Impact of Geography on Scottish Cancer Diagnoses in Primary Care: Results from a National Cancer Diagnosis Audit

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ABSTRACT- Word count 250 (limit 250)

Background

A recent meta-analysis of global research found cancer patients living in rural locations are 5% less likely to survive than their urban counterparts, a survival disadvantage that has never been satisfactorily explained.

Aims

[1] To describe and compare primary-care involvement in the diagnosis of cancer between rural and urban patients in Scotland.

[2] To compare the length of key diagnostic pathway intervals between rural and urban cancer patients in Scotland.

Methods

Participating GPs in the Scottish National Cancer Audit of cancer diagnosis (2017) collected data from primary-care medical records on the diagnostic pathway of patients diagnosed in 2014. Residential postcodes designated the patients as rural or urban dwellers. Key cancer diagnostic pathway intervals (primary, diagnostic, secondary, and treatment) were compared using binary logistic regression. Descriptive analysis included comparison of patient characteristics, and routes to diagnosis.

Results

73 Scottish general practices provided data on 1,905 cancer diagnoses. Rural patients did not have higher odds of prolonged diagnostic intervals compared to urban patients but were significantly more likely to have had a cancer alarm feature at presentation and three or more primary-care consultations prior to referral. Rural GPs were significantly more likely to perceive an avoidable delay in their patient's diagnostic pathway.

Conclusion

There was no evidence that rural patients were more likely to be subject to prolonged cancer diagnostic delays than urban patients. Rural patients may experience primary care differently in the lead-up to a cancer diagnosis. The effect on outcome is probably negligible, but further research is required to confirm this.

KEYWORDS: Cancer; clinical audit; diagnosis; delay; primary care; rurality

Main text word count = 3519

(Authors whose manuscripts exceed 3,000 words are asked to state this in their covering letter to the Editor-in-Chief)

1. INTRODUCTION

Rural-dwellers who develop cancer in Scotland (Campbell et al, 2000) and other developed countries have poorer outcomes (Coory et al, 2006; Pozet et al, 2008; Underhill et al, 2006; Westeel et al, 2007, Murage et al, 2018) but reasons why are unclear.

A systematic review and meta-analysis of studies comparing cancer survival between urban and rural residents found rural-dwellers were five per cent less likely to survive cancer than urban counterparts, with little evidence on underlying mechanisms (Carriere et al, 2018). The review included a narrative synthesis of potential explanations which concluded causes were obscure and likely to be complex and multifactorial.

Other research studies exploring urban versus rural cancer survival have been less definitive in establishing a rural cancer disadvantage, but are perhaps suggestive as to potential mechanisms. For example international studies comparing urban-rural survival in breast, lung and pancreatic cancer found that a rural survival disadvantage became non-significant once treatment received was controlled for (Mitchell et al, 2011, Johnson et al, 2014; Kirkegård et al, 2018). Also, studies from Australia and New Zealand concluded that their demonstration of no difference in rural-urban cancer survival reflected deliberate policies to counteract centralization of cancer services in urban areas (Bennett et al, 2007; Dasgupta et al, 2012).

Recent research in Scotland provides further new insight. Turner et al (2017), using geographic information systems (GIS) to locate patients with respect to healthcare services, explored associations between travel burden and cancer outcomes. Analysis including more than 12,000 cancer patients from across Northeast Scotland revealed a rural paradox. The most remote patients living more than an hour's travel from their cancer treatment centre were treated more quickly, but were significantly less likely to survive to one-year compared to those living closer, even adjusting for advanced cancer at presentation. This contradiction has not been satisfactorily explained.

It has been argued that initiatives to improve rural health should not focus solely on determining and responding to area-based explanations for rural inequalities and should instead target all potential risk determinants collectively (Smith et al, 2008). However 17.4% of Scotland's population (one million people) live rurally (Scottish Government, 2018) and such comprehensively unfocused policies risk being extremely costly, inefficient and ineffective. It seems prudent, therefore, to take every opportunity to elucidate precise targets for intervention.

In 2016-17, Cancer Research UK, together with NHS partners, the Royal College of General Practitioners (RCGP) and Macmillan Cancer Support, conducted a National Cancer Diagnosis

Audit (NCDA) in Scotland (Murchie et al, 2020). The aim of the NCDA was to understand primary care cancer diagnosis. This audit collected granular data on diagnostic pathway from primary care medical records on cancer patients diagnosed in 2014, supplemented by linkage to the Scottish Cancer Registry. This paper now compares 1,905 cancer patients included in the Scottish NCDA with respect to demographic characteristics, routes to diagnosis and key cancer pathway intervals to gain new information on potential reasons for Scotland's geographical cancer inequality. The NCDA provided a representative sample of cancers diagnosed in Scotland in 2014 with respect to key demographics, details of which are available from the ISD Scotland website (ISD Scotland, 2019).

2. METHODS

2.1 Study population and data collection

In late 2016 the Information Services Division (ISD), NHS Scotland, assigned all incident cancer cases from the whole of 2014 (excluding non-melanoma skin cancer) to their registered general practice at diagnosis using the Scottish Cancer Registry. NCDA participants were volunteer practices recruited following promotion by the RCGP, Cancer Research UK and Macmillan Cancer Support. Registration included signing Caldicott Data Release Forms to permit data-sharing with ISD. Approved practice leads (usually a GP) were securely sent pre-prepared Excel data-collection forms for eligible cancer diagnoses. Practices returned de-identified forms to ISD using secure NHS email. Forms were issued and returned between February and June 2017.

The eight-sectioned excel form, detailing patients' pathways to cancer diagnosis were pre-populated with Scottish Cancer Registry and Cancer Waiting Times data. This included cancer type, stage, date of cancer diagnosis, date of death, date of receipt of cancer referral from primary care, date of start of treatment, level of urgency, source of referral and method of first detection (Appendix I). Primary-care held medical records were used to validate dates and vital status. Residential postcodes enabled the Scottish Index of Multiple Deprivation (SIMD) grouped into one of five categories using quintiles and Scottish Government 2-fold and 6-fold Urban-Rural Classifications to be assigned to each patient(Scottish Government, 2018; Scottish Government, 2018).(Figure 1)

The form also gathered data on patient socio-demographic characteristics; presence of any co-morbidities (categorised into 0, 1-2, and 3 or more); number of consultations before referral; any primary care investigations; and any perceived avoidable delays in the referral pathway.

2.2 Analysis

The analysis reported adopted similar data-definitions as those reported in the Scottish NCDA baseline paper (Murchie et al, 2020). Symptoms and positive signs recorded in NCDA as having been present at first consultations were mapped onto site-specific Scottish Referral

Guidelines for Urgent Suspected Cancer by PM (Scottish Executive, 2014). The presence at first presentation of any single guideline symptom or positive sign for any cancer according to the Scottish guidelines was recoded to indicate "at least one alarm feature at presentation." Primary care-led investigations were grouped into blood, urinary, imaging, endoscopy and other tests.

Key cancer pathway intervals, (primary care, diagnostic, secondary care and treatment intervals) were calculated using available dates (Weller et al, 2012). Primary care interval (PCI) measures number of days from the date of first relevant presentation in primary care to the date of first GP referral. Diagnostic interval (DI) measures number of days from the first relevant presentation in primary care to date of cancer diagnosis. Secondary care interval (SCI) measures the number of days between GP referral to date of cancer diagnosis, and treatment Interval (TI) measures number of days from diagnosis to date treatment started. Any intervals of <0 and >730 days were excluded from further analysis. Medians and inter-quartile-ranges were calculated, as was the proportion of patients with intervals of more than 60 or 90 days.

The median number of consultations prior to referral was calculated, as was proportion of patients requiring three or more consultations before referral. Based on participating GPs' perception where they subjectively judged whether in hindsight, an "avoidable delay" had occurred, we described the health care setting and stage in the diagnostic pathway where the delay was attributed to.

In subsequent analysis the distribution of categorical variables was compared between rural and urban groups (using the Scottish 2-fold classification) using contingency tables and Chi-squared tests. Median pathway intervals were combined using appropriate non-parametric tests. To explore relatively prolonged pathway intervals for urban and rural participants eight binary variables >60 days or >90 days (yes or no) for each of the four key intervals (primary care, secondary care, diagnostic and treatment interval) were derived. Subsequently the univariate odds (rural vs urban) of a delay >60 and >90 days were calculated using univariate binary logistic function in SPSS V.23 (IBM, Armonk, NY, USA). Subsequently, multivariable analysis was conducted to calculate the adjusted odds (rural vs urban) for each interval being prolonged >60 and >90 days using the same SPSS V.23 function, but this time adding cancer site, deprivation, number of comorbidities, gender, and presence of at least one alarm feature to adjust for potential confounding. A further sensitivity analysis was conducted using the Scottish 6-fold urban rural classification (Appendix II).

3. RESULTS

Seventy-three Scottish general practices (7.7% of all Scottish general practices in 2017) submitted data on 1,905 cancer diagnoses (6.0% of cancers diagnosed in Scotland in 2014). Characteristics of this patient sample show that 76.4% were urban-dwelling and 23.6% were rural-dwelling. There were slightly more men (53.6%) than women in rural areas, and in urban areas, males 50.3%.

Age group distribution was similar in the two populations (rural median age 70 (IQR 60-78), urban 70 (IQR 60-77). Most rural patients tended to be from less deprived areas, SIMD categories 3 and 4, (68.2% v 30.7%). There were no great differences in cancer type apart from a slightly lower incidence in rural areas of lung cancer (15.1% v 20.0). Rural patients were also slightly more likely to have comorbidities. There was no significant variation in cancer stage at diagnosis (table 1).

Detection of cancer and route to diagnosis

There were no significant differences in how patients' cancer was detected between urban and rural areas. For most patients this was through clinical presentation (urban 91.6%, rural 92.7% respectively)(table 2).

Compared with urban patients, fewer rural patients were referred routinely (9.3% v 11.1%) or through emergency referral (21.5% v 19.8%), more were referred through the urgent-not for suspected cancer (12.0% v 8.8%) and urgent suspected cancer route (40.4% v 38.9%) although these differences were not statistically significant (table 2).

Alarm symptoms at presentation

There were no significant differences in presentation of alarm symptoms by cancer type at first consultation irrespective of locality, apart from urban patients with testicular or penile cancer (P=0.013), though numbers were very low (n=44). Across all cancers, rural patients were significantly more likely to have at least one alarm feature at presentation (P=0.044) (table 3).

Symptoms and signs, pre-referral consultations, and avoidable delay

No significant difference was found between urban and rural-dwellers in the number of symptoms at presentation, or in the number of positive signs and tests at presentation. However, rural patients had significantly more consultations before referral than urban patients (Median (IQR) 1, 1-3: P=0.016), and were also significantly more likely to have three or more consultations before referral (P= 0.002), (table 4).

A significantly higher proportion of rural patients (32.3% v 26.4%) were judged by their GP to have experienced an avoidable delay in their diagnostic journey compared with urban patients (P=0.001), and rural GPs were more likely to perceive that the avoidable delay had occurred in primary care. Rural GPs were also more likely to consider their own pre-referral clinical appraisal had been the source of the avoidable delay, and less likely to consider that the patient was responsible for delayed help-seeking (P=0.006), (table 4).

GP initiated investigations

Rural patients were significantly more likely to have investigations instigated by their GP at their first relevant consultation than urban patients (P=0.029), with rural GPs significantly more likely to initiate blood tests at this consultation than their urban counterparts (P<0.001), (table 5).

Key cancer diagnostic intervals

Median primary care interval was four days for urban patients (IQR 4, 0-22) and seven days for rural patients (IQR 7, 0-30) but this difference was not significant (p=0.181). Also, the odds of a prolonged primary care interval (longer than 60 days or longer than 90 days) were not significantly higher in rural patients in either unadjusted or adjusted analyses (table 6).

Median diagnostic interval was significantly longer (5 days) for rural patients (P=0.039), but rural patients were no more likely to have a prolonged diagnostic delay in the adjusted analysis (> 60 days (OR 0.821, CI.0.616-1.094)) and (> 90 days (OR 0.807, CI 0.581-1.122)), table 6.

There were no significant differences in treatment or secondary care interval between rural and urban patients.

4. DISCUSSION

Summary of key findings

Routes to diagnosis of rural and urban patients were similar. Rural patients were more likely to have alarm features of potential cancer at presentation, were seen more often before being referred, and were more likely to have blood tests ordered by their GP. Rural GPs were more likely to perceive that they had caused avoidable delays for their rural patients, and less likely to perceive that their patients had delayed in help-seeking. Despite this, rural patients were no more likely to have significantly longer cancer diagnostic intervals. The trend to slightly longer median primary care and diagnostic intervals observed in rural patients may reflect rural GPs being more likely to investigate before referral.

Comparison with other literature

In the systematic review by Carriere et al (2018) potential mechanistic explanations were included in a socio-ecological model comprising levels of culture and community; wider policy; healthcare institutions and patient factors. At the patient level, in the current study we found rural patients had more alarm features at presentation, consistent with an earlier study in Northeast Scotland where colorectal cancer patients were more likely to have alarm symptoms at presentation (Murage et al, 2018).

Research using large patient samples and based on cancer registry data have found rural patients are less likely to be referred urgently, more likely to be diagnosed as an emergency or at post-mortem, and more likely to have a screen-detected cancer (Campbell et al, 2000; Murage et al, 2019; Leung et al, 2015). In contrast, this study found no significant difference in the routes to diagnosis experienced by rural and urban patients, although the sample was gathered in a different way. Our findings are supported in part by two Danish studies. The first, a national cohort study of 37,872 patients looking at cancer delays and travel distance to health services, found travel distance from a patient's home to their GP was not associated with time intervals in the diagnostic journey, but was associated with increased travel distance to the hospital (Virgilsen, Møller, and Vedsted, 2019a). The second study, looking at cancer diagnostic facilities and cancer stage for 12 different cancers (n=256,663 patients), found no

pronounced associations between travel distance to the GP and tumour stage. However, for the easy-to-diagnose cancer types (rectum cancer, malignant melanoma, testis cancer and cervix) a longer travel distance to the hospital was associated with advanced disease while it lessened the odds for the hard-to-diagnose cancer types (stomach, pancreatic, lung and ovarian cancer) (Virgilsen, Møller, and Vedsted, 2019b).

Previous investigators have cited poorer access to investigations and specialist care as a potential cause of poorer rural cancer outcomes (Jones et al, 2010; Barisic 2016). A recent large English study also reported that rural patients were less likely to be referred using urgent suspected cancer pathways (Murage et al, 2019). GPs are influenced by context in their decision-making, and could conceivably factor in travel and cost burdens when deciding how to manage patients who might have cancer (Sladden, 1998; Bentham, 1982; Kostopolou, 2019). Our finding that rural patients were seen more often prior to referral, and were more likely to have blood-tests initiated by their GP is interesting in this context. It is consistent with a pan-European study that found rural GPs were just as likely to take diagnostic action at the initial consultation, but that the action taken may be considered in light of the travel and cost burden to the patient (Murchie et al, 2020). Rural GPs were also more likely to perform blood tests at the index consultation, and as the overall primary care delay is not significantly different, it is possible that rural GPs, mindful of the implications for their patients, are simply establishing greater certitude that referral is completely necessary. This action by rural GPs could also partly explain why alarm features at presentation (which included positive tests) were more likely for rural than urban patients. As in this study, in geographically similar New Zealand, rates of referral to secondary care by rural and urban GPs were similar (Hider et al, 2000).

A previous study in Northeast Scotland found that patients living furthest from hospitals actually had significantly shorter time to treatment for cancer (Turner et al, 2017). Together with the current results it does not appear that rural-dwelling cancer patients in Scotland are disadvantaged by longer diagnostic delays in primary care compared with those living in cities. Relevant also is a randomized trial in rural Western Australia where neither a community nor GP educational intervention succeeded in reducing total diagnostic cancer intervals (Emery et al, 2017). It could be that rural patients do not suffer prolonged delays in the diagnosis of their cancer, and that there is little scope to reduce delays relative to urban-dwellers any further.

Strikingly, rural GPs were significantly more likely to perceive that they, and not their patient, had delayed diagnosis in an avoidable way. This view is not supported by the objective data, so speculatively it may represent differences in the attitudes of rural GPs and the relationship they have with their patients. A recent focus group study concluded that rural German GPs formed closer relationships and felt greater responsibility for their patients (Pohontsch et al, 2018). It is conceivable that doctor-patient relationships are also closer in rural Scotland.

Strengths and limitations

This study is based on a large sample of patients from throughout Scotland diagnosed with a new primary cancer. The sample is representative of Scottish cancer patients with respect to gender, age and cancer site and key demographics and, for the purpose of this study, a good proportion of rural patients. Participating general practitioners have provided rich, granular and detailed information, giving a detailed narrative picture of each patients' diagnosis – information that is only available directly from patient records. This also enables access to variables which in previous rural vs urban cancer diagnosis research have only been speculated about. The study was also able to use the Scottish Government's Urban Rural classifications which categorize patients based on geographical factors likely to influence healthcare access and health outcomes. We have added further definition by presenting data using both the 2-fold and 6-fold classifications.

NCDA data was collected GPs or practice staff direct from their own patents' practice-held records. There is, therefore, the possibility of bias in data-entry particularly where the pre-diagnostic pathway was complex. On the other hand, the audit team allocated cases to practices for data extraction minimising the potential bias from self-selection of cases. Furthermore, most of the data gathered related to objective facts collected onto a structured data-collection proforma. To obtain a complete picture of cancer diagnosis in Scotland NCDA collected data about a heterogenous group of cancers which have different natural histories and can present in different ways which creates some challenges to interpreting the data. To mitigate this issue we have included cancer site as a potential confounder in the multivariable analysis of prolonged diagnostic intervals. The data are from 2014 and local health services continue to evolve. However, there have been no major changes in cancer diagnostics or rural healthcare delivery in Scotland that would make the situation any different now. Data is not available on patients' journeys prior to presenting to their GP. This is difficult to collect, but is an important consideration for future research since it is conceivable that geography could have a considerable impact on this. Rurality in Scotland differs considerably from elsewhere in the UK and the world, meaning the results may not be generalizable. On the other hand, Scotland has similar rural cancer inequity to elsewhere, so the current research represents a good starting point for researchers wishing to conduct similar or comparative research.

Implications for future research

Our data suggest rural patients may tend to be more symptomatic when presenting to their GPs and then experience their cancer diagnosis differently. Detailed research exploring the impact of geography on patient behaviour and decision-making when faced with potential cancer symptoms should follow.

Rural patients had similar routes to diagnosis as urban patients, were not diagnosed at a later stage and where key pathway delays were longer it was by a few days, which seems highly unlikely to have been clinically significant. From an international perspective, these data are incremental, adding definition to the socio-ecological model, and suggesting similar methods

should be replicated to explore geographical influences on primary care cancer diagnosis internationally.

Overall, and from a Scottish perspective, the current results are consistent with the NASCAR study, conducted in the Northeast of Scotland (Turner et al, 2017). They suggest that rurality in Scotland does not lead to later stage diagnosis, delayed diagnosis or delayed treatment. This suggests that future research might focus on pre-presentational and post-treatment survivorship pathways if it would uncover the root causes of cancer outcome inequality in Scotland.

5. Conclusion

In a descriptive analysis of Scottish Cancer diagnoses from 2014 rural patients may have experienced primary care differently in the lead-up to a cancer diagnosis. Against a background of greater cost and travel burden, rural patients appeared more symptomatic at presentation, and then in likely collaboration with rural GPs, were more likely to have blood tests and review appointments to establish the basis for referral. Contrary to objective evidence, rural GPs appeared more likely to judge themselves rather than patients to have avoidably delayed the cancer diagnosis. This suggests that rural GPs may have different attitudes and more trusting relationships with their patients than urban counterparts. Together, these observations raise important research questions about geographical influences on patient and GP behaviour which could be explored using enhanced datasets, questionnaires and qualitative research methods.

Overall, however time to diagnosis and treatment for rural patients was not significantly prolonged compared to city-dwellers. These data add to evidence suggesting that poorer rural cancer outcomes in Scotland are not caused by prolonged diagnostic pathways in primary care. Future research must therefore explore geographical influences on the entirety of the cancer journey, from symptom development and appraisal to survivorship care, if the root causes of geographical cancer inequality in Scotland are to be completely understood.

AUTHOR CONTRIBUTION

Peter Murchie: Conceptualisation; formal analysis; writing- original draft preparation, reviewing and editing; supervision. **Rosalind Adam**: writing- original draft preparation, reviewing and editing. **Wei Lynn Khor:** writing- original draft preparation, reviewing and editing. **Sarah Smith:** writing-original draft preparation, reviewing and editing. **Emma McNair:** conceptualisation, writing, reviewing and editing**. Ruth Swann:** conceptualisation, writing, reviewing and editing**. Jana Witt:** conceptualisation, writing, reviewing and editing **David Weller:** conceptualisation, writing, reviewing and editing.

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ETHICAL APPROVAL

The NCDA in Scotland received approval from the Public Benefit and Privacy Panel for Health of the Scottish NHS on 20th January 2017 (PBPP 1617-0061).

DATA MANAGEMENT

In full compliance with all regulatory and legal requirements data were stored, accessed and analysed within the National Data Safe Haven maintained by NHS National Services Scotland. Outputs were subject to disclosure checks by members of the Electronic Data Research and Innovation (eDRIS) team of the Information and Statistics Division, Scotland prior to release to the research team for inclusion in this manuscript.

COMPETING INTERESTS

No authors have competing interests to declare.

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TABLES

TABLE 1: SAMPLE COMPOSITION BY SCOTTISH URBAN RURAL 2-FOLD CLASSIFICATION (n=1905)

		TOTAL SCOTTISH CASES 2014[1]	TOTAL OF NCDA n(%)	Urban Areas N=1538 n(%)	Rural Areas N=476 n(%)
GENDER	**MALE**	15,528 (49.0)	973 (51.1)	732 (50.3)	241 (53.6)
	FEMALE	16,183 (51.0)	932 (48.9)	723 (49.7)	209 (46.4)
AGE GROUP (YEARS)	**0-24**	524 (1.7)	17 (0.9)	11 (0.8)	6 (1.3)
	25-49	2,746 (8.6)	175 (9.2)	139 (9.6)	36 (8.0)
	50-64	7,966 (25.1)	468 (24.6)	359 (24.7)	109 (24.2)
	65-74	9,492 (29.9)	528 (27.7)	396 (27.2)	132 (29.3)
	75-84	7,940 (25.0)	510 (26.8)	390 (26.8)	120 (26.7)
	>84	3,043 (9.6)	207 (10.9)	160 (11.0)	47 (10.4)
SIMD Category (based on quintiles)[2]	**1 (Most Deprived)**	29,458 (18.1)	441 (23.1)	400 (27.5)	41 (9.1)
	2	31,208 (19.2)	351 (18.4)	297 (20.4)	54 (12.0)
	3	33,241 (20.4)	323 (17.0)	211 (14.5)	112 (24.9)
	4	34,590 21.3)	431 (22.6)	236 (16.2)	195 (43.3)
	5 (Least Deprived)	33,939 (20.9)	359 (18.8)	311 (21.4)	48 (10.7)
CANCER SITE	**Bladder**	841 (2.7)	50 (2.6)	39 (2.7)	11 (2.4)
	Brain	443 (1.4)	23 (1.2)	16 (1.1)	7 (1.6)
	Breast	4,610 (14.5)	209 (11.0)	155 (10.7)	54 (12.0)
	Cancer of Unknown Primary[3]	Not available	29 (1.5)	18 (1.2)	11 (2.4)
	Colon	2,586 (8.2)	158 (8.3)	121 (8.3)	37 (8.2)
	Leukaemia	584 (1.8)	44 (2.3)	30 (2.1)	14 (3.1)
	Liver	572 (1.8)	56 (2.9)	47 (3.2)	9 (2.0)
	Lung	5,307 (16.7)	359 (18.8)	291 (20.0)	68 (15.1)
	Lymphoma	1,177 (3.7)	78 (4.1)	57 (3.9)	21 (4.7)
	Melanoma	1,248 (3.9)	79 (4.1)	62 (4.3)	17 (3.8)
	Multiple Myeloma	435 (1.4)	21 (1.1)	16 (1.1)	5 (1.1)
	Oesophageal	932 (2.9)	63 (3.3)	49 (3.4)	14 (3.1)
	Oral	896 (2.8)	51 (2.7)	40 (2.7)	11 (2.4)
	Other	2,909 (9.1)	96 (5.0)	80 (5.5)	16 (3.6)
	Other Gynae	1,767 (5.6)	75 (3.9)	54 (3.7)	21 (4.7)
	Ovarian	595 (1.9)	38 (2.0)	28 (1.9)	10 (2.2)
	Pancreatic	793 (2.5)	55 (2.9)	41 (2.8)	14 (3.1)
	Prostate	3,202 (10.1)	222 (11.7)	160 (11.0)	62 (13.8)
	Rectal	1,135 (3.6)	73 (3.8)	58 (4.0)	15 (3.3)
	Renal	1,006 (3.2)	71 (3.7)	50 (3.4)	21 (4.7)

	Stomach	673 (2.1)	55 (2.9)	43 (3.0)	12 (2.7)
CANCER STAGE[3]	**1**	Not available	207 (10.9)	164 (11.3)	43 (9.6)
	2	Not available	238 (12.5)	175 (12.0)	63 (14.0)
	3	Not available	237 (12.4)	173 (11.9)	64 (14.2)
	4	Not available	416 (21.8)	321 (22.2)	95 (21.1)
	Unknown	Not available	807 (42.4)	622 (42.7)	185 (41.1)
COMORBIDITIES[3]	**None**	Not available	475 (24.9)	373 (25.8)	102 (22.7)
	One	Not available	537 (28.2)	407 (28.2)	130 (29.0)
	Two	Not available	469 (24.6)	350 (24.3)	119 (26.5)
	Three or more	Not available	411 (21.6)	313 (21.7)	98 (21.8)
	Unknown	Not available	13 (0.7)	n<10	n<10

[1] Data on all Scottish cancer cases 2014 obtained from ISD Scotland. Cancer Incidence in Scotland Dashboard. https://www.isdscotland.org/Health-Topics/Cancer/Publications/2019-04-30/visualisation.asp

[2]SIMD Category totals and percentages relate to the period 2013-2017 combined. ISD does not publish deprivation data for individual years

[3] Data on cancer stage and individual comorbidities are not publically available from ISD Scotland

TABLE 2: METHOD OF FIRST DETECTION AND TYPE OF REFERRAL BY URBAN RURAL 2 FOLD CLASSIFICATION (n=1905)

	TOTAL OF NCDA n(%)	Clinical Presentation N= n(%)	Incidental Finding n(%)	Incidental Finding at Autopsy n(%)	Interval Cancer n(%)	Other n(%)	Not Known n(%)
TOTAL	1905 (100)						
URBAN-RURAL 2-FOLD CLASSIFICATION							
Urban	1455 (100)	1333 (91.6)	113 (7.8)	n≤5	n≤5	n≤5	n≤5
Rural	450 (100)	417 (92.7)	31 (6.9)	n≤5	n≤5	n≤5	n≤5
						P=0.360[1]	
	TOTAL OF NCDA n(%)	**Routine n(%)**	**Urgent – Not for Suspected Cancer n(%)**	**Urgent Suspected Cancer Referral n(%)**	**Emergency Referral n(%)**	**Other n(%)**	**Not known n(%)**
TOTAL	1905 (100)						
URBAN-RURAL 2-FOLD CLASSIFICATION							
Urban	1455 (76.4)	162 (11.1)	128 (8.8)	566 (38.9)	313 (21.5)	130 (8.9)	124 (8.5)88(5.7)
Rural	450 (23.6)	42 (9.3)	54 (12.0)	182 (40.4)	89 (19.8)	37 (8.2)	34 (7.6)31(6.5)
						P=0.445[1]	

[1] Pearson's Chi-Squared Test

TABLE 3: PRESENCE OF AT LEAST ONE SCOTTISH REFERRAL GUIDELINE ALARM FEATURES AT PRESENTATION BY INDIVIDUAL SITE GUIDELINE 2-FOLD URBAN RURAL CLASSIFCATION (n=1905)

		Urban Areas (N=1455) n(%)	Rural Areas (N=450) n(%)	Total (N=1905) n(%)	P Value (Chi-Squared test)[1]
At Least One Alarm Feature Present*	**Yes**	1119 (77.0)	367 (81.5)	1486 (78.0)	
	No	336 (23.0)	83 (18.4)	419 (22.0)	**P=0.044**

[1] Chi-squared test continuity correction

[2] Omitted for disclosure risk

TABLE 4: SYMPTOMS AND SIGNS AT PRESENTATION (n=1905), NUMBER OF PRE-REFERRAL CONSULTATIONS (n=1905) AND AVOIDABLE DELAYS (n=1669 – excluding 236 unknowns) BY 2-FOLD URBAN RURAL CLASSIFICATION

		Urban Areas	Rural Areas	P-value
Number of symptoms at presentation	**Median (IQR)**	1.0(1-2)	1.0(1-3)	
				P=0.140[1]
Number of positive signs or tests at presentation	**Median (IQR)**	0(0-1)	0(0-1)	
				P=0.326[1]
Median number of consultations before referral	**Media (IQR)**	1.0(1-2)	1.0(1-3)	
				P=0.016[1]
Three or more consultations before referral	**Yes n(%)**	286(19.7)	122(27.1)	
	No n(%)	1024(70.4)	293(65.1)	
	Unknown n(%)	145(10.0)	35(7.8)	P=0.002[2]
		Urban Areas N=1255 n(%)	**Rural Areas N=414 n(%)**	**TOTAL**
Avoidable Delay in Diagnostic Journey	**Yes**	348 (23.9)	137 (30.4)	485
	No	982 (73.6)	296 (67.7)	1184
				P=0.001[3]
Where Avoidable Delay Occurred	**Pre-consultation**	69 (19.8)	19(13.4)	89
	Primary Care	132 (38.0)	61(43.2)	195
	Secondary or Tertiary Care	136 (39.2)	57 (40.4)	193
	Not known	n<10	n<10	16
				P=0.058[2]
Stage of Journey Delayed	**Help-seeking**	78 (36.1)	23 (16.8)	101
	Clinical appraisal	39 (18.5)	30 (21.9)	69
	Investigation	91 (26.1)	33 (24.1)	124
	Investigation Reporting	28 (8.0)	n<10	36
	Referral	55 (15.8)	19 (13.9)	74
	Appointment	23 (6.6)	n<10	30
	Follow-up of Abnormal Result	26 (7.5)	11 (8.0)	37
	Not Known	n<10	n<10	14
				P=0.006[2]

[1] Mann Whitney U Test

[2] Pearson's Chi-Squared Test [3] Chi-squared test continuity correction

TABLE 5: GP INITIATIED INVESTIGATIONS BY 2-FOLD URBAN RURAL CLASSIFICATION (n=1846 excluding 59 unknowns. 120 inapplicable cases included as "no.")

		Urban Areas n(%)	Rural Areas n(%)	TOTAL
GP Led Investigation Occurred	**YES**	728 (51.7)	185 (42.1)	982
	NO	679 (48.3)	254 (57.9)	864
				P=0.029 [1]
GP Initiated Blood Tests	**YES**	499 (35.5)	199 (45.3)	698
	NO	908 (64.5)	240 (54.7)	1148
				P<0.001[1]
GP Initiated Urine Tests	**YES**	39 (2.1)	9 (2.1)	38
	NO	1378 (97.9)	430 (97.9)	1808
				P=1.000[1]
GP Initiated Imaging	**YES**	290 (20.6)	100 (22.8)	390
	NO	1117 (79.4)	339 (77.2)	1456
				P=0.366[1]
GP Initiated Endoscopy	**YES**	44 (3.1)	11 (2.5)	55
	NO	1363 (96.9)	428 (97.5)	1791
				P=0.612[1]
GP Initiated Other Tests	**YES**	48 (3.4)	23 (5.2)	71
	NO	1359 (96.6)	416 (94.8)	1775
				P=0.110[1]

[1]Chi-squared test continuity correction

TABLE 6: Key Cancer Diagnostic Intervals BY 2-FOLD URBAN RURAL CLASSIFICATION

Key Diagnostic Intervals	Large Urban Areas N(%)	Rural Areas N(%)	Median (IQR)		P value	Unadjusted Odds Ratio (CI)		**Adjusted Odds Ratio (CI)	
			Urban	Rural		Urban	Rural	Urban	Rural
Primary Care Interval	**N=987***	**N=327***							
Median interval days			4(0-22)	7(0-30)	P=0.181[1]				
> 60 days yes	105(10.6)	43(13.1)			P=0.253[2]	1	0.786(0.538-1.149)	1	0.837(0.550-1.273)
> 90 days yes	70(7.1)	31(9.5)			P=0.199[2]	1	0.729(0.468-1.135)	1	0.650(0.395-1.070)
Diagnostic Interval	**N=1191***	**N=381***							
Median interval days			29.0(13-66)	34.0(14-75)	P=0.039[1]				
> 60 days yes	326(27.4)	119(31.2)			P=0.164[2]	1	0.830(0.645-1.067)	1	0.821(0.616-1.094)
> 90 days yes	203(17.0)	77(20.2)			P=0.184[2]	1	0.811(0.606-1.086)	1	0.807(0.581-1.122)
Secondary Care Interval	**N=735***	**N=242***							
Median interval days			62(36-106)	62(34-105)	P=0.938[1]				
> 60 days yes	375(51.0)	124(51.2)			P=1.000[2]	1	0.991(0.741-1.326)	1	1.064(0.753-1.503)
> 90 days yes	235(32.0)	235(32.0)			P=0.478[2]	1	0.884(0.651-1.201)	1	0.971(0.671-1.406)
Treatment Interval	**N=932***	**N=291***							
Median interval days			39.5(20-69)	37.0(17-66)	P=0.350[1]				
> 60 days yes	275(29.5)	82(28.2)			P=0.718[2]	1	1.067(0.797-1.428)	1	0.993(0.705-1.400)
> 90 days yes	155 (16.6)	41 (14.1)			P=0.347[2]	1	1.216(0.838-1.765)	1	1.130(0.731-1.746)

[1] Mann Whitney U Test

[2] Chi-Squared Test Continuity Correction

*Intervals are restricted to 0-730 days and any intervals out with this range are excluded to minimise data errors. Patients with a cancer diagnosed through screening (n=109) are also excluded. Additionally, where relevant valid dates are not available intervals could not be calculated.

** Adjustments were made for cancer site, deprivation, number of comorbidities, gender, and presence of at least one alarm feature to adjust for potential confounding.

Figure 1: Scottish Government Urban Rural Classification 2-fold and 6-fold breakdowns

Scottish Government 2-fold Urban Rural Classification	
1 Urban Area	Settlements of 3,000 or more people
2 Rural Area	Areas with a population of less than 3,000 people
Scottish Government 6-fold Urban Rural Classification	
1 Large Urban Area	Settlements of 125,000 or more people
2 Other Urban Area	Settlements of 10,000 to 124,999 people.
3 Accessible Small Towns	Settlements of 3,000 to 9,999 people and within a 30 minute drive of a settlement of 10,000 or more
4 Remote Small Towns	Settlements of 3,000 to 9,999 people and with a drive time of over 30 minutes to a settlement of 10,000 or more
5 Accessible Rural	Areas with a population of less than 3,000 people, and within a 30 minute drive time of a settlement of 10,000 or more
6 Remote Rural	Areas with a population of less than 3,000 people, and with a drive time of over 30 minutes to a settlement of 10,000 or more

Adapted from: Scottish Government. Scottish Government Urban Rural Classification. https://www2.gov.scot/Topics/Statistics/About/Methodology/UrbanRuralClassification (Accessed 03/02/20)

Appendix I (Sample NCDA data collection form – attached Excel file)

Appendix II (Analysis by Scottish Urban Rural 6 Fold Classification)

Supplementary TABLE S1: SAMPLE COMPOSITION BY SCOTTISH URBAN RURAL 6-FOLD CLASSIFICATION (n=2014)

	TOTAL OF NCDA n(%)	Large Urban Areas N=780 n(%)	Other Urban Areas N=474 n(%)	Accessible Small Towns N=207 n(%)	Remote Small Towns N=77 n(%)	Accessible Rural Areas N=224 n(%)	Remote Rural Areas N=252 n(%)
TOTAL	1905						
GENDER							
MALE	973 (51.1)	377 (50.8)	215 (48.2)	101 (52.1)	39 (53.4)	105 (49.1)	136 (57.6)
FEMALE	932 (48.9)	365 (49.2)	231 (51.8)	93 (47.9)	34 (46.6)	109 (50.9)	100 (42.4)
AGE GROUP (YEARS)							
0-24	17 (0.8)	8 (1.0)	0(0)	n<10	n<10	n<10	n<10
25-49	175 (9.2)	78 (10.5)	38 (8.5)	18 (9.3)	n<10	21 (9.8)	15 (6.4)
50-64	468 (24.6)	194 (26.1)	111 (24.9)	45 (23.2)	n<10	53 (24.8)	56 (23.7)
65-74	528 (27.7)	190 (25.6)	128 (28.7)	52 (26.8)	26 (35.6)	66 (30.8)	66 (28.0)
75-84	510 (26.8)	196 (26.4)	117 (26.2)	57 (29.4)	20 (27.4)	53 (24.8)	67 (28.4)
>84	207 (10.9)	76 (10.2)	52 (11.7)	20 (10.3)	12 (16.4)	20 (9.3)	27 (11.4)
SIMD							
1 (Most Deprived)	441 (23.1)	292 (39.4)	96 (21.5)	13(6.3)	n<10	24 (11.2)	17 (7.2)
2	351 (18.4)	117 (15.8)	124 (27.8)	45(21.8)	14 (19.2)	26 (12.1)	28 (11.9)
3	323 (17.0)	75 (10.1)	60 (13.5)	45(21.8)	35 (47.9)	37 (17.3)	75 (31.8)
4	431 (22.6)	89 (12.0)	87 (19.5)	55(26.6)	n<10	98 (45.8)	97 (41.1)
5 (Least Deprived)	359 (18.8)	169 (21.8)	79 (17.7)	49(23.7)	16 (21.9)	29 (13.6)	19 (8.1)
CANCER SITE							
Bladder	50 (2.5)	22 (3.0)	11 (2.5)	n<10	n<10	n<10	n<10
Brain	23 (1.2)	n<10	n<10	n<10	n<10	n<10	n<10
Breast	209 (11.0)	73 (9.8)	48 (10.8)	28 (14.4)	n<10	33 (15.4)	21 (8.9)
Cancer of Unknown Primary	29 (1.5)	n<10	11(2.3)	n<10	n<10	n<10	n<10
Colon	158 (8.3)	59 (8.0)	34 (7.6)	23 (11.9)	n<10	15 (7.0)	22 (9.3)
Leukaemia	44 (2.3)	17 (2.3)	n<10	n<10	n<10	n<10	11 (2.3)
Liver	56 (2.9)	26 (3.5)	18 (4.0)	n<10	n<10	n<10	n<10
Lung	359 (18.8)	165 (22.2)	87 (19.5)	25 (12.9)	14 (19.2)	31 (14.5)	37 (15.7)
Lymphoma	78 (4.1)	30 (4.0)	19 (4.3)	n<10	n<10	10 (4.7)	11 (4.7)
Melanoma	79 (4.1)	24 (3.2)	23 (5.2)	12 (6.2)	n<10	n<10	12 (5.1)
Multiple Myeloma	21 (1.1)	12(1.6)	n<10	n<10	n<10	n<10	n<10
Oesophageal	63 (3.3)	30 (4.0)	13 (2.9)	n<10	n<10	n<10	n<10
Oral	51 (2.7)	25 (3.4)	10 (2.2)	n<10	n<10	n<10	n<10
Other	96 (5.0)	39 (5.3)	29 (6.5)	n<10	n<10	n<10	n<10

Other Gynae	75 (3.9)	25 (3.4)	21 (4.7)	n<10	n<10	n<10	12 (5.1)
CANCER STAGE[3]							
1	207 (10.9)	93 (12.5)	42 (9.4)	21 (10.8)	n<10	21 (9.8)	22 (9.3)
2	238 (12.5)	82 (11.1)	50 (11.2)	35 (18.0)	n<10	36 (16.8)	27 (11.4)
3	237 (12.4)	90 (12.1)	46 (10.3)	24 (12.4)	13 (17.8)	30 (14.0)	34 (14.4)
4	416 (21.8)	166 (22.4)	99 (22.2)	42 (21.6)	14 (19.2)	50 (23.4)	45 (19.1)
Unknown	807 (42.4)	311 (41.9)	209 (46.9)	72 (37.1)	30 (41.1)	77 (36.)	108 (45.8)
COMORBIDITIES[3]							
None	475 (25.1)	178 (24.2)	125 (28.2)	56 (29.2)	14 (19.4)	53 (24.9)	49 (20.8)
One	537 (28.4)	200 (27.2)	130 (29.3)	52 (27.1)	25 (34.7)	66 (31.0)	64 (27.1)
Two	469 (24.8)	178 (24.2)	110 (24.8)	43 (22.4)	19 (26.4)	51 (23.9)	68 (28.8)
Three or more	411 (21.7)	180 (24.5)	78 (17.6)	41 (21.4)	14 (19.4)	43 (20.2)	55 (23.3)
Unknown	13 (0.7)	n<10	n<10	n<10	n<10	n<10	n<10

Supplementary TABLE S2: METHOD OF FIRST DETECTION BY URBAN RURAL 6-FOLD CLASSIFICATION (n=1905)

	TOTAL OF NCDA	Clinical Presentation n(%)	Incidental Finding n(%)	Incidental Finding at Autopsy n(%)	Interval Cancer n(%)	Not Known n(%)	Other n(%)
TOTAL	1905						
URBAN-RURAL 6-FOLD CLASSIFICATION							
Large Urban Area	742	677 (91.2)	60 (8.1)	n<10	n<10	n<10	n<10
Other Urban Area	446	410 (91.9)	33 (7.4)	n<10	n<10	n<10	n<10
Accessible Small Town	194	179 (92.3)	15 (7.7)	n<10	n<10	n<10	n<10
Remote Small Town	73	67 (91.8)	n<10	n<10	n<10	n<10	n<10
Accessible Rural Area	214	196 (91.6)	17 (7.9)	n<10	n<10	n<10	n<10
Remote Rural Area	236	221 (93.6)	14 (5.9)	n<10	n<10	n<10	n<10
							P=0.570

[1] Pearson Chi-squared test

Supplementary TABLE S3: TYPE OF REFERRAL BY URBAN RURAL 6-FOLD CLASSIFICATION (n=1905)

	TOTAL OF NCDA n	Routine n(%)	Urgent – Not for Suspected Cancer n(%)	Urgent Suspected Cancer Referral n(%)	Emergency Referral n(%)	Other n(%)	Not Known n(%)
TOTAL	1905						
URBAN-RURAL 6-FOLD CLASSIFICATION							
Large Urban Area	742	96 (12.9)	67 (9.0)	271 (36.5)	177 (23.9)	61 (8.2)	62 (8.4)
Other Urban Area	446	46 (10.3)	38 (8.5)	171 (38.3)	98 (22.0)	50 (11.2)	39 (8.7)
Accessible Small Town	194	12 (6.2)	19 (9.8)	96 (49.5)	29 (14.9)	21 (10.8)	14 (7.2)
Remote Small Town	73	8 (11.0)	n<10	28 (38.4)	9 (12.3)	15 (20.5)	9 (12.3)
Accessible Rural Area	214	18 (8.4)	27 (12.6)	80 (37.4)	46 (21.5)	24 (11.2)	17 (7.9)
Remote Rural Area	236	24 (10.2)	27 (11.4)	102 (43.2)	43 (18.2)	18 (7.6)	17 (7.2)
							P=0.001[1]

[1] Pearson Chi-squared test

Supplementary TABLE S4: PRESENCE OF AT LEAST ONE SCOTTISH REFERRAL GUIDELINE ALARM FEATURES AT PRESENTATION BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1905)

		Large Urban Areas n(%)	Other Urban Areas n(%)	Accessible Small Towns n(%)	Remote Small Towns n(%)	Accessible Rural Areas n(%)	Remote Rural Areas n(%)	Total n(%)
At Least One Alarm Feature	**Yes**	575(38.7)	348(23.4)	147(9.9)	49(3.3)	175(11.8)	192(12.9)	1486
	No	167(39.9)	98(23.4)	47(11.2)	24(5.7)	39(9.3)	44(10.5)	419
								P=0.108[1]

[1] Pearson's Chi-squared test

Supplementary TABLE S5: NUMBER OF SYMPTOMS AND SIGNS AT PRESENTATION BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1905)

	Large Urban Areas n(%)	Other Urban Areas n(%)	Accessible Small Towns n(%)	Remote Small Towns n(%)	Accessible Rural Areas n(%)	Remote Rural Areas n(%)
Median Symptoms at presentation (IQR)	1(1-2)	1(1-2)	1(1-2)	1(0-2.5)	1(1-3)	1(1-2)
						P=0.467[1]
Median Positive Signs or Tests at Presentation (IQR)	0(0-1)	0(0-1)	0(0-1)	0(0-1)	1(0-1)	0(0-1)
						P=0.379[1]

[1] Kruskall Wallis Test

Supplementary TABLE S6: AVOIDABLE DELAYS BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1669, excluding 236 unknowns)

		Large Urban Areas N=677 n (%)	Other Urban Areas N=407 n (%)	Accessible Small Towns N=188 n (%)	Remote Small Towns N=58 n (%)	Accessible Rural Areas N=211 n (%)	Remote Rural Areas N=222 n (%)	TOTAL
Delay in Diagnostic Journey	**YES**	188 (27.8)	81 (19.9)	59 (31.4)	20 (34.5)	57 (27.0)	80 (36.0)	485
	NO	489 (72.2)	326 (80.1)	129 (68.6)	38 (65.5)	154 (73.0)	142 (64.0)	1278
							P<0.001[1]	
Where Delay Occurred	**Pre-consultation**	49 (26.1)	9 (11.1)	8 (13.6)	n<10	n<10	11 (13.8)	88
	Primary Care	64 (34.0)	37 (45.7)	25 (42.4)	n<10	29 (50.9.7)	32 (40.0)	193
	Secondary or Tertiary Care	70 (37.2)	29 (35.8)	26 (44.1)	10 (50.0)	20 (35.1)	33 (41.3)	188
	Not known	n<10	n<10	n<10	n<10	0 (0)	n<10	16
							P<0.035[1]	
Stage of Journey Delayed	**Help-seeking**	51 (27.1)	11 (13.6)	11 (18.6)	n<10	n<10	15 (18.8)	101
	Clinical appraisal	22 (11.7)	n<10	n<10	0 (0)	13 (22.8)	17 (21.3)	69
	Investigation	40 (21.3)	24 (29.6)	21 (35.6)	n<10	16 (28.1)	17 (21.3)	124
	Investigation Reporting	14 (7.4)	n<10	n<10	n<10	n<10	n<10	36
	Referral	27 (14.4)	19 (23.5)	n<10	n<10	n<10	11 (13.8.0)	74
	Appointment	13 (6.9)	n<10	n<10	n<10	n<10	n<10	30
	Delayed result follow-up	16 (8.5)	n<10	n<10	n<10	n<10	n<10	37
	Not known	n<10	n<10	n<10	n<10	n<10	n<10	14
							P=0.229[1]	

[1] Pearson's Chi-squared test

Supplementary TABLE S7: GP INITIATIED INVESTIGATIONS BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1860, excluding 45 unknowns)

		Large Urban Areas n (%)	Other Urban Areas n (%)	Accessible Small Towns n (%)	Remote Small Towns n (%)	Accessible Rural Areas n (%)	Remote Rural Areas n (%)	TOTAL
GP Led Investigation Occurred	**YES**	362 (50.3)	201 (46.4)	87 (44.6)	29 (40.8)	90 (43.4)	95 (40.6)	864
	NO	357 (49.7)	232 (53.6)	108 (55.4)	42 (59.2)	118 (56.7)	139 (59.4)	996
							P=0.087[1]	
GP Initiated Blood Tests	**YES**	246 (34.2)	157 (36.3)	69 (35.4)	32 (45.1)	92 (44.2)	108 (46.2)	704
	NO	473 (65.8)	276 (63.7)	126 (64.6)	39 (54.9)	116 (55.8)	141 (53.8)	1156
							P=0.004[1]	
GP Initiated Urine Tests	**YES**	19 (2.6)	n<10	n<10	n<10	n<10	n<10	40
	NO	700 (97.4)	428 (98.8)	190 (97.4)	70 (98.6)	204 (98.1)	228 (97.4)	1820
							P=0.630[1]	
GP Initiated Imaging	**YES**	139 (19.3)	103 (23.8)	33 (16.9)	15 (21.1)	47 (22.6)	54 (23.1)	391
	NO	580 (80.7)	330 (76.2)	162 (83.1)	56 (78.9)	161 (77.4)	180 (76.9)	1469
							P=0.296[1]	
GP Initiated Endoscopy	**YES**	24 (3.3)	16 (3.7)	n<10	n<10	n<10	n<10	60

	NO	695 (96.7)	417 (96.3)	191 (97.9)	69 (97.2)	201 (96.6)	227 (97.0)	1800
							P=0.936[1]	
GP Initiated Other Tests	**YES**	16 (2.2)	18 (4.2)	12 (6.2)	n<10	n<10	18 (7.7)	74
	NO	703 (97.8)	415 (95.8)	194 (93.8)	66 (93.0)	203 (97.6)	216 (92.3)	1786
							P=0.001[1]	

[1] Pearson's Chi-squared test

Supplementary TABLE S8: NUMBER OF PRE-REFERRAL CONSULTATIONS BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1905)

		Large Urban Areas N=742 n(%)	Other Urban Areas N=446 n(%)	Accessible Small Towns N=194 n(%)	Remote Small Towns N=73 n(%)	Accessible Rural Areas N=214 n(%)	Remote Rural Areas N=236 n(%)
MEDIAN NUMBER OF CONSULTATIONS BEFORE REFERRAL	**Median (IQR)**	1(1-2)	1(1-2)	1(1-3)	2(1-2)	1(1-3)	20(1-3)
							P=0.108[1]
THREE OR MORE CONSULTATION BEFORE REFERRAL	**YES**	136(18.3)	86(19.3)	53(27.3)	11(15.1)	52(24.3)	70(29.7)
	NO	528(71.2)	317(71.1)	133(68.6)	46(63.0)	146(68.2)	147(62.3)
	UNKNOWN	78(10.5)	43(9.6)	8(4.1)	16(21.9)	16(7.5)	19(8.1)
							P=0.004[2]

[1] Kruskall Wallis test

[2] Pearson's Chi-squared test

Supplementary TABLE S9: PRIMARY CARE INTERVAL BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1314)*

		Large Urban Areas N=504* n(%)	Other Urban Areas N=291* n(%)	Accessible Small Towns N=146* n(%)	Remote Small Towns N=46* n(%)	Accessible Rural Areas N=157* n(%)	Remote Rural Areas N=170* n(%)
PRIMARY CARE INTERVAL (IQR)	**MEDIAN (IQR)**	3(0-21)	4(0-20)	8(0.75-32.25)	5.5(0.75-24)	7(0-24)	7(0-33.25)
							P=0.163[1]
PRIMARY CARE INTERVAL > 60 DAYS	**YES**	55(10.9)	27(9.3)	18(12.3)	5(10.9)	15(9.6)	28(16.5)
	NO	449(89.1)	264(90.7)	128(87.7)	41(89.1)	142(90.4)	142(83.5)
							P=0.265[2]
PRIMARY CARE INTERVAL > 90 DAYS	**YES**	42(8.3)	14(4.8)	12(8.2)	n<5	n<5	20(11.8)
	NO	462(91.7)	277(95.2)	134(91.8)	44(95.7)	146(93.0)	150(88.2)
							P=0.128[2]
UNADJUSTED ODDS OF PCI > 60 DAYS	**OR (95% Cis)**	1	1.185(0.735-1.911)	0.813(0.466-1.418)	1.038(0.395-2.729)	1.151(0.632-2.096)	0.616(0.379-1.000)
UNADJUSTED ODDS OF PCI > 90 DAYS	**OR (95% Cis)**	1	1.731(0.945-3.172)	0.929(0.785-1.779)	2.073(0.486-8.836)	1.205(0.606-2.396)	0.670(0.386-1.163)
ADJUSTED ODDS OF PCI > 60 DAYS* **	**OR (95% Cis)**	1	1.128(0.682-1.866)	0.792(0.433-1.449)	1.051(0.381-2.902)	1.196(0.623-2.298)	0.638(0.369-1.105)
ADJUSTED ODDS OF PCI > 60 DAYS* **	**OR (95% Cis)**	1	1.568(0.831-2.958)	0.851(0.419-1.729)	2.094(0.465-9.422)	1.027(0.482-2.187)	0.591(0.312-1.118)

[1] Kruskall Wallis test

[2] Pearson's Chi-squared test

* Intervals are restricted to 0-730 days and any intervals out with this range are excluded to minimise data errors.. Additionally, where relevant valid dates are not available intervals could not be calculated.

Supplementary TABLE S10: DIAGNOSTIC INTERVAL BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1572)*

		Large Urban Areas N=597* n(%)	Other Urban Areas N=374* n(%)	Accessible Small Towns N=166* n(%)	Remote Small Towns N=54* n(%)	Accessible Rural Areas N=187* n(%)	Remote Rural Areas N=194* n(%)
DIAGNOSTIC INTERVAL (IQR)	**MEDIAN (IQR)**	29(12-67)	28(13-64)	31(15-64)	23(11-66.75)	30(14-61)	35.5(14.75-87)
							P=0.133[1]
DIAGNOSTIC INTERVAL > 60 DAYS	**YES**	166(27.8)	98(26.2)	46(27.7)	16(29.6)	47(25.1)	72(37.1)
	NO	431(72.2)	276(73.8)	120(72.3)	38(70.4)	140(74.9)	122(62.9)
							P=0.097[2]
DIAGNOSTIC INTERVAL > 60 DAYS	**YES**	106(17.8)	58(15.5)	31(18.7)	8(14.8)	30(16.0)	47(24.2)
	NO	491(82.2)	316(84.5)	135(81.3)	46(85.2)	157(84.0)	147(75.8)
							P=0.178[2]
UNADJUSTED ODDS OF DI > 60 DAYS	**OR (95% Cis)**	1	1.059(0.794-1.411)	0.922(0.635-1.339)	0.889(0.491-1.610)	1.125(0.779-1.632)	0.636 (0.456-0.889)
UNADJUSTED ODDS OF DI > 90 DAYS	**OR (95% Cis)**	1	1.142(0.811-1.609)	0.844(0.552-1.291)	1.150(0.548-2.414)	1.113(0.720-1.722)	0.647(0.443-0.944)
ADJUSTED ODDS OF DI > 60 DAYS* **	**OR (95% Cis)**	1	1.048(0.768-1.430)	0.954(0.631-1.443)	0.930(0.486-1.779)	1.159(0.764-1.757)	0.620(0.422-0.911)
ADJUSTED ODDS OF DI > 90 DAYS* **	**OR (95% Cis)**	1	1.094(0.760-1.575)	0.850(0.535-1.352)	1.231(0.559-2.709)	1.10(0.681-1.779)	0.641(0.416-0.988)

[1] Kruskall Wallis test

[2] Pearson's Chi-squared test

* Intervals are restricted to 0-730 days and any intervals out with this range are excluded to minimise data errors. Additionally, where relevant valid dates are not available intervals could not be calculated.

Supplementary TABLE S11: SECONDARY CARE INTERVAL BY 6-FOLD URBAN RURAL CLASSIFCATION (n=977)*

		Large Urban Areas N=384 n(%)*	Other Urban Areas N=203 n(%)*	Accessible Small Towns N=113 n(%)*	Remote Small Towns N=35 n(%)*	Accessible Rural Areas N=110 n(%)*	Remote Rural Areas N=132 n(%)*
SECONDARY CARE INTERVAL (IQR)	**MEDIAN (IQR)**	62.5(34-109)	62(38-95)	56(36.5-104)	63(34-138)	61.5(33-98.25)	62.5(34-106.75)
							P=0.990[1]
SECONDARY CARE INTERVAL > 60 DAYS	**YES**	199(51.8)	105(51.7)	53(46.9)	18(51.4)	56(50.9)	68(51.5)
	NO	185(48.2)	98(48.3)	60(53.1)	17(48.6)	54(49.1)	64(48.5)
							P=0.969[2]
SECONDARY CARE INTERVAL > 90 DAYS	**YES**	129(33.6)	58(28.6)	35(31.0)	13(37.1)	36(32.7)	48(36.4)
	NO	255(66.4)	145(71.4)	78(69.0)	22(62.9)	74(67.3)	84(63.6)
							P=0.702[2]
UNADJUSTED ODDS OF SCI > 60 DAYS	**OR (95% Cis)**	1	0.985(0.702-1.381)	1.180(0.779-1.788)	1.005(0.503-2.008)	1.026(0.672-1.568)	1.018(0.688-1.507)
UNADJUSTED ODDS OF SCI > 90 DAYS	**OR (95% Cis)**	1	1.221(0.846-1.764)	1.072(0.687-1.671)	0.849(0.414-1.741)	1.032(0.657-1.620)	0.881(0.585-1.327)
ADJUSTED ODDS OF SCI > 60 DAYS* **	**OR (95% Cis)**	1	0.889(0.606-1.302)	1.175(0.722-1.912)	1.320(0.597-2.915)	1.054(0.637-1.743)	1.098(0.690-1.749)
ADJUSTED ODDS OF SCI > 90 DAYS* **	**OR (95% Cis)**	1	1.139(0.751-1.727)	1.056(0.625-1.786)	1.073(0.464-2.478)	1.079(0.628-1.852)	0.969(0.592-1.589)

[1] Kruskall Wallis test

[2] Pearson's Chi-squared test

* Intervals are restricted to 0-730 days and any intervals out with this range are excluded to minimise data errors. Additionally, where relevant valid dates are not available intervals could not be calculated.

Supplementary TABLE S12: TREATMENT INTERVAL BY 6-FOLD URBAN RURAL CLASSIFCATION (n=1223)*

		Large Urban Areas N=483* n(%)	Other Urban Areas N=271* n(%)	Accessible Small Towns N=137* n(%)	Remote Small Towns N=41* n(%)	Accessible Rural Areas N=137* n(%)	Remote Rural Areas N=154* n(%)
TREATMENT INTERVAL (IQR)	**MEDIAN (IQR)**	42(20-71)	37(20-60)	35(18-70)	43(25-86.5)	36(20.5-69.5)	39(14-66.25)
							P=0.478[1]
TREATMENT INTERVAL > 60 DAYS	**YES**	150(31.1)	67(24.7)	42(30.7)	16(39.0)	35(25.5)	47(30.5)
	NO	333(68.9)	204(75.3)	95(69.3)	25(61.0)	102(74.5)	107(69.5)
							P=0.260[2]
TREATMENT INTERVAL > 60 DAYS	**YES**	86(17.8)	35(12.9)	24(17.5)	10(24.4)	21(15.3)	20(13.0)
	NO	397(82.2)	236(87.1)	113(82.5)	31(75.6)	116(84.7)	134(87.0)
							P=0.256[2]
UNADJUSTED ODDS OF TI > 60 DAYS	**OR (95% Cis)**	1	1.397(0.999-1.952)	1.020(0.678-1.536)	0.793(0.418-1.503)	1.274(0.830-1.958)	1.051(0.711-1.554)
UNADJUSTED ODDS OF TI > 90 DAYS	**OR (95% Cis)**	1	1.485(0.972-2.269)	1.021(0.621-1.679)	0.740(0.353-1.550)	1.167(0.694-1.963)	1.479(0.877-2.496)
ADJUSTED ODDS OF TI > 60 DAYS* **	**OR (95% Cis)**	1	1.239(0.855-1.796)	0.851(0.526-1.376)	0.708 (0.338-1.480)	1.128(0.687-1.854)	0.863(0.545-1.367)
ADJUSTED ODDS OF TI > 60 DAYS* **	**OR (95% Cis)**	1	1.395(0.874-2.228)	0.849(0.470-1.531)	0.663(0.278-1.582)	1.033(0.566-1.884)	1.224(0.667-2.243)

[1] Kruskall Wallis test

[2] Pearson's Chi-squared test

* Intervals are restricted to 0-730 days and any intervals out with this range are excluded to minimise data errors. Additionally, where relevant valid dates are not available intervals could not be calculated.