

Accepted Manuscript

British Journal of General Practice

Cancer detection via primary care urgent referral in England 2009/10 to 2018/19 and the association with practice characteristics

Round, Thomas; Ashworth, Mark; L'Esperance, Veline; Møller, Henrik

DOI: <https://doi.org/10.3399/BJGP.2020.1030>

To access the most recent version of this article, please click the DOI URL in the line above.

Received 17 November 2020

Revised 13 May 2021

Accepted 17 May 2021

© 2021 The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 License (<http://creativecommons.org/licenses/by/4.0/>). Published by British Journal of General Practice. For editorial process and policies, see: <https://bjgp.org/authors/bjgp-editorial-process-and-policies>

When citing this article please include the DOI provided above.

Author Accepted Manuscript

This is an 'author accepted manuscript': a manuscript that has been accepted for publication in British Journal of General Practice, but which has not yet undergone subediting, typesetting, or correction. Errors discovered and corrected during this process may materially alter the content of this manuscript, and the latest published version (the Version of Record) should be used in preference to any preceding versions

Cancer detection via primary care urgent referral in England 2009/10 to 2018/19 and the association with practice characteristics

Thomas Round, BSc, MRCP, GP and NIHR Doctoral Research Fellow^{1,2}, Mark Ashworth, DM, MRCP, FRCGP, Reader in Primary Care Research¹, Veline L'Esperance, BM, MSc, MPH, MRCP, FHEA, GP and NIHR Doctoral Research Fellow¹, Henrik Møller, Professor of Cancer Epidemiology³

¹Primary Care, School of Population Health and Environmental Sciences, King's College London, Addison House, Guys Campus, London SE1 1UL

²National Cancer Registration and Analysis Service (NCRAS), Public Health England (PHE), Wellington House, London SE1 8UG

³School of Cancer and Pharmaceutical Sciences, King's College London, Guys Campus, London SE1 9RT

Corresponding author: thomas.round@kcl.ac.uk

Abstract word count 250

Paper word count (excluding tables/figures/supplementary content) 3163

Abstract

Background

There is substantial variation in use of urgent suspected cancer referral (two week wait/2WW) between practices.

Aim

To examine change in use of 2WW referrals in England over ten years (2009/10 to 2018/19) and practice and population factors associated with cancer detection.

Design and Setting

Retrospective cross-sectional study of English general practices and their 2WW referral and cancer waiting times (CWT) detection data (all cancers other than non melanoma skin cancers) 2009/10 to 2018/19.

Methods

Descriptive statistics of changes over ten years in 2WW referral data. Yearly linear regression models to determine the association between cancer detection rates and quintiles of practice and population characteristics. Predicted cancer detection rates were calculated and the difference between lowest (Q1) to highest (Q5) quintiles.

Results

Over the ten years studied there were 14.89m 2WW referrals (2.2m 2018/19), 2.68m new cancer diagnoses of which 1.26m were detected following 2WW. The detection rate increased from 41% to 52%. In 2018/19 an additional 66,172 cancers were detected via 2WW compared to 2009/10. Higher cancer detection via 2WW referrals was associated with larger practices and those with younger GPs. From 2016/17 onwards more deprived practice populations were associated with decreased cancer detection.

Conclusions

From 2009/10 to 2018/19 2WW referrals increased on average by 10% year on year. Higher cancer detection was found in larger practices, with relatively younger GPs and more recently, less deprived populations. COVID-19 has led to significant impacts on 2WW referral activity and the impact on patient outcomes will need to be studied.

Keywords

Cancer, early diagnosis, primary care, general practice, referral and consultation

How this fits in

There is considerable variation in use of urgent suspected cancer referrals (2WW) between general practices in England, with increased use associated with improved cancer patient outcomes. There has been limited research into practice and population characteristics associated with cancer detection via 2WW referral pathways. Over the ten year period up to 2018/19 yearly 2WW referrals more than doubled to over 2.24 million leading to an increase in cancer detection and 66,172 additional cancers diagnosed via 2WW in 2018/19 compared to 2009/10. Higher cancer detection via 2WW referrals was associated with larger practices and those with younger GPs, though the relationship with GP age was attenuated in more recent years. Of concern are decreases in 2WW referrals during the COVID-19 pandemic and the appearance of potential disparity in cancer detection, with lower rates in practices serving more deprived populations.

Background

Most of those with cancer present symptomatically to primary care (1), although the diagnosis of cancer in general practice is not straightforward (2, 3). International variations in cancer survival have been partly attributed to healthcare system differences in primary care (4). In particular whether systems with prominent primary care 'gate-keeping' may result in longer diagnostic intervals and poorer outcomes for patients with cancer (5, 6).

Concerns about diagnostic delays led to the implementation of urgent referral pathways in England (7). These are based on National Institute for Health and Care Excellence (NICE) referral guidelines initially published in 2005 (8) and updated in 2015 (9). A primary care referral for suspected cancer aims for cases to be seen by a specialist or have a diagnostic test within 2 weeks of referral (i.e. 2 week wait or 2WW referral). For many cancers there is good evidence that the time to diagnosis and treatment is reduced for patients referred urgently (10, 11). There are significant variations in use of 2WW between practices (12), with referral route an important potential predictor of time to diagnosis (13, 14).

Higher practice use of 2WW is associated with reduced cancer patient mortality (15) and in reduced late stage cancers at diagnosis (16). Higher practice referral rates (2006-2008) for upper gastrointestinal (GI) endoscopy was also found to be associated with improved patient outcomes (17). A cross sectional study of practice characteristics associated with use of both 2WW and endoscopy referrals in 2013 suggested that practice-level attributes explained a substantial amount of between-practice variation (18).

A more detailed analysis has been called for to understand the variation in use of 2WW pathways (7, 12, 19) and the characteristics of primary care associated with higher practice cancer detection (15,

16), including confirming whether previously found associations (for 2013) (18) are consistent over longer and more recent time periods.

Methods

Design and setting

Retrospective cross-sectional study of national cancer and general practice data in England for financial years 2009/10 to 2018/19.

National and practice cancer data

The national Cancer Waiting Time (CWT) system in England is used to monitor cancer waiting times targets and is a record of cancer registration (20). This includes all patients diagnosed with cancer (ICD-10 codes C00–C97), excluding non melanoma skin cancer (C44). National level data on cancer registrations and 2WW referrals are available from NHS England (21), whilst practice 2WW cancer detection rate data are available from Public Health England (PHE) National Cancer Registration and Analysis Service (NCRAS) ‘fingertips’ (22) practice profiles, which are generated where the practice list size is at least 1000. 2WW referral metrics are available at a national and individual practice level and include:

Detection rate (DR) — proportion of CWT-recorded cancers (0 to 100%) resulting from a 2WW referral (i.e. the sensitivity of referral).

Conversion rate (CR) — proportion of urgent referrals for suspected cancer that result in a diagnosis of cancer (i.e. the positive predictive value [PPV] for cancer among the patients referred).

We focussed on the CWT 2WW referral indicator of ‘cancer detection’ at a practice level (i.e. the sensitivity of selection of patients for urgent referral) which is significantly associated with cancer patient outcomes (16).

Practice characteristics

Descriptive data for all practices in England were obtained from NHS Digital (23) for the ten financial years studied as described in previous publications (24-26). Data included workforce information (e.g. mean age of practice GPs), practice characteristics such as list size, list size per full-time equivalent (FTE) GP and the demographic characteristics of registered patients.

Estimates of the proportions of patients from ethnic minority groups were obtained for the location of each practice, adjusted for Lower Layer Super Output Area (LLSOA) data for the practice postcode. Deprivation data for each general practice was attributed as the mean of the Index of Multiple Deprivation (IMD) scores weighted by the proportion of practice patients resident in each LLSOA. Quality Outcomes Framework (QOF) data were also obtained from NHS digital, based on achievement of a series of targets relating to long-term condition management and public health goals (27). We examined whether and how these practice and population characteristics (see table 3 for variables) were associated with cancer detection via 2WW referral pathways.

For 2018/19 there were 6873 practices in England, with 92 (1.3%) excluded, mainly due to missing referral data, with 6781 practices were included for analysis (see supplementary figure 1).

Supplementary table 2 provides a detailed breakdown of exclusions from 2009/10 to 2018/19.

Statistical analysis

Data on yearly cancer registrations and 2WW referral metrics were extracted from NHS England and PHE 'fingertips' for descriptive analysis. Variable descriptions and analysis were performed utilising STATA (version 16). Practice and population variables were stratified into quintiles (i.e. five equal groups) for analysis similar to previously described methods (16, 28). Multicollinearity was tested using the variance inflation factor (VIF) (29), which was <2 (mean 1.33) for all included variables, suggesting no significant multicollinearity. Linear and multiple linear regression models were used to

explore the association between practice variable quintiles and cancer detection for each study year, starting from 2018/19 and then the previous nine financial years. P values were calculated for significance of differences in predicted cancer detection between variable quintiles. Values were expressed as percentage point differences between lowest (Q1) and highest (Q5) quintiles for each variable.

Results

Cancer diagnoses and 2WW referral data 2009/10 to 2018/19

Over the ten years studied there were 14.89m 2WW referrals, 2.68m new cancer registrations of which 1.26m were detected via urgent referral (see table 1). Total 2WW referrals more than doubled to over 2.24 million in 2018/19 (see figure 1), with an average yearly increase of 10%. However, the yearly conversion rates decreased from 10.8% to 7.3% (see supplementary figure S3, CWT database registered cancers increased from 234,138 in 2009/10 to 313,525 in 2018/19, a 34% relative increase over 10 years. Cancer detection via 2WW referral increased from 41% in 2009/10 to 52% in 2018/19, leading to an increase in cancers diagnosed following 2WW referral from 97,760 (2009/10) to 163,932 (2018/19). There were an additional 66,172 cancers detected via 2WW compared to 2009/10 (a 68% relative increase). If cancer detection rate had been maintained at 41% (rather than yearly increases) 165,899 fewer cancers would have been detected via 2WW over the ten year period.

Variable summary

The distribution of practice and population characteristics for the practices included are summarised in table 2. Over ten years studied there was a reduction in the number of practices, with consequent increase in list size (from 6910 to 8307). There was an increase in the average registered patients per FTE GP to over 2300, although the method of recording this variable changed in 2015/16 (30). GP

mean age (range, 47-48 years), IMD score (range, 25.6-26.2) and the proportion of registered patients aged over 65 (16%) were relatively stable over this time period, whilst the proportion of registered white ethnicity patients decreased from 89% to 84% over the study period. Maximum available practice QOF points decreased over time from 1000 (2009/10) to 559 (2014/15 onwards).

2018/19 cancer detection and predictors

The univariable linear regression associations between practice characteristic quintiles and cancer detection are shown in table 3. Variables positively associated with higher cancer detection rates, included practice list size (+4 percentage points higher cancer detection from lowest (Q1) to highest (Q5) quintiles), QOF score (+3), proportion of patients aged over 65 years (+5) and proportion of white patients (+3). As an example cancer detection rates increased from 50% for practices in the lowest quintile of list size (mean of 3,207 patients) to 54% for practices in the highest quintile (mean of 16,847 patients). Variables negatively associated with cancer detection rates included registered patients per FTE GP (-2 percentage points difference Q1 to Q5), GP average age (-3) and IMD score (-5).

For the multivariable linear regression models all variables remained significantly associated (consistently positively or negatively) with cancer detection rates with the exception of QOF score and patient ethnicity. Overall, differences in detection rate between Q1 and Q5 were attenuated after adjustment for covariates. The largest cancer detection rate Q1-Q5 differences were found for practice list size (+2), GP average age (-2), deprivation (-4) and older patients (+3).

Difference in predicted cancer detection rates between practice variable quintiles 2009/10 to

2018/19

Cancer detection analyses for quintiles of practice characteristics in univariable and multiple linear regression models were carried out for each previous financial year to 2009/10 (yearly data tables available on request). The percentage point difference in cancer detection rates for practice variables between lowest (Q1) to highest quintiles (Q5) for each year is described in tables 4 and 5, obtained from univariable and multiple linear regression models respectively.

In the univariable regression models (table 4) increasing numbers of patients per FTE GP, GP average age and practice deprivation (IMD score) all had significant negative associations with cancer detection. Though the Q1 to Q5 difference from 2009/10 to 2018/19 reduced for patients per FTE GP (from -6 to -2) and GP average age (-7 to -3), whilst for deprivation the quintile difference increased (from -3 to -5). Positive associations with increased cancer detection rates were found for increased practice list size, QOF score and the proportion of patients aged over 65 years.

In the multivariable linear regression models (table 5), the most consistent association with increased cancer detection was for larger practices, with younger GPs, serving older populations. Over the study period differences in cancer detection between Q1-Q5 for GP age became less pronounced (from -6, 2009/10 to -2, 2018/19), whilst deprivation initially lacked significance, but was significantly associated with reduced cancer detection (-4 percentage point difference) from 2016/17 onwards.

Excluded practices

The characteristics of excluded practices, included those with missing referral data are included in supplementary table 4, with the total number of excluded practices reducing from 588 (2009/10) to 92 (2018/19). They were smaller (mean list size <3000), had older GPs (mean age 52), lower QOF scores and served younger and more deprived, multi-ethnic populations.

Discussion

Summary

2WW referrals in England more than doubled over the ten year time period studied to over 2.24 million in 2018/19, with a subsequent increase in cancer detection rates (41% to 52%) and decrease in conversion rate (10.8% to 7.3%). This led to 66,172 additional cancers detected following 2WW referral in 2018/19 compared to 2009/10.

Predicted 2WW cancer detection was consistently associated with larger practice list size (positive association) and increasing GP age (negative association), although over the study period there was a narrowing in the difference of cancer detection between practices with younger and older GPs. In the last three years of study, cancer detection rates were consistently lower in more deprived areas, an effect not seen in earlier years.

Strengths and limitations

The strengths of this study include utilising large national databases in England including all 2WW referrals and cancers registered within CWT database, and data on the majority of practices England over ten years.

The CWT database contains diagnosis and treatment information on cancer patients who were offered treatment within the NHS, whichever diagnosis route they came through (20, 21). However, not all cancer patients are included in the CWT. Data from adults diagnosed with colorectal, lung or ovarian cancer in England (2009–2013) were linked from CWT to cancer registry, mortality, and Hospital Episode Statistics data. The authors found approximately 80% of patients were included (31). Patients not recorded in CWT were more likely to be in the youngest or oldest age groups, have

more comorbidities, have been diagnosed through emergency presentation, have late or missing stage, and have much poorer survival. NCRAS routes to diagnosis data includes cancer registrations following GP referral (2WW or routine), screening, outpatient or inpatient elective, death certification and if diagnosed within 28 days of emergency activity (32). The most recent data to 2017 (33) showed that over half of all cancers are diagnosed following a GP referral, and there have been reductions in diagnosis following emergency activity to under 20% of all cancers. Approximately 4% of cancer registrations are via an unknown route.

Practice level characteristics were extracted from quality assured national published datasets (27, 34) and we utilised established methodology (25, 26). We had no access to patient-level data, so could not adjust for the characteristics of patients that were investigated or referred at the individual level, although we used practice-level measures of ethnicity and deprivation, adjusted for LSOA of residence of the registered population. The studied associations may be affected by practices not included in our analyses, although this reduced over time to less than 2% (table 1). The number of practices with missing 2WW referral data also reduced over the ten years studied from 3.2% to 0.5%, suggesting increased robustness of the PHE NCRAS data. There were also changes over the time period studied in how some practice characteristics were calculated, such as in 2015/16 NHS England changed how FTE GP was calculated (30).

Variation in practice with respect to cancer referrals is more complex than publicly reported metrics suggest (including detection rate) (35, 36) and no single indicator captures quality of care.

Comparison with existing research

There have been substantial increases in the proportion of cancer patients diagnosed following 2WW referral and a subsequent decrease in those diagnosed via emergency routes (37), in whom there are worse outcomes (32). There are also large differences in the number of 2WW referrals

based on cancer site and patient demographics (38). Following revised NICE 2WW referral guidance (2015) (39) there have been further substantial increases in referrals and related pressure on diagnostic services and diagnostic intervals (40).

Previous studies utilised data from a single year (2013) examined the association between practice 2WW and endoscopy use with GP patient survey data (41) and general practice characteristics (18). Practice-level attributes explained a substantial amount of between-practice variance in 2WW but little of the variance in endoscopy, with urgent referral found to be higher in training practices (42) and those with younger GPs (18).

There have been several studies into 2WW referral metrics, including detection rate, which have found year-on-year random variation (19), with significant observed differences in case-mix (43), and variation in referral selection accuracy and thresholds (44). GPs and practices are not working in isolation, with influences from the wider healthcare system (35, 36). Research has shown English GPs are potentially less likely to investigate and refer for suspected cancer (6) compared to GPs in similar high income countries. There is also an association between practice 2WW referral metrics and individual GP referral thresholds (45).

The broader literature on referrals suggests much variation is unexplained (46, 47), with conflicting evidence about the relationship between practice size and GP characteristics on referral rates (46, 48), and the impact of GP and practice characteristics on potential delays in cancer diagnosis (49). Our study has suggested that GP age has become less important as a predictor of cancer detection over time. One explanation is the diffusion of NICE referral guidance into clinical practice of individual GPs (10), with GPs of all ages more likely to follow guideline compliant practice.

A previous study found older patients (over 85 years) and more deprived patients were less likely to be referred (50), though there has been conflicting evidence at a practice level (46, 51). Our findings

of an association between practice deprivation and reduced cancer detection in recent time periods is a concern, particularly given continuing evidence for the persistence of the 'inverse care law' (52, 53).

Implications and Conclusions

This study has shown a substantial increase in yearly 2WW referrals of 10% per year to over 2 million per year in 2018/19. The average English general practice makes over 300 2WW referrals per year or approximately 65 per FTE GP. This has been associated with an increase in the proportion of cancers detected following GP 2WW referral from 41% to 52% and a reduction in the 2WW conversion rate from over 10% to 7%. This increase in referral activity has likely led to improved cancer patient outcomes (16). Health service waiting time targets are considered to be important indicators of the quality of cancer care (46), and even after a period of constrained resources and increases in referrals, the English healthcare system maintained (in 2018/19) 92% of urgently referred patients being seen by a specialist within 2 weeks of referral (21).

For the more recent financial year (2019/20) (54) there were 2,386,815 2WW referrals in England with overall detection rate further increasing to 53.5% and conversion rate to 6.7%, with the largest numbers of referrals for suspected skin (509,668), lower GI (443,534) and breast (435,253) cancers. PHE NCRAS has published 2WW pathway specific detection and conversion rates (55) with substantial variation between different 2WW pathways. This suggests some pathways are working more effectively than others, with international evidence showing a the UK cancer survival gap (between other comparable countries) reducing for breast cancer but not for some other cancers (4). This suggests scope for focusing on specific cancer types where increased triage testing and diagnostic access in primary care might make the most impact (16).

The most recent (2019/20) conversion rate for all 2WW referrals in England was just under 7% (i.e. 7 in 100 referrals diagnosed with cancer). Whilst the NICE 2WW guidelines in 2015 (9) specified a risk threshold to consider referral of 3%, patients would opt for investigation or referral at a lower risk threshold of 1% (56). With longer term aims of faster diagnostic standards and a greater proportion of early stage diagnoses (57), there are clear issues around finite staff, diagnostic access and capacity across primary and secondary care (58-60). This includes understanding the health economic impacts of increasing referrals and reduced referral thresholds, the potential risks of this including patient anxiety, iatrogenic harms and overdiagnosis.

During the COVID-19 pandemic there have been reductions in cancer screening, 2WW referrals and access to diagnostic tests, with likely negative impact on cancer diagnoses and outcomes (61, 62). It is therefore imperative to maintain gains made over the last ten years in the use of suspected cancer pathways. This includes clear and consistent messaging to the public that they should contact primary care services if they have worrying symptoms, and that whilst primary care is under pressure, assessment and urgent referral pathways are continuing although may be delivered in a different way (for example telephone/online consultations) (63, 64).

Conclusions

Against a backdrop of a more than doubling of 2WW referrals over the 10-year study period there is a consistent significant association between lower cancer detection and smaller practices with older GPs, though over time there was less observed variation particularly with GP age. The more recent significant association between increased practice deprivation and lower cancer detection is a cause for concern. Work to understand the significance of these findings for primary care staff and their patients is called for, including potential interventions to continue to facilitate cancer detection via primary care referral particularly given the recent impacts of the COVID-19 pandemic.

Additional Information

Ethical approval: Ethics committee approval not required for research based on routine data.

Data Availability: The analysis is based on routine practice level data from the NHS. Practice level referral data is available from PHE fingertips <https://fingertips.phe.org.uk/profile/cancerservices> . No additional data are available from the authors.

Conflict of Interest: All authors have completed the Unified Competing Interest form (available on request) and declare: TR has an honorary contract with National Cancer Registration and Advisory Service (NCRAS) Public Health England (PHE), and is supported by a National Institute for Health Research (NIHR) Doctoral Research Fellowship grant and previously a Royal Marsden Partners (RMP) Research Fellowship. Since October 2020 TR has been an Associate Editor for British Journal of General Practice (BJGP), and had no Editorial role in reviewing this manuscript. There are no other relationships or activities that could appear to have influenced the submitted work.

Funding: Dr Thomas Round is funded by a National Institute for Health Research (NIHR) Doctoral Research Fellowship (DRF) DRF-2016-09-054 for this research project and also supported by a Royal Marsden Partners (RMP) Research Fellowship. The views expressed are those of the author(s) and not necessarily those of the NIHR, NHS, RMP, PHE or the Department of Health and Social Care.

Authorship: TR, MA and HM conceived the study. TR, MA and HM drafted the study protocol, and contributed to the final protocol and analysis plan. TR analysed the data, and all authors contributed to the interpretation of the results. TR led the writing of the manuscript to which all authors contributed. TR is the guarantor.

Acknowledgements: This study was supported by a patient and public involvement (PPI) steering group which provided input to the programme of research (NIHR funded DRF). Study results and implications were discussed with patients with cancer, carers and lay people at meetings, workshops and conferences.

References

1. Swann R, McPhail S, Witt J, Shand B, Abel GA, Hiom S, et al. Diagnosing cancer in primary care: results from the National Cancer Diagnosis Audit. *Br J Gen Pract.* 2018;68(666):e63-e72.
2. Hamilton W, Sharp D. Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Family practice.* 2004;21(1):99-106.
3. Lyratzopoulos G, Wardle J, Rubin G. Rethinking diagnostic delay in cancer: how difficult is the diagnosis? *BMJ.* 2014 Dec 10;349.
4. Coleman M, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet.* 2011;377(9760):127-38.
5. Vedsted P, Olesen F. Are the serious problems in cancer survival partly rooted in gatekeeper principles? An ecologic study. *Br J Gen Pract.* 2011;61(589):e508-e12.
6. Rose PW, Rubin G, Perera-Salazar R, Almberg SS, Barisic A, Dawes M, et al. Explaining variation in cancer survival between 11 jurisdictions in the International Cancer Benchmarking Partnership: a primary care vignette survey. *BMJ Open.* 2015;5(5):e007212.
7. Emery JD, Shaw K, Williams B, Mazza D, Fallon-Ferguson J, Varlow M, et al. The role of primary care in early detection and follow-up of cancer. *Nat Rev Clin Oncol.* 2014;11(1):38.
8. National Institute for Health and Care Excellence (NICE). Referral guidelines for suspected cancer. 2005.
9. National Institute for Health and Care Excellence (NICE). Suspected cancer: recognition and referral NICE guideline [NG12]. 2015.
10. Neal R, Din N, Hamilton W, Ukoumunne O, Carter B, Stapley S, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: analysis of data from the UK General Practice Research Database. *Br J Cancer.* 2014;110(3):584-92.
11. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *British journal of cancer.* 2009;101(S2):S5-S8.
12. Meechan D, Gildea C, Hollingworth L, Richards MA, Riley D, Rubin G. Variation in use of the 2-week referral pathway for suspected cancer: a cross-sectional analysis. *Br J Gen Pract.* 2012;62(602):e590-e7.
13. Jensen H TM, Olesen F, Overgaard J, Vedsted P. Cancer suspicion in general practice, urgent referral and time to diagnosis: a population-based GP survey and registry study. *BMC cancer.* 2014;30(14(1)):636.
14. Larsen MB, Hansen RP, Hansen DG, Olesen F, Vedsted P. Secondary care intervals before and after the introduction of urgent referral guidelines for suspected cancer in Denmark: a comparative before-after study. *BMC Health Serv Res.* 2013;13(1):348.
15. Møller H, Gildea C, Meechan D, Rubin G, Round T, Vedsted P. Use of the English urgent referral pathway for suspected cancer and mortality in patients with cancer: cohort study. *BMJ.* 2015;351:h5102.
16. Round T, Gildea C, Ashworth M, Møller H. Association between use of urgent suspected cancer referral and mortality and stage at diagnosis: a 5-year national cohort study. *Br J Gen Pract.* 2020;70(695):e389-e98.
17. Shaihi M, Thompson E, Kapoor N, Powell G, Sturgess RP, Stern N, et al. Variation in gastroscopy rate in English general practice and outcome for oesophagogastric cancer: retrospective analysis of Hospital Episode Statistics. *Gut.* 2014;63(2):250-61.
18. Mendonca SC, Abel GA, Gildea C, McPhail S, Peake MD, Rubin G, et al. Associations between general practice characteristics with use of urgent referrals for suspected cancer and endoscopies: a cross-sectional ecological study. *Fam Pract.* 2019;36(5):573-80.

19. Abel G, Saunders CL, Mendonca SC, Gildea C, McPhail S, Lyratzopoulos G. Variation and statistical reliability of publicly reported primary care diagnostic activity indicators for cancer: a cross-sectional ecological study of routine data. *BMJ Qual Saf.* 2018;27(1):21-30.
20. NHS Digital. Cancer Waiting Times Data Collection (CWT) 2020 [Available from: <https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-collections/cancerwaitingtimescwt>].
21. NHS England. Cancer Waiting Times Annual Reports [Available from: <https://www.england.nhs.uk/statistics/statistical-work-areas/cancer-waiting-times/cwt-annual-reports/>].
22. Public Health England (PHE). Cancer Services Profile [Available from: <https://fingertips.phe.org.uk/profile/cancerservices>].
23. NHS Digital. Data and information [Available from: <https://digital.nhs.uk/>].
24. Ashworth M, Seed P, Armstrong D, Durbaba S, Jones R. The relationship between social deprivation and the quality of primary care: a national survey using indicators from the UK Quality and Outcomes Framework. *Br J Gen Pract.* 2007;57(539):441-8.
25. Ashworth M, Schofield P, Seed P, Durbaba S, Kordowicz M, Jones R. Identifying poorly performing general practices in England: a longitudinal study using data from the quality and outcomes framework. *J Health Serv Res Policy* 2011;16(1):21-7.
26. L'Esperance V, Sutton M, Schofield P, Round T, Malik U, White P, et al. Impact of primary care funding on secondary care utilisation and patient outcomes: a retrospective cross-sectional study of English general practice. *Br J Gen Pract.* 2017;67(664):e792-e9.
27. NHS Digital. Quality Outcomes Framework (QOF). Disease prevalence and care quality achievement rates. 2020 [Available from: <https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/general-practice-data-hub/quality-outcomes-framework-qof>].
28. Møller H, Coupland VH, Tataru D, Peake MD, Mellemgaard A, Round T, et al. Geographical variations in the use of cancer treatments are associated with survival of lung cancer patients. *Thorax.* 2018;73(6):530-7.
29. Thompson CG, Kim RS, Aloe AM, Becker BJ. Extracting the variance inflation factor and other multicollinearity diagnostics from typical regression results. *Basic Appl Soc Psych.* 2017;39(2):81-90.
30. NHS Digital. Statistical Change Notice relating to General and Personal Medical Services in England workforce statistics 2016 [Available from: https://digital.nhs.uk/binaries/content/assets/legacy/pdf/b/h/statistical_change_notice_relating_to_general_and_personal_medical_services_in_england_workforce_sta.pdf].
31. Di Girolamo C, Walters S, Gildea C, Majano SB, Coleman MP, Rachet B, et al. Which patients are not included in the English Cancer Waiting Times monitoring dataset, 2009–2013? Implications for use of the data in research. *Br J Cancer.* 2018;118(5):733-7.
32. Elliss-Brookes L, McPhail S, Ives A, Greenslade M, Shelton J, Hiom S, et al. Routes to diagnosis for cancer—determining the patient journey using multiple routine data sets. *Br J Cancer.* 2012;107(8):1220-6.
33. National Cancer Registration and Analysis Service (NCRAS), Public Health England (PHE). Routes to Diagnosis 2017 [Available from: http://www.ncin.org.uk/publications/routes_to_diagnosis].
34. NHS Digital. General Practice Workforce 2020 [Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/general-and-personal-medical-services>].
35. Round T, Abel G. Seeing the wood and the trees: the impact of the healthcare system on variation in primary care referrals. *BMJ Qual Saf.* 2020;274-276.
36. Burton C, O'Neill L, Oliver P, Murchie P. Contribution of primary care organisation and specialist care provider to variation in GP referrals for suspected cancer: ecological analysis of national data. *BMJ Qual Saf.* 2020;29(4):296-303.

37. Herbert A, Abel GA, Winters S, McPhail S, Elliss-Brookes L, Lyratzopoulos G. 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.* 2019;69(687):e724-e30.
38. Zhou Y, Mendonca S, Abel G, Hamilton W, Walter FM, Johnson S, et al. Variation in 'fast-track' referrals for suspected cancer by patient characteristic and cancer diagnosis: evidence from 670 000 patients with cancers of 35 different sites. *Br J Cancer.* 2018;118(1):24.
39. Hamilton W, Hajioff S, Graham J, Schmidt-Hansen M. Suspected cancer (part 2—adults): reference tables from updated NICE guidance. *BMJ.* 2015;350.
40. Price S, Spencer A, Zhang X, Ball S, Lyratzopoulos G, Mujica-Mota R, et al. Trends in time to cancer diagnosis around the period of changing national guidance on referral of symptomatic patients: A serial cross-sectional study using UK electronic healthcare records from 2006–17. *Cancer Epidemiol.* 2020;69:101805.
41. Lyratzopoulos G, Mendonca SC, Gildea C, McPhail S, Peake MD, Rubin G, et al. Associations between diagnostic activity and measures of patient experience in primary care: a cross-sectional ecological study of English general practices. *Br J Gen Pract.* 2018;68(666):e9-e17.
42. Weston C, Ahluwalia S, Bassett P, Lock J, Durbaba S, Ashworth M. GP training practices in England: a description of their unique features based on national data. *Educ Prim Care.* 2017;28(6):313-8.
43. Murchie P, Chowdhury A, Smith S, Campbell NC, Lee AJ, Linden D, et al. General practice performance in referral for suspected cancer: influence of number of cases and case-mix on publicly reported data. *Br J Cancer.* 2015;112(11):1791.
44. Burton CD, McLernon DJ, Lee AJ, Murchie P. Distinguishing variation in referral accuracy from referral threshold: analysis of a national dataset of referrals for suspected cancer. *BMJ open.* 2017;7(8):e016439.
45. Kostopoulou O, Nurek M, Cantarella S, Okoli G, Fiorentino F, Delaney BC. Referral Decision Making of General Practitioners: A Signal Detection Study. *Med Decis Making.* 2019;39(1):21-31.
46. O'Donnell CA. Variation in GP referral rates: what can we learn from the literature? *Fam Pract.* 2000;17(6):462-71.
47. Sullivan CO, Omar RZ, Ambler G, Majeed A. Case-mix and variation in specialist referrals in general practice. *Br J Gen Pract.* 2005;55(516):529-33.
48. Forrest CB, Nutting PA, Von Schrader S, Rohde C, Starfield B. Primary care physician specialty referral decision making: patient, physician, and health care system determinants. *Med Decis Making.* 2006;26(1):76-85.
49. Hansen RP, Vedsted P, Sokolowski I, Søndergaard J, Olesen F. General practitioner characteristics and delay in cancer diagnosis. a population-based cohort study. *BMC Fam Pract.* 2011;12(1):100.
50. McBride D, Hardoon S, Walters K, Gilmour S, Raine R. Explaining variation in referral from primary to secondary care: cohort study. *BMJ.* 2010;341:c6267.
51. Hippisley-Cox J, Hardy C, Pringle M, Fielding K, Carlisle R, Chilvers C. The effect of deprivation on variations in general practitioners' referral rates: a cross sectional study of computerised data on new medical and surgical outpatient referrals in Nottinghamshire. *BMJ.* 1997;314(7092):1458.
52. Hart JT. The inverse care law. *Lancet.* 1971;297(7696):405-12.
53. McLean G, Guthrie B, Mercer SW, Watt GC. General practice funding underpins the persistence of the inverse care law: cross-sectional study in Scotland. *Br J Gen Pract.* 2015;65(641):e799-e805.
54. NHS England. Waiting Times for Suspected and Diagnosed Cancer Patients: 2019-20 Annual Report. 2020.
55. National Cancer Registration and Analysis Service (NCRAS), Public Health England (PHE). Urgent Suspected Cancer Referrals: Conversion and Detection Rates 2020 [Available from: http://www.ncin.org.uk/cancer_type_and_topic_specific_work/topic_specific_work/tww_conversion_and_detection].

56. Banks J HS, Bigwood L, Peters TJ, Walter FM, Hamilton W. Preferences for cancer investigation: a vignette-based study of primary-care attendees. *Lancet Oncol.* 2014;Feb 28(15(2)):232-40.
57. NHS England. The NHS long term plan. 2019.
58. Report of the Independent Cancer Taskforce. *Achieving World-Class Cancer Outcomes: A strategy for England 2015-2020.* 2015.
59. Mike Richards RT, Rebecca Fisher and Catherine Turton *Unfinished business: An assessment of the national approach to improving cancer services in England 1995–2015.* The Health Foundation; 2019.
60. Round T. Primary care and cancer: facing the challenge of early diagnosis and survivorship. *Eur J Cancer Care.* 2017;26(3):e12703.
61. Sud A, Torr B, Jones ME, Broggio J, Scott S, Loveday C, et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. *Lancet Oncol.* 2020;21(8):1035-44.
62. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol.* 2020;21(8):1023-34.
63. Jones D, Neal RD, Duffy SR, Scott SE, Whitaker KL, Brain K. Impact of the COVID-19 pandemic on the symptomatic diagnosis of cancer: the view from primary care. *Lancet Oncol.* 2020;21(6):748-50.
64. Round T, L'Esperance V, Bayly J, Brain K, Dallas L, Edwards JG, et al. COVID-19 and the multidisciplinary care of patients with lung cancer: an evidence-based review and commentary. *Br J Cancer.* 2021.

Table 1: Practice cancer referral data 2009/10 to 2018/19: 2WW referrals, CWT recorded cancers, detection and conversion rates

Financial years	Total 2WW referrals (% yearly change)	CWT recorded cancers (% yearly change)	2WW cancers recorded in CWT (% yearly change)	2WW cancer detection rate (% yearly change)	2WW cancer conversion Rate
2009/10	903,011	234,138	97,760	41%	10.8%
2010/11	999,688 (11%)	240,572 (3%)	103,023 (5%)	43% (5%)	10.3%
2011/12	1,101,823 (10%)	250,456 (4%)	110,400 (7%)	45% (5%)	10.0%
2012/13	1,215,813 (10%)	254,061 (1%)	114,945 (4%)	46% (2%)	9.5%
2013/14	1,353,618 (11%)	262,414 (3%)	122,229 (6%)	48% (4%)	9.0%
2014/15	1,545,767 (14%)	266,723 (2%)	126,637 (4%)	47% (-2%)	8.2%
2015/16	1,722,952 (11%)	276,555 (4%)	133,958 (6%)	49% (4%)	7.8%
2016/17	1,862,994 (8%)	284,655 (3%)	141,790 (6%)	50% (2%)	7.6%
2017/18	1,947,568 (5%)	294,514 (3%)	149,046 (5%)	51% (2%)	7.7%
2018/19	2,245,524 (15%)	313,525 (6%)	163,932 (10%)	52% (2%)	7.3%
Ten-year total number of referrals or cancers	14,898,758	2,677,613	1,263,720		
Change in financial year 2018/19 compared to 2009/10	1,342,513 (249% relative increase)	79,387 additional cancers (34% relative increase)	66,172 additional cancers (68% relative increase)	11 percentage point increase (27% relative increase)	3.5 percentage point decrease (48% relative decrease)

Figure 1: 2WW referrals and detection rate (CWT) in England 2009/10 to 2018/19

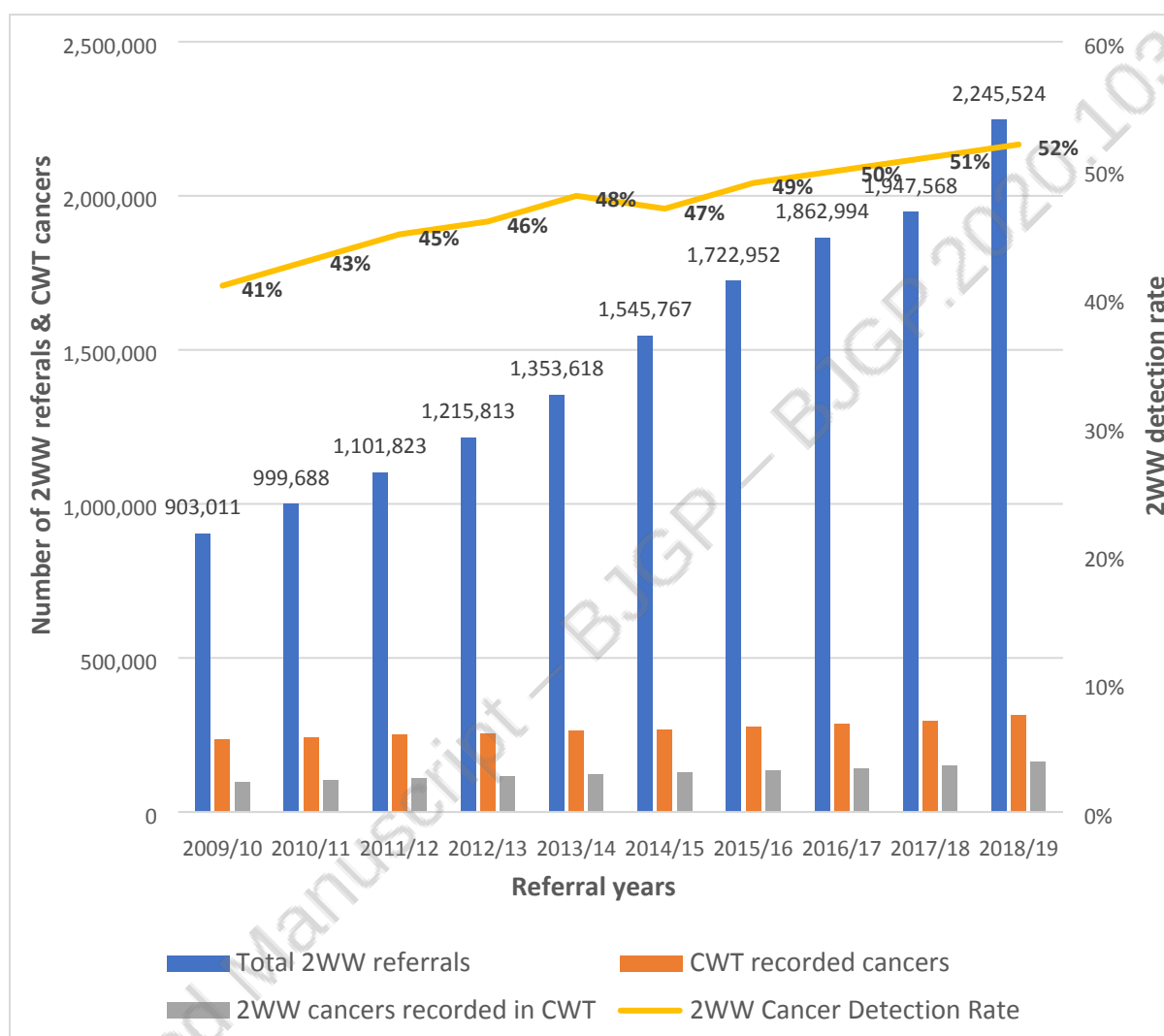


Table 2: GP practice characteristics in England 2009/10 to 2018/19 included in analysis

	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19
Number of practices included	7717	7730	7725	7739	7706	7428	7446	7233	6987	6781
2WW Detection Rate (DR)	41%	43%	45%	46%	48%	47%	49%	50%	51%	52%
Practice list size (mean)	6910	6973	7050	7145	7230	7491	7669	7690	8307	8717
List per FTE GP (mean)	1808	1851	1824	1847	1851	1879	2339	2342	2358	2304
GP average (mean) age	47.6	47.5	47.4	47.8	47.9	47.6	47.1	47.3	47.7	47.0
QOF score (mean) (out of maximum points available)	958 (1000)	950 (1000)	973 (1000)	964 (1000)	844 (900)	531 (559)	535 (559)	540 (559)	539 (559)	540 (559)
Practice IMD Score (mean)	25.9	26	25.8	26.2	26.2	26.1	26.1	26.1	26.1	25.6
Patients aged >65 years (%)	16%	16%	16%	17%	16%	16%	16%	16%	17%	17%
Ethnicity (white %)	89%	88%	83%	83%	84%	85%	84%	83%	84%	83%

Table 3: Predicted cancer detection (with 95% confidence intervals) for variable quintiles 2018/19 for both linear and multiple linear regression, and percentage point difference in predicted cancer detection from Q1 to Q5

Practice variable quintiles	2018/19 Practice variable quintile mean	Linear regression Predicted cancer detection (95% CI)	Q1-Q5 percentage point difference	Multiple linear regression Predicted cancer detection (95% CI)	Q1-Q5 percentage point difference
	Practice List Size (mean 8717)				
1	3207	50% (49-50%)		51% (50-51%)	
2	5423	52% (51-52%)		52% (52-53%)	
3	7686	53% (53-54%)		53% (52-54%)	
4	10427	53% (53-54%)		53% (42-43%)	
5	16847	54% (53-54%)		53% (42-43%)	
		P<0.001	+4	P<0.001	+2
	List per FTE GP (mean 2304)				
1	1297	53% (53-54%)		53% (52-54%)	
2	1566	54% (53-55%)		53% (53-54%)	
3	1934	52% (52-53%)		52% (52-53%)	
4	2403	51% (50-52%)		51% (51-52%)	
5	4468	51% (51-52%)		52% (52-53%)	
		P<0.001	-2	P=0.002	-1
	GP average age (mean 47)				
1	38.9	53% (52-54%)		53% (52-54%)	
2	42.9	54% (53-54%)		53% (52-54%)	
3	46.2	53% (52-54%)		53% (52-53%)	
4	50.3	52% (51-53%)		52% (51-53%)	
5	54.2	50% (49-51%)		51% (51-52%)	
		P<0.001	-3	P=0.002	-2
	QOF Mean Score (mean 540.1)				
1	495.5	51% (50-51%)		52% (51-53%)	
2	540.4	52% (51-53%)		53% (52-53%)	
3	550.2	52% (52-53%)		52% (51-53%)	
4	554.1	53% (53-54%)		53% (52-53%)	
5	558.4	53% (53-54%)		53% (53-53%)	
		P<0.001	+2	P=0.113	+1
	IMD score 2019 (mean 25.6)				

1	6.9	54% (54-55%)		54% (53-54%)	
2	14.1	54% (53-55%)		54% (53-54%)	
3	21.8	53% (52-53%)		53% (52-53%)	
4	32.1	51% (51-52%)		52% (51-52%)	
5	53.2	49% (49-50%)		50% (50-51%)	
		P<0.001	-5	P<0.001	-4
	Patients aged >65 (mean 17%)				
1	8%	50% (50-51%)		51% (50-52%)	
2	13%	51% (51-52%)		52% (51-53%)	
3	17%	52% (52-53%)		52% (52-53%)	
4	20%	53% (52-53%)		52% (52-53%)	
5	26%	55% (54-56%)		54% (54-55%)	
		P<0.001	+5	P<0.001	+3
	Ethnicity (white) (mean 89%)				
1	49%	51% (50-51%)		53% (52-54%)	
2	80%	52% (51-53%)		53% (52-53%)	
3	92%	52% (52-53%)		52% (52-53%)	
4	97%	53% (52-54%)		52% (51-53%)	
5	98%	54% (53-54%)		52% (51-53%)	
		P<0.001	+3	P=0.092	-1

Table 4: Percentage difference in predicted cancer detection from Q1 to Q5 in linear regression models, years 2009/10 to 2016/17 (all statistically significant, P<0.001)

	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19
Practice list size	+5	+6	+4	+3	+5	+4	+5	+4	+4	+4
List per FTE GP	-6	-4	-4	-2	-3	-3	-2	-2	-1	-2
GP average age	-7	-7	-6	-6	-5	-5	-4	-4	-3	-3
QOF score	+5	+4	+3	+2	+2	+3	+2	+2	+2	+2
IMD score	-3	-3	-2	-1	-3	-3	-3	-4	-5	-5
Patients aged>65	+5	+5	+2	+2	+3	+3	+3	+3	+3	+5
Ethnicity (%white)	+6	+5	+2	+2	+3	+3	+2	-1	+2	+3

Table 5: Percentage point difference in predicted cancer detection from Q1 to Q5 in multiple linear regression models, years 2009/10 to 2016/17 (*if not significant)

	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19
Practice list size	+2	+2	+2	+1	+3	+3	+3	+4	+2	+2
List per FTE GP	-3	0*	-2	-1	-1	-1*	-1*	-1*	-1*	-1
GP average age	-6	-6	-4	-5	-3	-4	-3	-3	-2	-2
QOF score	+3	+3	+1	0	+1	+1	+1	+1*	+1	+1*
IMD score	-1*	-1*	0*	-1*	-2*	-1*	-1*	-4	-4	-4
Patients aged>65	+2	+2	-1	+1	-1*	+2	+2	+2	+2	+3
Ethnicity (%white)	+2	+3	+1	-1*	+2	+1	-1	-2	-1	-1*