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To cite this article: Susan J.M. van Boxtel-Wilms, Kees van Boven, J.H. Hans Bor, J. Carel Bakx, Peter Lucassen, Sibo Oskam & Chris van Weel (2016) The value of reasons for encounter in early detection of colorectal cancer, European Journal of General Practice, 22:2, 91-95, DOI: 10.3109/13814788.2016.1148135

To link to this article: http://dx.doi.org/10.3109/13814788.2016.1148135
The value of reasons for encounter in early detection of colorectal cancer

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KEY MESSAGES
- Research into the reasons for encounter is a new method using a patient-centred reason for seeking care to study the predictive value for potentially bad outcomes.
- By using reasons for encounter, diagnostic criteria for GPs can be improved.

ABSTRACT
Background: Symptoms with a high predictive power for colorectal cancer (CRC) do not exist.
Objective: To explore the predictive value of patients’ reason for encounter (RFE) in the two years prior to the diagnosis of CRC.
Methods: A retrospective nested case-control study using prospectively collected data from electronic records in general practice over 20 years. Matching was done based on age (within two years), gender and practice. The positive likelihood ratios (LR+) and odds ratios (OR) were calculated for RFE between cases and controls in the two years before the index date.
Results: We identified 184 CRC cases and matched 366 controls. Six RFEs had significant LR+ and ORs for CRC, which may have high predictive power. These RFEs are part of four chapters in the International Classification of Primary Care (ICPC) that include tiredness (significant at 3–6 months prior to the diagnosis; LR+ 2.6 and OR 3.07; and from 0 to 3 months prior to the diagnosis; LR+ 2.0 and OR 2.36), anaemia (significant at three months before diagnosis; LR+ 9.8 and OR 16.54), abdominal pain, rectal bleeding and constipation (significant at 3–6 months before diagnosis; LR+ 3.0 and OR 3.33; 3 months prior to the diagnosis LR+ 8.0 and OR 18.10) and weight loss (significant at three months before diagnosis; LR+ 14.9 and OR 14.53).
Conclusion: Data capture and organization in ICPC permits study of the predictive value of RFE for CRC in primary care.

ARTICLE HISTORY
Received 10 December 2014
Revised 19 January 2016
Accepted 20 January 2016

KEYWORDS
Reason for encounter; primary care; colorectal cancer; diagnosis

Introduction
Colorectal carcinoma is one of the most prevalent types of cancer in the developed world. In The Netherlands, colorectal cancer (CRC) is the second most prevalent type of cancer in women and the third in men. The annual incidence was 6–8 per 10 000 persons.[1–4]

Most of the patients diagnosed with CRC will initially visit their general practitioner (GP) with symptoms such as rectal bleeding, anaemia and change of bowel habit.[3,4] These symptoms have a wide range in sensitivity and specificity, which depends on age and gender.[5–7] For example, the sensitivity for rectal bleeding ranged from 0.25 to 0.86, while the specificity ranged from 0.25 to 0.88.[8–10] In combination with the low incidence of CRC in primary care this results in problems in predicting CRC in primary care.[3,10] For example, for rectal bleeding the positive predictive value in primary care patients ranges from 2.16 in women aged 50–59 years to 7.69 for men aged 70–79 years.[6] Although combinations of symptoms improve the sensitivity, they diminish specificity.[8]

Generally, patient symptoms have been found to have low positive predictive value, giving little
guidance to GPs for distinguishing between self-lim-
iting and severe conditions. It is desirable to improve
the diagnostic process. A promising example is the rea-
son for encounter (RFE), a literal description of why the
patient has consulted the GP.[11,12] The International
Classification of Primary Care (ICPC) captures RFE and
allowed us to answer the following question: do pri-
mary care patients with colorectal cancer (CRC) differ
from others in their reason for encounter in the two
years prior to the diagnosis of CRC?[13]

Methods
Design
We performed a retrospective nested case-control
study using prospectively collected data from elec-
tronic records in general practice over 20 years from
which new CRC patients were identified and compared
with two matched controls sampled from the same
population. We used all data from the different
encounter types (face-to-face encounters, telephone
encounters and repeat prescriptions) with the excep-
tion of letters, that were routinely gathered during
contacts with patients of nine GPs participating in a
practice-based research network (Transition
Project).[14] We excluded administrative records.

Data source
Data prospectively and routinely registered in the
Transition Project were collected and analysed. The
Transition Project is a practice-based research network
of currently nine Dutch GPs in five practices with 15
000 patients started in 1985.[15] In the Transition
Project GPs routinely code each episode of care
according to the ICPC in an episode structure.[13,16,17]
With this classification the GP codes each patient’s RFE,
the diagnosis and the interventions (referral, prescrip-
tion, examinations). The Transition Project is the only
practice based research network in which the RFE is
coded (Box 1).[12,13,18] The ICPC classification has pro-
ven to be a very proper tool with high validity for
eventual diagnoses, and RFE which reflects the
patients’ perspective.[19] The Transition Project is
highly reliable due to the well-defined diagnostic crite-
rion and because the electronic system gives a warning
in a case of error or inconsistency.[12,20,21]

Population
We included all patients diagnosed with a new episode
of CRC between 1 January 1992 and 31 December
2011. All patients had to have at least two years of
record information before the diagnosis. Patients were
compared with controls without CRC matched for age
(within 2 years), gender and practice; the controls also
had to have at least two years of records before the
index date and an encounter with their GP within one
month of the index date. The index date was the date
on which the GP registered the diagnosis CRC either
after receiving a letter from a specialist or after being
told by the patient. We selected two controls per CRC
case.

Procedure
The data were analysed as a retrospective nested case-
control study. The index dates (of diagnosis) were
extracted from the Transition Project. We compared
cases and controls in four periods: a period of 3
months before diagnosis, [1] 3–6 months prior to diag-
nosis, [2] 6–12 months prior to diagnosis [3] and 1–2
years prior to diagnosis [4]. We analysed the data with
SPSS 18. Mean numbers of encounter and episode
were calculated. In order to compare the case and con-
trol group the episode CRC was excluded for these
mean numbers.

All ICPC codes were analysed separately as well as
the broader ICPC chapters or categories of diagnostic
codes.

All RFEs and the clustering of RFEs within ICPC
chapters were considered in the analyses.

We calculated the positive likelihood ratios (LR+) and
odds ratios (OR). Confidence interval (95% CI) was
calculated.

Results
We identified 186 patients from the five practices
within the Transition Project. Two cases had only one
control and, for two cases, we could not find a control;
the ones without a control were excluded. Thus, 184
patients were compared with 366 controls. Of the
patients, 57.1% (105) were male. The mean age at
diagnosis was 70.05 years. For controls, the mean age
was 69.87 years (Table 1).

Table 1. Characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Case</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (percentage)</td>
<td>184</td>
<td>366</td>
<td>0.86</td>
</tr>
<tr>
<td>Male</td>
<td>105 (57.1%)</td>
<td>206 (56.7%)</td>
<td></td>
</tr>
<tr>
<td>Mean age at index date in years (standard deviation in years)</td>
<td>70.05 (13.24)</td>
<td>69.87 (13.25)</td>
<td>0.88</td>
</tr>
<tr>
<td>Mean number per patient (standard deviation) of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>encounter</td>
<td>21.77 (16.84)</td>
<td>20.46 (18.11)</td>
<td>0.41</td>
</tr>
<tr>
<td>episode</td>
<td>11.17 (7.61)</td>
<td>10.22 (7.75)</td>
<td>0.17</td>
</tr>
</tbody>
</table>
Table 2. RFE as start of an episode for cases and controls per chapter per time-period expressed as OR.

<table>
<thead>
<tr>
<th>Chapter of RFE</th>
<th>Period</th>
<th>Cases (n = 184)</th>
<th>Controls (n = 366)</th>
<th>OR (95%) CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0–3mth</td>
<td>40</td>
<td>41</td>
<td>2.36</td>
<td>1.46–3.82</td>
</tr>
<tr>
<td></td>
<td>3mth–6mth</td>
<td>21</td>
<td>16</td>
<td>3.07</td>
<td>1.49–6.31</td>
</tr>
<tr>
<td></td>
<td>6mth–1y</td>
<td>31</td>
<td>53</td>
<td>1.24</td>
<td>0.74–1.54</td>
</tr>
<tr>
<td>B</td>
<td>0–3mth</td>
<td>43</td>
<td>85</td>
<td>1.01</td>
<td>0.66–1.54</td>
</tr>
<tr>
<td></td>
<td>3mth–6mth</td>
<td>9</td>
<td>2</td>
<td>16.54</td>
<td>2.08–131.42</td>
</tr>
<tr>
<td></td>
<td>6mth–1y</td>
<td>2</td>
<td>1</td>
<td>4.00</td>
<td>0.36–44.11</td>
</tr>
<tr>
<td></td>
<td>1y–2y</td>
<td>4</td>
<td>5</td>
<td>1.60</td>
<td>0.37–5.96</td>
</tr>
<tr>
<td>D</td>
<td>0–3mth</td>
<td>101</td>
<td>25</td>
<td>18.10</td>
<td>9.43–34.75</td>
</tr>
<tr>
<td></td>
<td>3mth–6mth</td>
<td>33</td>
<td>22</td>
<td>3.33</td>
<td>1.87–5.96</td>
</tr>
<tr>
<td></td>
<td>6mth–1y</td>
<td>33</td>
<td>43</td>
<td>1.59</td>
<td>0.99–2.56</td>
</tr>
<tr>
<td></td>
<td>1y–2y</td>
<td>45</td>
<td>73</td>
<td>1.32</td>
<td>0.85–2.06</td>
</tr>
<tr>
<td>T</td>
<td>0–3mth</td>
<td>15</td>
<td>2</td>
<td>14.53</td>
<td>3.32–63.62</td>
</tr>
<tr>
<td></td>
<td>3mth–6mth</td>
<td>4</td>
<td>4</td>
<td>2.26</td>
<td>0.48–10.42</td>
</tr>
<tr>
<td></td>
<td>6mth–1y</td>
<td>8</td>
<td>11</td>
<td>1.46</td>
<td>0.59–3.62</td>
</tr>
<tr>
<td></td>
<td>1y–2y</td>
<td>11</td>
<td>23</td>
<td>0.95</td>
<td>0.44–2.04</td>
</tr>
</tbody>
</table>

Table 3. Specific RFE as start of an episode for cases and controls per time-period expressed as OR.

<table>
<thead>
<tr>
<th>RFE</th>
<th>Period</th>
<th>Cases (n = 184)</th>
<th>Controls (n = 366)</th>
<th>OR (95%) CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness</td>
<td>0–3mth</td>
<td>19</td>
<td>9</td>
<td>4.22</td>
<td>1.91–9.33</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0–3mth</td>
<td>5</td>
<td>0</td>
<td>11.50</td>
<td>3.98–33.25</td>
</tr>
<tr>
<td>Constipation</td>
<td>3–6mth</td>
<td>33</td>
<td>4</td>
<td>8.67</td>
<td>2.47–30.41</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>0–3mth</td>
<td>33</td>
<td>0</td>
<td>1.70</td>
<td>0.53–3.47</td>
</tr>
<tr>
<td>Weight loss</td>
<td>0–3mth</td>
<td>8</td>
<td>1</td>
<td>15.06</td>
<td>1.88–120.81</td>
</tr>
</tbody>
</table>

The mean number of encounters (repeat prescriptions included) and the CRC episode excluded) for all RFE chapters was 21.77 for cases and 20.46 for controls. The mean number of new started episodes was 21.77 for cases and 20.46 for controls per time-period expressed as OR.

Differences between cases and controls

Reasons for encounter. In the period 1–2 years before the index date there were no differences in RFE except for rectal bleeding (LR+ 5.3 and OR 7.30, both with wide confidence intervals; see Tables 3 and 5 for the specified RFEs). Three to six months prior to the index date RFE in the chapter containing abdominal pain, rectal bleeding and constipation was significantly higher in CRC patients (LR+ 3.0 and OR 3.33; see Tables 2 and 4). In the period 3–6 months prior to the index date, significant differences in the chapter containing tiredness became visible (LR+ 2.6 and OR 3.07). In the 3 months before the index date differences in RFE were found in 4 of the ICPC chapters, namely the chapters containing tiredness (LR+ 2.0 and OR 2.36), anaemia (LR+ 9.8 and OR 16.54), abdominal pain, rectal bleeding and constipation (LR+ 8.0 and OR 18.10) and weight loss (LR+ 14.9 and OR 14.53).

Discussion

Main findings

RFEs belonging to chapter A ‘general/unspecified’ (most important RFE tiredness), chapter B ‘blood/immunology’ (most important RFE ‘I think I have an anaemia’), chapter D ‘digestive’ (most important RFEs abdominal pain, rectal bleeding and constipation) and chapter T ‘endocrine/metabolic’ (most important RFE weight loss).
belonging to chapter A and D 6 months prior to the diagnosis. Most LR+ is below 10 and not important. The higher LR+ for weight loss and local abdominal pain could be expected because we started our study from the diagnosis CRC. The differences between RFEs in the cases and the controls disappeared after 6 months prior to the diagnosis of CRC. Other RFEs did not show differences between cases and controls, for example ‘change of faeces/bowel movements,’ ‘diarrhoea,’ ‘abdominal mass NOS’ and ‘abdominal distension’.

**Comparison with existing literature**

The LR+ and the ORs of some specified RFEs in our study compared with the LR+ of the symptoms reported by Hamilton show the same trend.[7] They become more discriminatory near the time of diagnosis. Because CRC does not have symptoms with a high predictive power, RFE could be of potential importance. To demonstrate or to exclude this, more data with higher sample sizes are needed. Since this is the first study regarding RFE and CRC, we investigated RFE on the level of ICPC chapter to provide a general picture. Due to the relatively small numbers, we could only make reliable statements with wide confidence intervals concerning specified ICPC codes six months prior to the diagnosis. Since certain ICPC chapters proved significant association with CRC, further research should be focused on more specified RFE or combinations of RFE with patient characteristics to begin to understand patterns in primary care. A systemic review found that patients in primary care had a higher risk of CRC if rectal bleeding was accompanied by weight loss or change in bowel habit.[22] By adding RFE to these combinations, it is likely that pooled positive predictive values can be improved. Displaying symptoms as RFEs emphasizes the importance of patients’ spontaneous expressed reasons to contact the GP for diagnosing cancer. Recording the RFE indicates the direction for history taking, physical examination and further diagnostics. The ICPC system is essential for this search for potentially meaningful patterns because the system gives an insight in the encounters of patients. It is possible patterns can be identified in other diseases.

**Strengths and limitations**

This is the first study comparing RFE of cases and controls in the period before the diagnosis CRC in a relatively large sample.

An advantage of the Transition Project is that the system provides reliable RFE data as a result of the well-defined diagnostic criteria and automatic warning systems to prevent double coding and the high concordance in RFE between patient and GP.[12,19–21]. Therefore, we were able to study the patients’ perspective. This provides unique information for new methods of recognizing CRC in real life general practice consultations. The latter is especially valuable because we think strengthening the diagnostic process of CRC should be investigated in real life conditions.

We found that two specific RFE had a high LR+ in the 3 months before diagnosis (local abdominal pain and weight loss). The other LR+ show a moderate to small LR+ and are therefore clinically not relevant.

The odds ratios of the specific RFEs have a high number (between 4 and 15.06) and are therefore promising. However, due to the relatively small population the CIs are wide. Therefore, the clinical relevance of the described numbers is not yet clear.

A limitation of our study is that the index date may be less reliable due to delays in informing the GP. It is possible that as a result the cases have a higher number of encounters due to the recently diagnosed CRC and consequently a higher number of RFE.

The Transition Project does not register the socioeconomic state of patients; therefore, we matched cases with controls of the same practice since most Dutch GP practices are organized geographically.

**Future perspectives**

Studying the relationship between RFEs and diagnoses within episodes has tremendous potential for providing better diagnostic criteria to GPs, which is an important task of primary care. GPs also have insight in individual patients’ risk profiles, such as life style and family history of colon cancer, and the diagnostic process would in particular benefit from relating reasons for encounter to individual ‘risk profile’.

**Conclusion**

The study has explored the differences in reasons for encounter between matched patients in shared geography with and without CRC. Significant differences are found between the two groups regarding specific symptoms apart and related to ICPC chapters. Studies like this may strengthen diagnostic tools in primary care and may be further strengthened by exploring reasons for encounter with patients’ individual risk profiles, for example regarding hereditary conditions.
Acknowledgements
We would like to thank the following GPs for their contribution to the Transition Project: A Dam, P Dijkstra, A Groen, J De Haan, A Honseelaar-de Groot, D Janssen, G Polderman, T Polman, K Stolp, N Valken and M Woerdeman.

Declaration of interest
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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