The value of reasons for encounter in early detection of colorectal cancer

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The value of reasons for encounter in early detection of colorectal cancer

Susan J.M. van Boxtel-Wilms, Kees van Boven, J.H. Hans Bor, J. Carel Bakx, Peter Lucassen, Sibo Oskam and Chris van Weel

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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+ 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.

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-limiting and severe conditions. It is desirable to improve the diagnostic process. A promising example is the reason 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 primary 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 electronic 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 exception 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, prescription, 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 proven 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 criteria 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 diagnosis, [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 control 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>
<thead>
<tr>
<th>Table 1. Characteristics of patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Number (percentage)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Mean age at index date in years (standard deviation in years)</td>
</tr>
<tr>
<td>Mean number per patient (standard deviation) of</td>
</tr>
<tr>
<td>encounter</td>
</tr>
<tr>
<td>episode</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%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0–3mth</td>
<td>42</td>
<td>41</td>
<td>2.36</td>
<td>1.46–3.82</td>
</tr>
<tr>
<td>3mth–6mth</td>
<td>21</td>
<td>16</td>
<td>3.07</td>
<td>1.49–6.31</td>
<td>0.00*</td>
</tr>
<tr>
<td>6mth–1y</td>
<td>31</td>
<td>53</td>
<td>1.24</td>
<td>0.74–1.54</td>
<td>0.42</td>
</tr>
<tr>
<td>1y–2y</td>
<td>43</td>
<td>85</td>
<td>1.01</td>
<td>0.66–1.54</td>
<td>0.97</td>
</tr>
<tr>
<td>B</td>
<td>0–3mth</td>
<td>9</td>
<td>2</td>
<td>16.54</td>
<td>2.08–131.42</td>
</tr>
<tr>
<td>3mth–6mth</td>
<td>2</td>
<td>1</td>
<td>4.00</td>
<td>0.36–44.11</td>
<td>0.26</td>
</tr>
<tr>
<td>6mth–1y</td>
<td>6</td>
<td>6</td>
<td>2.00</td>
<td>0.65–6.20</td>
<td>0.23</td>
</tr>
<tr>
<td>1y–2y</td>
<td>4</td>
<td>5</td>
<td>1.60</td>
<td>0.37–5.96</td>
<td>0.48</td>
</tr>
<tr>
<td>D</td>
<td>0–3mth</td>
<td>101</td>
<td>25</td>
<td>8.0</td>
<td>5.4–12.0</td>
</tr>
<tr>
<td>3mth–6mth</td>
<td>33</td>
<td>22</td>
<td>3.33</td>
<td>1.87–5.96</td>
<td>0.00*</td>
</tr>
<tr>
<td>6mth–1y</td>
<td>33</td>
<td>43</td>
<td>1.59</td>
<td>0.99–2.56</td>
<td>0.06</td>
</tr>
<tr>
<td>1y–2y</td>
<td>45</td>
<td>73</td>
<td>1.32</td>
<td>0.85–2.06</td>
<td>0.21</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>3mth–6mth</td>
<td>4</td>
<td>4</td>
<td>2.26</td>
<td>0.48–10.42</td>
<td>0.30</td>
</tr>
<tr>
<td>6mth–1y</td>
<td>8</td>
<td>11</td>
<td>1.46</td>
<td>0.59–3.62</td>
<td>0.42</td>
</tr>
<tr>
<td>1y–2y</td>
<td>11</td>
<td>23</td>
<td>0.95</td>
<td>0.44–2.04</td>
<td>0.90</td>
</tr>
</tbody>
</table>

A = general/unspecified  
B = blood/immunology  
D = digestive  
T = endocrine/metabolic  
* = P < 0.05.  
0–3mth = from 1 day after index date until 3 months prior to the diagnosis.

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%)</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>Local abdominal pain</td>
<td>3–6mth</td>
<td>23</td>
<td>4</td>
<td>11.21</td>
<td>3.98–33.25</td>
</tr>
<tr>
<td>Constipation</td>
<td>0–3mth</td>
<td>13</td>
<td>3</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>6.87</td>
<td>2.47–30.41</td>
</tr>
<tr>
<td>3–6mth</td>
<td>8</td>
<td>2</td>
<td>8</td>
<td>1.70</td>
<td>1.10–2.31</td>
</tr>
<tr>
<td>1y–2y</td>
<td>8</td>
<td>3</td>
<td>7.30</td>
<td>1.53–34.71</td>
<td>0.01*</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 11.17 for cases and 10.22 for controls (Table 1).

Most cases (97%) were referred within 90 days from the start of complaints related to the cancer by their GP, four cases were referred between 91 and 180 days and two cases were referred more than a year after the start of the complaints. One CRC patient refused a referral.

Although we studied all ICPC codes and the 17 ICPC chapters, due to the small numbers of patients and large confidence intervals, we only present findings for six reasons for encounter and the four chapters that showed differences between cases and controls: 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 also chapter T ‘endocrine/metabolic’ (most important RFE weight loss).

Table 4. RFE as start of an episode for cases and controls per chapter per time-period expressed as LR+.

<table>
<thead>
<tr>
<th>RFE</th>
<th>Period</th>
<th>Cases (n = 184)</th>
<th>Controls (n = 366)</th>
<th>LR+ (95%)</th>
<th>CI (95%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness</td>
<td>0–3mth</td>
<td>42</td>
<td>41</td>
<td>2.0</td>
<td>1.4–3.0</td>
<td>0.00*</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0–3mth</td>
<td>21</td>
<td>16</td>
<td>2.6</td>
<td>1.4–4.9</td>
<td>0.00*</td>
</tr>
<tr>
<td>Local abdominal pain</td>
<td>3mth–6mth</td>
<td>9</td>
<td>2</td>
<td>9.8</td>
<td>2.0–41.0</td>
<td>0.00*</td>
</tr>
<tr>
<td>Constipation</td>
<td>0–3mth</td>
<td>101</td>
<td>25</td>
<td>8.0</td>
<td>5.4–12.0</td>
<td>0.00*</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>3mth–6mth</td>
<td>33</td>
<td>22</td>
<td>3.0</td>
<td>1.8–5.0</td>
<td>0.00*</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0–3mth</td>
<td>33</td>
<td>43</td>
<td>1.5</td>
<td>1.0–2.3</td>
<td>0.00*</td>
</tr>
<tr>
<td>Weight loss</td>
<td>0–3mth</td>
<td>15</td>
<td>2</td>
<td>1.49</td>
<td>3.4–6.45</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

Table 5. Specific RFE as start of an episode for cases and controls per time-period expressed as LR+.

<table>
<thead>
<tr>
<th>RFE</th>
<th>Period</th>
<th>Cases (n = 184)</th>
<th>Controls (n = 366)</th>
<th>LR+ (95%)</th>
<th>CI (95%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness</td>
<td>0–3mth</td>
<td>19</td>
<td>9</td>
<td>4.1</td>
<td>1.9–9.1</td>
<td>0.00*</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0–3mth</td>
<td>5</td>
<td>0</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Local abdominal pain</td>
<td>3mth–6mth</td>
<td>8</td>
<td>4</td>
<td>4.0</td>
<td>1.2–13.0</td>
<td>0.00*</td>
</tr>
<tr>
<td>Constipation</td>
<td>0–3mth</td>
<td>13</td>
<td>3</td>
<td>8.6</td>
<td>2.5–29.9</td>
<td>0.00*</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>3mth–6mth</td>
<td>8</td>
<td>2</td>
<td>8.0</td>
<td>1.7–37.1</td>
<td>0.00*</td>
</tr>
<tr>
<td>1y–2y</td>
<td>8</td>
<td>3</td>
<td>5.3</td>
<td>1.4–19.6</td>
<td>0.00*</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>0–3mth</td>
<td>8</td>
<td>1</td>
<td>15.9</td>
<td>2.0–126.3</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

**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,’ ‘diar-
rhoea,’ ‘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 diagno-
sis. Because CRC does not have symptoms with a high
predictive power, RFE could be of potential impor-
tance. 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 pic-
ture. 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 sys-
temic 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 posi-
tive 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 indi-
cates the direction for history taking, physical examin-
ation and further diagnostics. The ICPC system is
essential for this search for potentially meaningful pat-
tens 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 con-
trols in the period before the diagnosis CRC in a rela-
tively 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 con-
cordance in RFE between patient and GP.[12,19–21].
Therefore, we were able to study the patients’ perspec-
tive. This provides unique information for new meth-
ods 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 popula-
tion 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 num-
ber of encounters due to the recently diagnosed CRC
and consequently a higher number of RFE.

The Transition Project does not register the socio-
ceconomic 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 provid-
ing 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 rea-
sons for encounter to individual ‘risk profile’.

Conclusion
The study has explored the differences in reasons for
encounter between matched patients in shared geog-
raphy 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 pro-
files, for example regarding hereditary conditions.
Acknowledgements

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Declaration of interest

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

References


