York Health Economics Consortium

Accelerating early identification of cancer in primary care using an artificial intelligence driven solution

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Keywords

General practice; cancer; diagnosis

How this fits in

It has long been understood that early diagnosis is important for cancer outcomes. Reducing delays in referral from primary care is an important measure in supporting this aim. An analysis of nationally collated data over one year shows an increase in the cancer detection rate among referrals in CCGs where C the Signs was used.

ABSTRACT

Background: Early identification of cancer symptoms and prompt referral are associated with better treatment outcomes, including reduced mortality.

Aim: An analysis of cancer referral data was undertaken to test whether C the Signs (a digital, artificial intelligence-driven tool) would support GPs to make more accurate assessments of potential cancer symptoms.

Design and Setting: Nationally collated comparative data on cancer referrals from Public Health England (PHE) were analysed. This covered the period of a trial of C the Signs in three clinical commissioning groups (CCGs) in one NHS region. Non-participating CCGs in the same region were used as comparators.

Method: Data on cancer referrals from primary care were accessed from the PHE website, corresponding as closely as possible to the trial period. Two comparator groups were used: all the non-participating CCGs and three CCGs matched to the trial group on previous performance on the measures of interest: detection rates; emergency presentation rates; referral rates; conversion rates.

Results: The trial CCGs showed significantly greater increase in cancer detection rates compared to the pre-trial year, relative to both comparators ($p<0.05$). There was also a significant increase in the detection rate when compared to the matched CCGs ($p<0.05$).

Conclusion: A tool that can help general practitioners to more accurately identify potential cancer symptoms would be an important service in attempts to improve early detection. This study shows that the use of artificial intelligence may have a role to play in this endeavour. C the Signs has the potential to contribute to achieving this goal.

1. INTRODUCTION

One in two people in the UK will be diagnosed with cancer at some point in their lifetime (1). Survival of most cancers is linked to the stage at diagnosis. Cancer diagnosed in the early stages (Tumour Nodes Metastases (TNM) stage 1 or 2) has considerably better outcomes than cancer diagnosed in late stages (TNM stage 3 or 4). Net five-year survival (accounting for background mortality) for breast cancer, is 97.9% for cases diagnosed at stage 1 and 26.2% for cases diagnosed at stage 4 (2). For prostate cancer the figures are 100% for stage 1 and 49% for stage 4 (3) and for bowel cancer the figures are 91.7% for stage 1 and 10.3% for stage 4 (4). Only 53.7% of patients are currently diagnosed at TNM stages 1 or 2 in the UK (5).

Diagnosing cancer can be challenging, however (6,7). In the early stages of cancer, symptoms can be vague and non-specific, overlapping with other conditions, which can lead to cancers being overlooked or missed. Approximately 20% of patients are diagnosed with cancer in the emergency department, the majority with late stage disease (8). 40% of patients diagnosed in the emergency department will survive to one year. These findings highlight an important cohort of patients who could have benefitted from earlier identification and referral.

Primary care is the first point of contact for patients, with 90% of patient contact with the National Health Service (NHS) taking place in general practice (9). Yet, on average, general practitioners (GPs) diagnose only eight new cases of cancer each year (10). A recent study evaluating over 1.4 million patients diagnosed with cancer demonstrated the importance of the GP in early stage diagnosis, by showing that higher rates of referral for suspected cancer is associated with lower mortality for the four most common types of cancer, one-third to half of which is likely to be explained by earlier stage at diagnosis (11). An audit conducted in 2017 identified that about one-third of patients report multiple GP consultations (three or more) before emergency presentation, with this being more likely in harder-to-suspect cancers or atypical presentations (12). A significant event audit in 2015 found that while 64.4% of cases diagnosed in the emergency department had presented to their GP in the preceding 12 months, delay in referral can be attributed, albeit in part, to the complexity of presentation or coexisting patient factors (13). Both studies concluded that interventions such as clinical decision support tools in general practice could be useful in reducing emergency cancer presentations.

C the Signs is a clinical decision support tool for GPs to use during a patient consultation. It uses artificial intelligence, mapped with the latest research, to support the early identification of the cancer(s) a patient is at risk of, and which investigation or referral may be appropriate. The tool uses a systematic approach that stratifies patients according to their risk of cancer, using signs, symptoms, demographic data, risk factors and other clinical markers.

This paper reports the results of an observational trial which sought to test the hypothesis that C the Signs would support GPs to make more accurate assessments of potential cancer symptoms. This would be apparent in an increased cancer detection rate in primary care and a decreased emergency presentation rate, compared to before C the Signs was available, observable in nationally published data.

2. METHODS

Three clinical commissioning groups (CCGs) in the East of England (EoE) participated in the trial, and supported communication to practices through CCG newsletters and local GP meetings. C the Signs was made available to all GPs free of charge, without any incentivisation. (There will be a charging model in place in future implementation sites). The tool was accessed from a website and on mobile application, with the trial running from July 2017 to June 2018.

The number of users and level of engagement were tracked throughout the trial period. The tool recorded each time the tool was used, capturing the clinical presentations of patients assessed and the 'pathways' that were recommended. C the Signs did not record the diagnostic outcome of each patient risk assessed and referred. Impact was measured using two indicators: the primary care cancer detection rate and the emergency presentation rate as reported by Public Health England's National Cancer Registration and Analysis Service (NCRAS) data (14), available approximately one year after the time period on which it reports.

The detection rate measures the number of reported new cancer cases treated that resulted from a two week wait (2ww) referral, expressed as a percentage of all new cancer cases treated at practices in the CCG. The emergency presentation rate measures the number of persons diagnosed with cancer via an emergency route, expressed as a rate per 100,000 persons registered at practices in the CCG. The detection rate is taken as a proxy measure for early diagnosis, as the cancer was suspected by a primary care clinician, and hence a higher rate is considered desirable. The emergency presentation rate is a proxy measure for late diagnosis and a lower rate is considered desirable. These two indicators are the strongest predictors of stage shift from TMN 3 and 4, to TMN 1 and 2, and are used by NHS England and Public Health England (PHE) as markers to track improvements in early cancer diagnosis.

A further two measures were also considered: the referral rate (the number of 2ww referrals for suspected cancer expressed as a rate per 100,000 persons registered at practices in the CCG) and the conversion rate (the number of 2ww referrals that resulted in a diagnosis of cancer, expressed as a percentage of all 2ww referrals at practices in the CCG). These have been shown to correlate strongly with the detection rate (15).

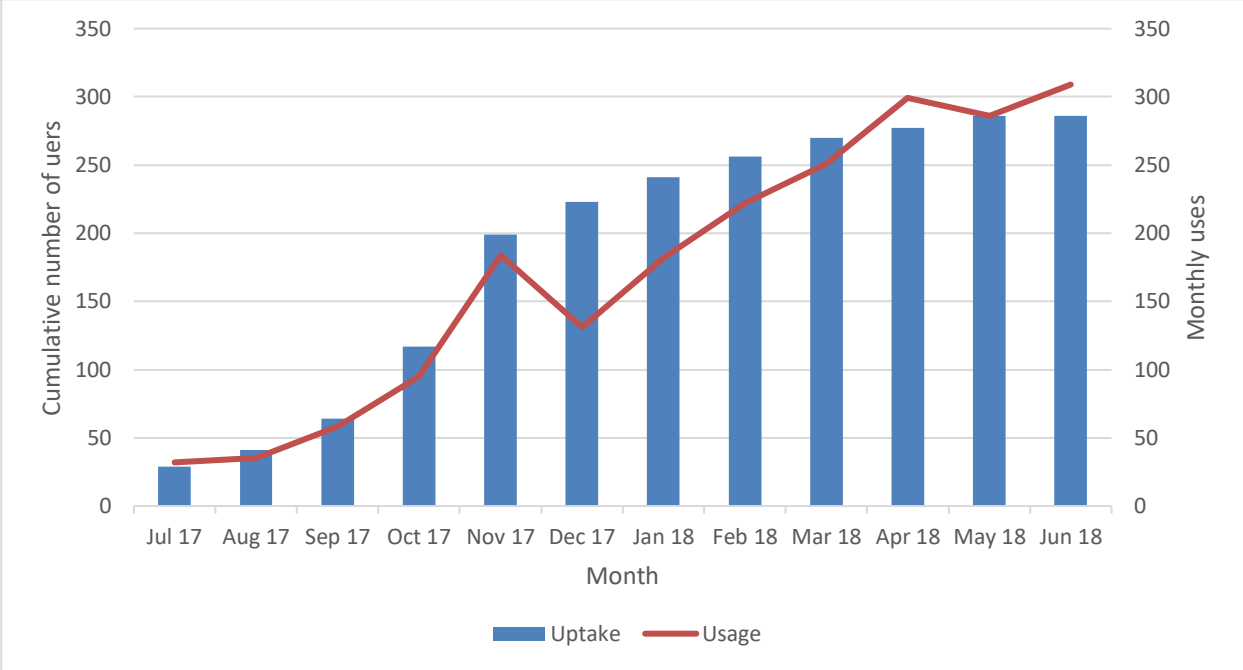
Two comparator groups were used to assess any impact of the tool: the rest of the CCGs in the EoE region (17 in total) where the tool was not adopted; and three CCGs from the EoE Region that were matched with the trial CCGs, based on similar, previous performance on the measures of interest. The least sum of squares method was used to select the CCGs with the closest trend to the trial CCGs over the previous five years (2011-12 to 2016-17).

For each of the metrics, the change in the values between 2016/17 and 2017/18 was calculated. The results for each measure were statistically analysed. Mann-Whitney Tests (MW-test) were used for pairwise comparisons of non-normally distributed data, whereas Two Sample T-tests (t-test) were used for normally distributed data. The analysis used one-tailed tests of significance, which assesses the change in one direction (i.e. an increase or a decrease).

3. RESULTS

Over the twelve months of the trial, a total of 286 primary care practitioners adopted the tool, from 85 practices, across the three CCGs. This represents 71% of all practices in the combined CCGs. The majority of users were GPs (260 of the total), with 16 nurse practitioners and 10 other healthcare professionals among users. Figure 3.1 shows the cumulative uptake by practitioners and the monthly levels of usage of the tool (not cumulative).

Figure 3.1 Cumulative uptake of C the Signs by practitioners and non-cumulative uses per month across the three CCGs



There was a steady rise in the cumulative number of practitioners using the tool over the period, with a levelling off at the end, which may reflect the total achievable level of uptake. The monthly usage also shows a mostly steady increase, reflecting the number of users, with the exception of a dip in December 2017. The total number of patients risk assessed was 2,084 for the full year of the trial, triggering 5,121 suspected cancer pathways.

Table 3.1 shows the values for each output measure under consideration in the trial CCGs and for both of the comparator groups. The rates for each of the measures were lower for the trial CCGs than the average for the rest of the CCGs in the EoE Region and for the matched CCGs. The percentage change in the trial year, compared to the previous year are presented in Table 3.2 for the four measures considered in this paper.

Table 3.1 Average values for detection rate, emergency presentations, referral rate and conversion rate for the trial CCGs and two comparator groups (trial year and preceding year)

	Average values			
	Detection rate (as percentage of new cancer cases treated)	Emergency presentation rate (per 100,000 persons)	Referral rate (per 100,000 persons)	Conversion rate (percentage of 2ww referrals)
Trial CCGs 2016/17	47.4%	85	2,513	7.7%
Trial CCGs 2017/18	50.5%	79	2,651	7.3%
Rest of EoE CCGs 2016/17	51.6%	95	3,277	8.5%
Rest of EoE CCGs 2017/18	51.7%	90	3,383	8.4%
Matched CCGs 2016/17	53.8%	80	2,949	8.8%
Matched CCGs 2017/18	55.0%	83	3,151	8.5%

Source: https://fingertips.phe.org.uk/

Table 3.2 Percentage change in detection rate, emergency presentations, referral rate and conversion rate for the trial year, comparing 2017/18 to the previous year

	Percentage change from previous year			
	Detection rate	Emergency Presentation rate	Referral rate	Conversion rate
Trial CCGs	6.39%	-7.09%	5.48%	-5.63%
Rest of EoE CCGs	0.23% *	-5.75%	3.24% *	-2.00%
Matched CCGs	2.17% *	2.90%	6.84%	-2.66%

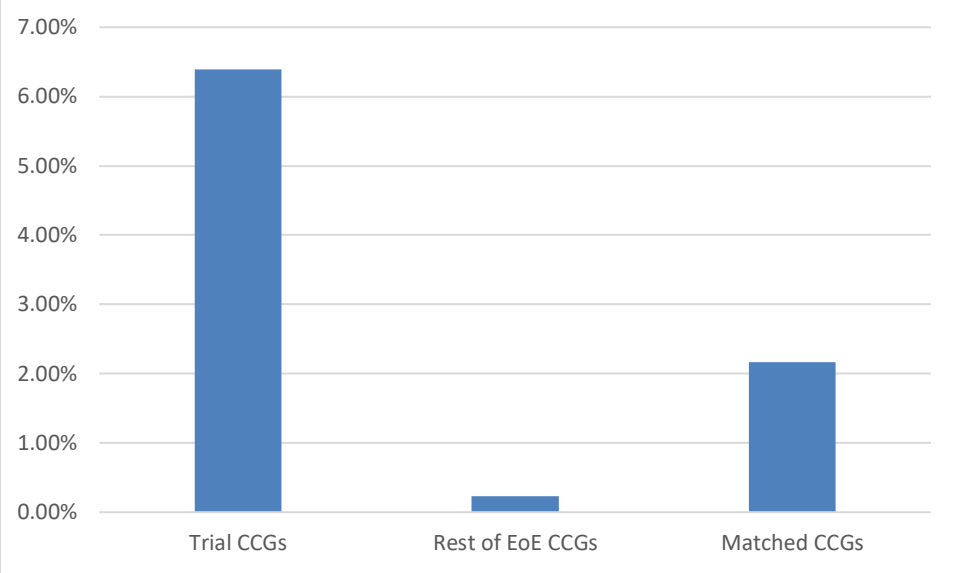
* Indicates a significant difference ($p<0.05$) relative to the trial group for one-way tests

These results indicate that, when compared to the rest of the CCGs in EoE, there was a significant increase in the average cancer detection rate and referral rates for the trial CCGs between the trial year and the previous year ($p<0.05$). There was also a significant increase in the detection rate when compared to the matched CCGs ($p<0.05$), but no significant difference was observed in the referral rate.

The emergency presentations decreased, but this was not found to be statistically significant. The conversion rate also decreased against both comparator groups. This change was found not to be statistically significant.

In the trial CCGs, the rate of cancer detection in primary care improved significantly by 6.39% ($P <0.05$). This compares to 0.23% in the rest of the East of England, and 2.17% in the matched controls (Figure 3.2).

Figure 3.2: Rate of cancer detection in primary care



Economic analysis

The economic analysis seeks to elucidate the possible economic consequences of any impact that might be attributed to an intervention. In this case that impact is the increase in the cases of cancer that are diagnosed at early rather than late stages. The evidence for the costs of early and late diagnoses are taken from the paper by Birtwistle *et al.* (17). This looked at the lifetime treatment costs for treating four common cancer types: colon, rectal, lung and ovarian cancer. Using their figures, a weighted average cost for early stage and late stage cancer is calculated, shown in Table 3.3.

Table 3.3 Costs of early and late stage cancer diagnosis at 2014 prices

	Diagnosis at stages 1-2	Diagnosis at stages 3-4	Difference
Weighted average cost of treatment for four cancer types	£6,549	£11,252	£4,703

Using inflation rates for health care (18), this cost difference is estimated at 2019/20 prices to be £4,960 per case. That figure can be applied to the impact on the detection rate, reported above. The difference in detection rates compared to the two comparator groups is shown in Table 3.4.

Table 3.4 Difference in the change in detection rates from 2016-17 to 2017-18 for the trial group and both comparator groups

	Trial group	Comparator group	Difference
EoE CCGs comparator	6.39%	0.23%	6.17%
Matched CCGs comparator	6.39%	2.17%	4.23%

Cost of C the Signs

For this trial the tool was offered free of charge to practitioners. For commercial use, C the Signs report that the cost is £0.18 per person registered on practice lists in a CCG. This includes availability of the system to clinicians, attendance at practice lunchtime learning sessions for introducing the system and training purposes, and attendance at existing cancer team meetings at CCG level. This gives a cost per CCG in the trial as shown in Table 3.5.

Table 3.5 List size and imputed cost for CCGs in the trial

CCG	Total list size at 01/12/19 [1]	Cost per year
CCG A	657,000	£118,260
CCG B	239,000	£43,020
CCG C	240,000	£43,200
Total	**1,136,000**	**£204,480**

Economic impact

The number of new cases treated (the denominator for the detection rate) in 2016-17 was 2,238, as reported in the PHE data. [2] Applying the difference to the number of cases reported in 2016-17, gives the following economic impact.

Table 3.6 Economic impact of differences in detection rates from 2016-17 to 2017-18 for both comparator groups (£4,960 at 2019/20 prices)

	Number of cases for 2016/17	Increase relative to EoE CCGs comparator (6.17%)	Increase relative to Matched CCGs comparator (4.23%)
Total cases for trial CCGs	2,238	138	95
Saving		£684,551	£469,293
Net saving (Saving minus cost of using C the Signs)		**£480,071**	**£264,813**

Note: the numbers presented have been rounded, so the results may appear slightly different from those found

[1] From: https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/general-practice-data-hub/patients-registered-at-a-gp-practice

[2] https://fingertips.phe.org.uk/ (accessed 07/01/20)

A return on investment has been calculated using the formula:

$$\text{Return on investment (ROI):} \quad \frac{\sum \text{discounted Benefits} - \sum \text{discounted costs}}{\sum \text{discounted costs}}$$

(Where ∑ = sum of)

This gives the results:

- ROI relative to EoE CCGs comparator: $\frac{£684,551 - £204,480}{£204,480} = 2.3$

- ROI relative to Matched CCGs comparator: $\frac{£469,293 - £204,480}{£204,480} = 1.3$

4. DISCUSSION

Summary

The rate of cancer detection in primary care in the trial CCGs improved significantly compared to the rest of the EoE region. As improvements in cancer detection following referrals from primary care correlate strongly with early cancer detection (11), this is likely to represent diagnostic stage shift in the trial CCGs.

There was a reduction in emergency presentations resulting in a new cancer diagnosis (7.09%), in line with long term trends. This was greater in the C the Signs group than in the rest of the EoE region and matched CCGs, although this did not reach a level of significance. The downward trend in emergency presentations in all groups matches the improvement in detection rates seen, suggesting possible shift towards earlier diagnosis. As emergency presentation rates fluctuate year on year across NHS England, a longer trial over a larger area would assist in understanding the attribution of observed effects to interventions aimed at increasing cancer detection.

Referral rates increased by 5.48% which was a statistically significant increase compared to the rest of the EoE Cancer Alliance. However, the trial CCGs conducted fewer referrals per 100,000 population in 2017/18 (2,651) compared to any of the comparators (and 21.7% less than the EoE Cancer Alliance), so this increased demand may not represent a substantial burden on secondary care. In addition, we saw a greater fall in conversion rates of 5.63% compared to comparators, but this did not reach the level of significance.

Increasing referrals from primary care for suspected cancer is a national priority which should contribute to improved cancer survival rates in the future. In order to detect cancers earlier and achieve better outcomes for patients, the threshold for GP referral for patients with suspected cancer was reduced from 11% to 3% in 2015. As expected, in order to increase the cancer detection rate, GP 2ww referral rates have increased, and conversion rates to cancer diagnosis have dropped (16). While the rate of referrals in the study area has increased, it remains below the regional and national average. This may suggest there has been an improvement in the appropriateness of referrals, although this would require further research to evaluate. There may be other consequences of the strategy to increase referrals for suspected cancer, such as increased demand on diagnostic services and on secondary care outpatient clinics. Conversely, an increase in earlier diagnoses can lead to reductions in treatment costs (17).

C the Signs saw positive engagement of clinicians during the study period, with 286 healthcare professionals signing up (82.17% of users signed up in the first three months). Users were from 85 practices, 71% of the total across the three participating CCGs. Mobile apps and websites can present a challenge in clinical practice, particularly given the limited time available during clinical consultations. The level of uptake of the tool (71% of practices within the trial area), without incentivisation or direct advertisement, illustrates the likability and usability of the tool.

Assigning an economic value to early diagnosis (as compared to late diagnosis) shows a net saving over one year of £480,071 or £264,813 with an ROI of 2.3 or 1.3 respectively, across this group of three CCGs. This indicates £2.30 or £1.30 of value for every £1.00 invested in the intervention. It is noted that not all of this value (the non-medication costs) may be realised as cash releasing savings. However, the non-cash releasing savings may contribute to relieving pressure on services, or increase the ability of services to meet demand. Beyond the economic impact, the benefits of earlier diagnosis for patients include more positive prognosis, with higher chances of survival and less intrusive treatment.

Strengths and limitations

For an intervention such as C the Signs it would be very complex to perform a controlled trial. A real world evaluation such as this gives an indication of the impact C the Signs can have, but acknowledges that there are other possible factors which may influence the measures used here, such as a local pressure to improve performance in cancer detection. However, no other such interventions in the early diagnosis of cancer were reported in the trial areas during the period. Continued study would be beneficial, to provide further evidence of the association of C the Signs with improved performance on cancer detection and emergency presentation rates.

Use of the tool in this trial began in July 2018 and ran for a full year. However, the available data on the measures used in this analysis relates to the financial year April 2017 to March 2018. Therefore, the referral data includes three months at the start of the period, during which C the Signs was not in use and the data are not available by month, so it has not been possible to analyse the partial year for which the tool was in use and for which data are available. The result of this would be to supress any attributed impact of the tool.

A longer-term study of the use of this tool will be helpful in clarifying the role of C the Signs in the observed changes in detection and referral rates, as well as in identifying potential changes in conversion and emergency presentation rates. In addition, a longer trial period would be beneficial to understand the effect of large fluctuations in emergency presentation rates from year to year.

Comparison with existing literature

Existing literature identifies the importance of early diagnosis for improved cancer outcomes. This study confirms the key role of primary care and supports the use of clinical decision tools to assist primary care clinicians in their referral practice.

Implications for research and/or practice

The early detection of cancer is a high, national priority in the NHS. A tool that can help general practitioners to more accurately identify potential cancer symptoms would be an important service in attempts to improve early detection. This study shows that the use of artificial intelligence may have a role to play in this endeavour and C the Signs has the potential to contribute to achieving this goal. Further research could also look at whether the benefits in terms of better cancer detection rates are outweighed by the implementation costs of interventions to improve primary care referral practice.

Competing interests

Dr Payling and Dr Bakshi are Co-founders of C the Signs. C the Signs is an NHS England funded initiative through the Small Business Research Initiative and was piloted for free across the three sites. Jo Hanlon, Jo Setters and Joe Moss are members of staff at York Health Economics Consortium, which was funded by C the Signs to conduct the analysis described in the manuscript. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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