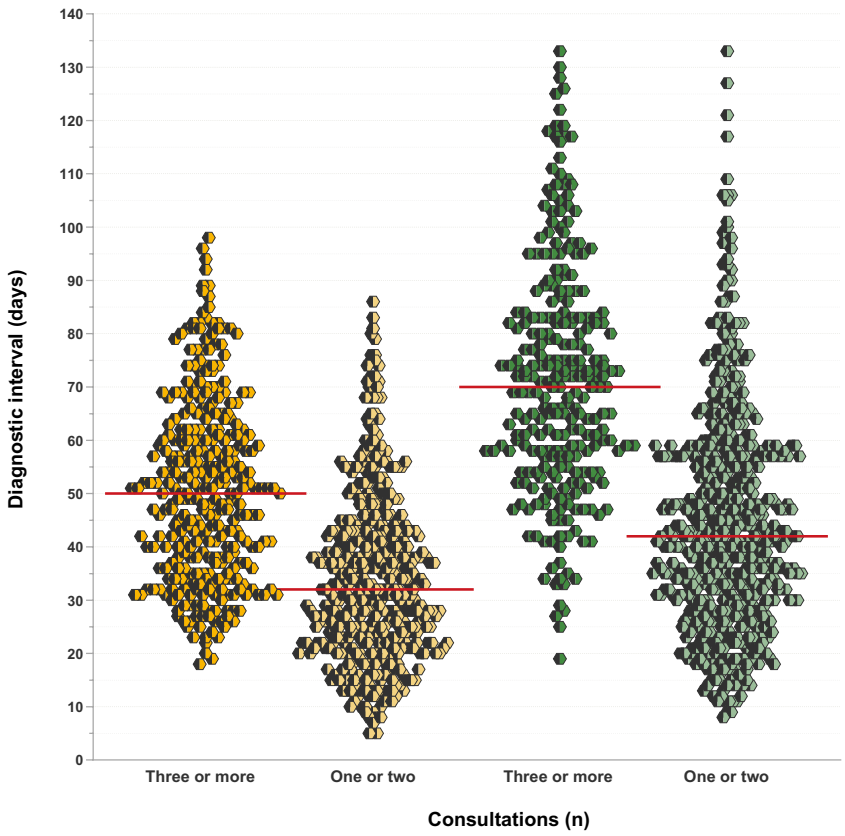

Fig. S3. Scatter dot plots representing the overall median diagnostic interval (days) in emergency and nonemergency presenters according to number of prereferral consultations. Emergency presenters with three or more vs. one or two consultations are illustrated with dark orange and lighter orange symbols, respectively. Nonemergency presenters are represented by dark green symbols (three or more consultations) and lighter green symbols (one or two consultations). Horizontal red lines in each data set indicate the median.

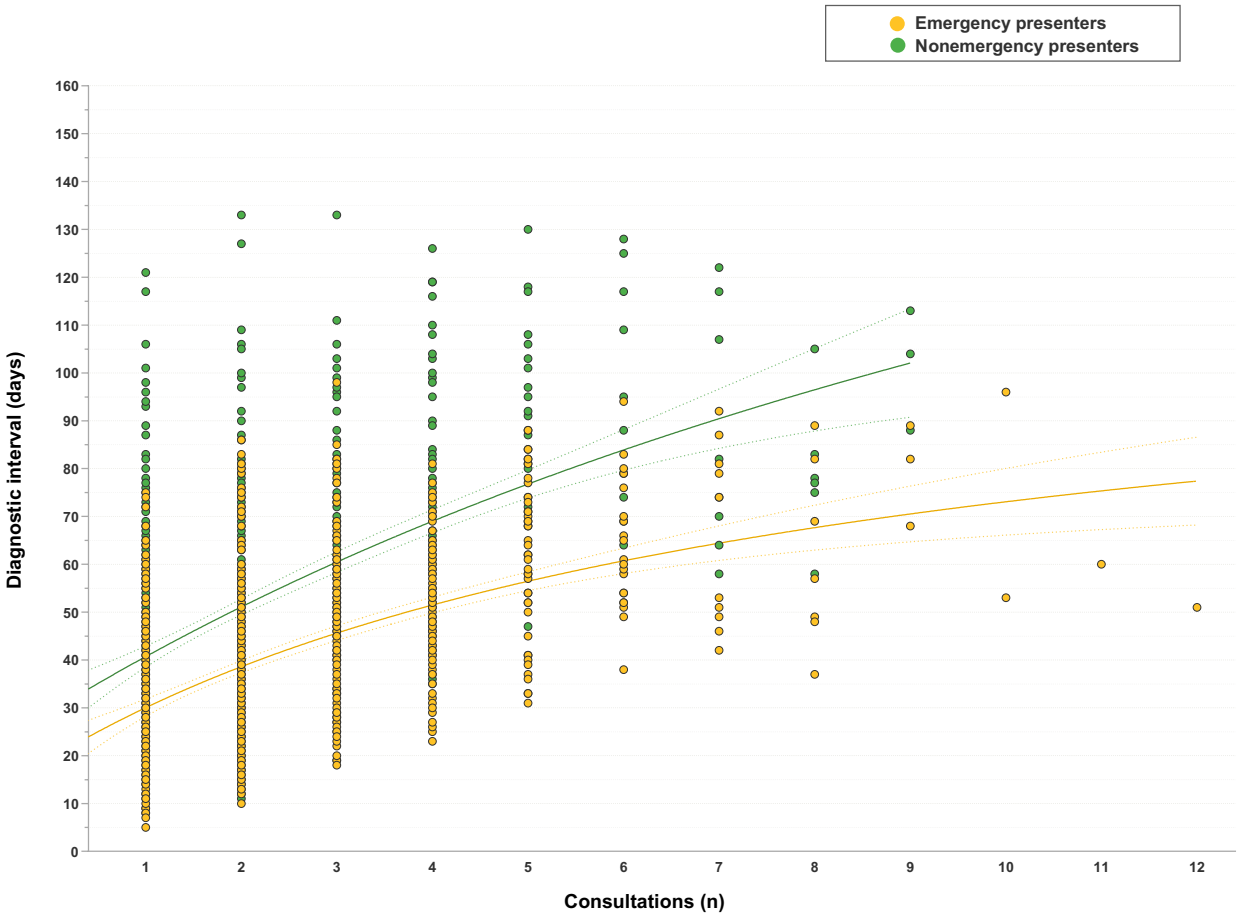

Fig. S4. Correlation plot portraying the association between the diagnostic interval (days) and the number of prereferral consultations for all emergency and nonemergency presenters. Correlation analysis showed a moderately strong positive association.