Maastricht University

Rectal bleeding, a danger signal?

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Rectal bleeding, a danger signal?

Bloedverlies per anum, een alarmsignaal?

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Rectal bleeding, a danger signal?

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Aan mijn vader

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1. Introduction

Is overt blood loss per rectum (rectal bleeding) a danger signal?
According to public health education programmes aiming at early diagnosis of colorectal cancer and according to most medical literature, it is. Rectal bleeding is thought to be a symptom of early rather than late colorectal cancer[1] and every instance of rectal bleeding, in particular in patients over 40, demands careful clinical investigation by endoscopy, roentgenography and laboratory means.[2-5] This can also be illustrated by a recent editorial in the Lancet saying that "rectal bleeding is always alarming, with the fear of cancer being uppermost in the patient's mind". "Only the foolhardy look no further: even when an obvious cause for bleeding is found initially, all too often another lesion lurks more proximally".[6] Similarly, "patients with rectal bleeding must be considered as having a carcinoma until the opposite is proven" as was recently advised in a Dutch magazine.[7]
However, voices have been raised cautioning against public education programmes designed to use rectal bleeding as a 'screening test' for colorectal cancer.[8] Rectal bleeding is not rare in healthy people and the incidence of cancer of the colon and rectum is relatively low with 0.5 cases per 1000 people per year.[9] The incidence of colon cancer is about 30 per 100,000 people per year, equally for men and women, and the incidence of rectum cancer is 22 for men and 14 for women per 100,000 per year.[9] General practitioners (GPs), on the whole, consider invasive diagnostic investigations to be indicated only when there are reasons to suspect cancer.[10,11]
The general practitioner is used to facing patients who have a fear of cancer[12], and he or she has to decide who can be reassured, and who should be further investigated.[13] Estimates of probability are crucial in this diagnostic process. Intuitive probability assessments are susceptible to biases.[14] The application of a clinical epidemiologic point of view can aid in rational clinical practice.[15]

Colorectal cancer is a major health problem with 2000 deaths each year in the Netherlands.[16]

The overall 5-year survival, according to 'Survival Epidemiology and End Results' (SEER) in the United States (1970-1983), was only 14% for rectum cancer and 51% for colon cancer in the years 1973 to 1980[17] and has shown little improvement recently despite the introduction of new surgical techniques and adjuvant chemotherapy.[18] The reason mentioned for lack of improvement in survival is that in most cases the disease had already reached an advanced stage by time of diagnosis.[18] However, it is not clear whether a delay in diagnosis in symptomatic patients, like those with overt rectal bleeding, is related to a worse prognosis.[19,20]

In a time with growing investment in preventive and screening activities it seems obvious that seeking a diagnosis as early as possible may do more good than harm. However, it becomes necessary to prevent unnecessary anxiety and medicalization among healthy people and to guard against overdiagnosis with excessive health care costs.[21,22,23] Data to give decision making in general practice a scientific basis are not sufficiently on hand.[24,25]

Aim of the study

The main purpose of the present study was to collect quantitative data which will contribute to rational diagnosing of patients presenting with rectal bleeding in general practice. The main question in this study was: is it possible to discriminate effectively between patients with rectal bleeding who have colorectal cancer and those who do not; or at least to discriminate between those who need invasive investigations and those who do not?

The following questions relevant for clinical decision making were asked:

1. What is the incidence of rectal bleeding in general practice?
2. What is the prior probability of malignant disease in patients presenting with rectal bleeding in general practice? What are the frequencies of other sources of rectal bleeding?
3. What is the predictive value of (combinations of) signs, symptoms and simple laboratory tests for colorectal cancer in general practice?

Another question of interest concerns the prior probability and predictive value in referred patients, which may be different from that in general practice and partly reflect the efficacy of the referral process.[24-28] The opportunity to collect data in general internists' outpatient clinics was used to answer the following question.

4. What is the predictive value of (combinations of) signs, symptoms and simple laboratory tests for inflammatory bowel disease or neoplasm in an outpatient internal medicine clinic?

A study of this kind needs the participation of a large number of GPs since colorectal cancer is relatively rare. Such participation was expected to be possible in the area of Maastricht and the southern part of Limburg due to some favourable circumstances:

- A stimulation of extramural research by means of the "Innovation Funding" from the Dutch Ministry of Education and Science.
- The research interest in clinical epidemiology and rational diagnosis in the Department of General Practice of the University of Limburg.
- A positive attitude towards the improvement of rational diagnosis in primary care and better communication between GPs and medical specialists. Considerable stimulus for this is provided by the Diagnostic Coordinating Centre (DCC) Maastricht, which cooperates with all GPs in the Maastricht area,[29] and also communicates with many other GPs in the region.
- The possibility to cooperate with a study on non-acute abdominal complaints in general practice and outpatient clinics, initiated by the Department of General Practice at the University of Limburg, funded by the Dutch Ministry of Welfare, Health and Cultural Affairs.
- The presence of a project with the aim of evaluating and improving rational diagnosing of patients referred for endoscopy of the upper intestinal tract, initiated by FJTE Vismans, internist.[30]

After initiation, the rectal bleeding study was allied to the non-acute abdominal complaints study. The latter study is presented separately in a thesis by JWM Muris and R Starmans.

Structure of this thesis

The results of a literature search regarding the occurrence and significance of rectal bleeding in the general population and in general practice are found in Chapter 2.
In the literature the term rectal bleeding is usually applied to overt blood loss per anum or per rectum, but rectal bleeding in general may also mean occult blood loss. When 'rectal bleeding' is mentioned in this thesis this means overt ano-rectal blood loss seen by the patient.
In order to illuminate the location of the clinical aspects regarding patients with rectal bleeding in general practice in the Netherlands, the state of the art of the diagnostic approach is discussed in Chapter 3.
In Chapter 4 the methodology of the empirical part of the study is described.
In the following chapters the results are presented. Chapter 5 deals with the incidence and the diagnostic outcome of patients presenting with rectal bleeding in general practice. Chapter 6 deals with the predictive value of signs and symptoms in general practice. Chapter 7 reports about the predictive value of signs, symptoms and simple laboratory tests in patients presenting with rectal bleeding in an outpatient clinic.
Results are discussed in Chapter 8 and implications for the diagnostic process in general practice and recommendations for further studies are highlighted.
The results are summarized in English and in Dutch in Chapter 9.

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2. The occurrence and significance of overt blood loss per rectum in the general population and in medical practice

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ABSTRACT

To determine the occurrence and significance of overt blood loss per rectum a Medline literature search was undertaken. The incidence of this symptom in the general population is reported to be about 20 per 100 people per year, the 'consultation incidence' in general practice is about 6 per 1000 and the incidence of referral to a medical specialist is estimated to be about 7 per 10000 per year. The clinical significance of the symptom varies within different populations: the predictive value of overt rectal blood loss for colorectal malignancy can be estimated to be less than 1 in 1000 in the general population, around 2 in 100 in general practice and up to 36 in 100 in the referred patients. How the manifestation of the bleeding (and other signs and symptoms) influence the care seeking and referral behaviour, leading to increasing prior probabilities, is unknown.

Introduction

Overt blood loss per anum or per rectum (haematochezia) is common in general practice. Its aetiology is usually not serious but it may also be the first symptom of a colorectal malignant disorder. Although it is open to debate whether the prognosis of symptomatic colorectal malignant disease may be improved by earlier diagnosis,[1-13] the finding of a carcinoma will often raise the question if it would have been possible to detect it earlier.[14] Partly because of this there is considerable disagreement as to the optimal diagnostic management. Some advocate a full examination of every patient with blood loss per rectum (sigmoidoscopy in combination with barium enema or coloscopy) in order to rule out the possibility of a malignant tumour,[15-28] whereas others favour a more conservative approach.[11,29] The general practitioner is faced with the task to select patients in such a way that the costs and benefits of ancillary tests are reasonably balanced.

We conducted a literature study on the occurrence (i.e. the incidence and characteristic manifestations) of blood loss per rectum and its predictive value with respect to colorectal tumours in order to find data that may of use in this selection process.

Method

A literature study was undertaken by means of a Medline search (CD-ROM) in Index Medicus and Excerpta Medica and a manual search in the Family Medicine Literature Index (Famli). For the publication years 1984 to 1991 the following key words were used: "bleeding per rectum", "colorectal neoplasm" (Famli),"anal/rectal/colorectal bleeding", "anal/rectal/colorectal/gastrointestinal haemorrhage", "anal/rectal/colorectal blood loss". In some cases the search was restricted by adding the key words "colorectal polyps" and "colorectal carcinoma" (CD-ROM). Additional sources were traced on the basis of references. Also, handbooks and Dutch publications, among which those of several Dutch general practice registration projects, were consulted.

The literature thus traced was assessed systematically on the following points:
- overt blood loss per rectum (nature of bleeding)
- the description of the population: age, sex, manner of selection
- the definition of blood loss used: in, on, or mixed with the stool, in the toilet or on the toilet paper, bright or dark red
- the period of time, the frequency, and the amount of blood loss
- the method of research: oral interview, written questionnaire, sample, population screening
- the country of origin

Altogether, 8617 references were found by CD-ROM. Studies discussing only occult blood loss or upper abdominal pathology were excluded. Also left out were studies dealing with blood loss as a side-effect of medication or surgery, with bleeding per rectum in children and with very specialistic diagnostic methods and therapeutic techniques. Approximately 2% of the studies seemed to be relevant within the scope of this study. The key word "rectal bleeding" yielded most of the references selected, and these were obtained from the Index Medicus. Excerpta Medica and Famli hardly added new references. Reports on the occurrence of overt blood loss were few as compared to those on occult blood loss. Even less in number were papers related to general practice: from CD-ROM and Famli only two references were found, and these turned out to be part of the same study.

Results

General population

Incidence

Nine studies were found relating to the general population. In these studies the occurrence of blood loss per rectum in "healthy" people, whose general practitioner was often not aware of the problem is reported (Table 1).

Table 1. Occurrence of rectal bleeding in the general population

Author*	population	method	occurrence
Wadsworth, 1971 [32]	≥ 21 year England	N=2153, random sample interviews, response rate 86.6%	2.4% previous 2 weeks blood in faeces
Jones, 1976 [37]	≥40 year, healthy people, exclusion of known bowel disease or surgery Australia	N=112, random sample questionnaire and interviews response rate?	38% "ever"
Gill, 1979 [31]	3 general practices The Netherlands	N=8211, questionnaire 72%	1.7% previous 2 weeks blood in faeces
Silman, 1983 [34]	≥ 40 year, male employees England	N=916, questionnaire + Hemoccult, response rate 50.7%	11.8% previous 3 months
Farrands, 1984 [36]	45-75 year, exclusive "colorectal pathology known by GP" England	N=527, questionnaire, response rate 34%	6.6% previous 6 months
Chapuis, 1985 [29]	≥ 50 year, "healthy men" Australia	N=319, interviews, response rate 85%	15% previous 6 months
Dent, 1986 [35]	≥ 30 year, "healthy people" Australia	N=202, random sample interviews, response rate 45%	16% previous 6 months
Kewenter, 1989 [30]	60-64 year Sweden	N=9040, random sample response rate 66%	12.9% previous 6 months
Jones, 1992 [33]	20-90 year England	N=1620, questionnaire response rate 71%	20% previous year 40-60 year: 10%

* First author only

The largest study is that of Kewenter et al.[30] It concerns a population screening in which persons between the ages of 60 and 64 were sent a postal questionnaire and Haemoccult tests. The response rate in the randomly selected sample was 66% (9040 subjects). Among other things, it was asked whether the subject had noticed any blood loss per rectum within the last half year. In 12.9% of subjects this was the case. This study is the only one with a follow-up period of two years, intended to identify any adenomas and carcinomas. In an almost equally large study by Gill,[31] patients belonging to the practices of three general practitioners were asked about their stools by means of a written questionnaire. Of the 8211 people who answered the prestructured questions (response 72%), 1.7% claimed to have detected blood in the faeces at least once during the preceding two weeks. In the study of Wadsworth et al 2153 adults (random sample, response 87%) were interviewed and asked, among other things, about blood in the stool during the last two weeks.[32] Of these 2.4% replied affirmatively. The study of Kewenter differs from those of Gill and Wadsworth particularly with regard to two points:

- selection of respondents with respect to age (in the study of Kewenter)
- the period of time enquired after (six months versus two weeks)

It is unclear whether these two factors are sufficient to account for the discrepancy in the results.

Like the studies of Gill and Wadsworth, a recent study of Jones and Lydeard concerns a population with an age and sex distribution that is representative of general practice.[33] The conclusion of the study is that the prevalence of rectal blood loss amounts to 20% a year. Among people between the ages of 40 and 60, the prevalence is lower: 10%. The remaining studies, dealing with smaller numbers, yield incidence figures that are similar to that of Kewenter: Silman et al,[34] Chapuis et al,[29] and Dent et al.[35] These three studies cover periods of 3-6 months. In the first two there is selection by age and gender: men of 40-50 years of age and older. The study of Dent et al involves men and women of over 30 years. Thus it seems reasonable to assume that 12-16% of the Western European and Australian adult population at large will affirm at any moment in time to have experienced blood loss per rectum in the past six months; for a year period, 20% will do so and for a 2 week period around 2%.

Farrands and Hardcastle[36] and Jones[37] present figures that deviate from the above percentages. In a study with a low response rate (34%) Farrands and Hardcastle report rectal bleeding in 6.6% of the respondents during the last 6 months. In both studies, known intestinal disorders were an exclusion criterion. The percentages found may therefore have been higher if the total population had been considered, particularly in the study of Farrands where known haemorrhoids were possibly excluded as well. In the study of Jones[37], the smallest of all, a frequency of 38% was found when the period of 6 months was extended to "ever".

Manifestation of blood loss

Only Jones reports on the frequency and volume of rectal bleeding.[37] In approximately half of the cases the frequency of blood loss was more than five times; usually it was only a drop (79%). In 21% there was medium (18%) or heavy (3%) bleeding. The blood was usually noticed "on the toilet paper" (84%) and/or "on the stool" (63%).
Other authors do not report on frequency, length of time, or amount of blood loss. In some instances the various manifestations of bleeding are mentioned. The occurrence of blood "in" or "mixed with the stool" varies widely: 100%, 27%, and 3% of reported bleeding.[31,34,35] Two authors indicate that the blood is mostly "on the paper", "in the toilet" or "on the stool" (73%-97%).[34,35] Usually the colour is bright red. In 23%-29% the blood is dark red.[30,34] Finally, it is remarkable that many people (19-43%) seldom or never inspect their faeces or the toilet paper.[31,35]

Diagnostic value

The predictive value of blood loss per rectum for the presence of rectal or sigmoid neoplasms (adenomas and carcinomas), as reported in the various studies, is presented in Table 2; it varies from 3 to 8% for adenomas and from 0 to 0.95% for carcinomas.

Table 2. Predictive value of rectal bleeding for adenomatous and malignant tumours in the rectum or sigmoid

Author*	predictive value %	comments	gold standard	number of patients
Silman, 1983 [34]	6	adenoma ≥ 1 cm no malignancy	flexible sigmoidoscopy and barium enema	108
Farrands, 1984 [36]	3	adenoma 0,5 - 1 cm no malignancy	flexible sigmoidoscopy and double contrast X-ray of the colon	35
Chapuis, 1985 [29]	8	adenoma ≥ 1 cm no malignancy	flexible sigmoidoscopy (30 cm)	48
Kewenter, 1989 [30]	4.3	adenoma 3.3% malignancy 0.95%	follow-up of 2 years. if occult blood test was positive: sigmoidoscopy and double contrast X-ray of the colon.	1164

* First author only

In 346 people with dark red bleeding, Kewenter et al found three adenomas but no carcinomas (predictive value 0.9%).[30] In 818 people with bright red blood loss in the same study, 11 carcinomas and 35 adenomas were identified (predictive value 5.6%). In contrast, Silman et al more frequently found an adenoma in patients with dark red (16%, 4 out of 25) rather than bright red blood loss (2.4%, 2 out of 83).[34] Chapuis et al screened 319 "healthy" men of over fifty years of age by means of sigmoidoscopy and an interview.[29] They calculated that the sensitivity and specificity of rectal blood loss for rectal or sigmoid adenomas was 33% and 86%, respectively (likelihood ratio for positive (LR^+) or negative findings (LR^-) 2.36 and 0.78 respectively). Silman et al obtained a sensitivity of 86% and a specificity of 89% for colorectal adenomas greater than 1 cm in diameter ($LR^+=7.82$, $LR^-=0.16$).[34]

General practice

Incidence

The literature search yielded no references with respect to the incidence of overt blood loss per rectum in the general practice population. As a substitute we analysed the data from a number of registration projects carried out in Dutch general practices. Results are summarized in Table 3.

Table 3. Morbidity rates in Dutch general practices; incidence per 1000 persons in the population per year.

Diagnoses	*Sources*			
	National Study 1991 [38] (symptoms) diagnoses	Transition Project 1991 [41] reasons for encounter	Monitoring Project 1984 [40] diagnoses	CMR 1985 [39] diagnoses
Rectal bleeding [NOS]	0.4	4	0.6 - 0.9	-
Haemorrhoid(s)	6.8	4	8.2 - 7.6	12.1
Malignant colorectal neoplasm	0.0*	0.0**	0.2 - 1.1**	0.6
Fissura ani, perianal abscess	3.2	0.2	2.2	1.4
Diverticulosis/-itis	1.6	0	2.4	
Chronic enteritis/colitis	0.8	0.1	0.5 - 0.2	
Others				2.0#
Total sum of rectal bleeding and disorders where rectal bleeding could be a symptom	12.8	8.3	14.1 - 14.4	16.1

* Prevalence = 4
** Malignant neoplasm intestine
# Others (a.o. diverticulosis, colitis)

The National Study[38] records diagnoses. In cases in which no diagnosis is made by the end of an illness episode, the symptom is registered. The incidence of "rectal blood loss, not other specified [NOS]" amounted to 0.4 per 1000 persons per year.
Moreover, a disorder in which rectal blood loss may have been a prominent symptom was diagnosed in 12.8 persons per 1000 per year. The Continuous Morbidity Registration of the Nijmegen Institute[39] does not include "blood loss per rectum" as a separate category. However, a similar incidence of 16.1 per 1000 for diagnoses associated with this symptom was reported. The figures of the Monitoring Project[40] are also in the same range. The Transition Project[41] registers reasons for encounter rather than diagnoses. Consequently, the incidence of rectal blood loss as reason for encounter is higher in this study and the incidence of haemorrhoids is correspondingly lower.

We have become aware of data from partly unpublished studies regarding lower abdominal pathology in general practice, that may be of use to approximate the incidence of overt rectal blood loss. Bekker et al[42] investigated the indications for proctoscopy and found an incidence of 4 per 1000 per year. Unpublished data of Fuller[43] and of Nørrelund[44] point to incidence rates of rectal bleeding of 8 per 1000 in England and 6 per 1000 in Denmark, respectively.
Taken together these data indicate that the incidence of rectal bleeding in general practice lies between 4 and 8 cases per 1000 per year.

Manifestation and diagnostic value

No epidemiologic data were found concerning the manifestation and the precise diagnostic value of rectal bleeding in general practice. Most registration projects lack not only a gold standard for diagnosis but also a diagnostic follow-up. An exception is the Transition project[41] which gives an indication of the most frequent final diagnoses (top 5) made during subsequent visits. In illness episodes starting with "rectal bleeding" as reason for encounter, the following final diagnoses are made: in 30% "haemorrhoids", in 26% "no cause

found", in 18% "anal fissure or abscess", in 4% "constipation", and in 4% "other, nonspecific diagnoses". Colorectal carcinomas and adenomas are not given and therefore must have been found in less than 4% of cases of blood loss per rectum.
Hodgkin[45] indicated a ratio of 1:20 for the relationship between trivial and serious causes of blood loss per rectum. This would mean a predictive value of approximately 5% for "serious causes".

Referred patients

Incidence

Little has been reported on the incidence of blood loss per rectum in referred populations. Moreover, this will be highly dependent on the referral situation that is to be investigated: first or second referral centre, medical or surgical service, urban or rural populations. For the situation in the Netherlands Lamberts[41] recorded a referral percentage for this complaint of 14%. On the basis of this percentage, it can be calculated that around 0.56 patients per 1000 persons are referred per year because of blood loss per rectum (14% of the incidence of 4 per 1000 per year in general practice). With an assumption of a higher incidence rate of rectal blood loss in general practice, for example 6 per 1000, an estimation of an incidence of referred patients with rectal blood loss of is around 0.84 per 1000 per year.

Diagnostic value

Numerous reports have described the relative frequency of diagnoses in patients presenting with rectal blood loss. Again these results are partly dependent on the referral situation but may nevertheless be of use to obtain an impression of the efficacy and efficiency of the selection proces. Results of 26 reports are summarised in Table 4. In the Australian study,[46] the predictive value of blood loss per rectum for the presence of tumours was 19%: for malignancy 11% and for adenomas 8%.

Table 4. Reported frequencies of sources of rectal blood loss in referred patients (population and manifestation if available)

		Primary diagnoses							
Studies first author	population	malignancy %	polyps %	IBD⁺ %	diverticulosis/ -itis %	fissura ani abscess %	haemorrhoids %	other %	unknown cause %
Noer, 1961 [47]	N=221 moderate bleeding	39	10	18	28			5	
Williams, 1977 [16]	N=311 referred patients	4	2	5		18	54	10	7
Boley, 1979 [48]	N=84 >65 year minor bleeding	8	11	1	35	2	7	24	12
Brand, 1980 [49]	N=306 gastroenterologic outpatients	8	≥5mm:14 <5mm:10	4	"alone":21	exclusion	exclusion	angiodys- plasia:4	39
Shinya, 1982 [50]	N=2200 referral centre	19	32	6	<1		27	10	6
Dehn, 1982 [51]	N=110 proctologic outpatients	5	5	4	3	15	65		3
Boley, 1984 [52] *	N=99 >60 year major bleeding	9 (incl.polyps)			43			angiodys- plasia:20 others:21	11
McCallum, 1984 [53]	N=248 20-89 year	3	adenoma:8 hyperplast.:8						
Bat, 1985 [20] *	N=194 haemorrhoids proctocologic service	6	14		21		100 2nd/3rd degree	3	

Table 4 continued

		Primary diagnoses							
Studies first author	population	malignancy %	polyps %	IBD+ %	diverticulosis/ -itis %	fissura ani abscess %	haemorrhoids %	other %	unknown cause %
Brouwer, 1985 [54]	N=110 surgical outpatients	4	25	13	15	perianal disorders:25		5	13
Goulston, 1986 [22] *	N=145 frontiers 1st-2nd line	11	8	2	3	5	72	3	
Tedesco, 1987 [18]	N=285 40-87 year	11				exclusion	exclusion		
Guillem, 1987 [55]	N=224 chronic bleeding	18	adenoma:23	8	16	anal lesions:30		5	
Pines, 1987 [24] *	N=387 >40 year prolonged bleeding	1.2	22				100 2nd/3rd degree		
Swarbrick, 1987 [56]	N=237 unexplained bleeding	10	16	10	17	exclusion	exclusion	2	45
Irvine, 1988 [57]	N=71 referred patients	7	27	5	25		17	4	15
Tate, 1988 [58]	N=49 referred patients	18							

Table 4 continued

		Primary diagnoses							
Studies first author	population	malignancy %	polyps %	IBD+ %	diverticulosis/ -itis %	fissura ani abscess %	haemorrhoids %	other %	unknown cause %
Cheung, 1988 [25] * #	N=337 >40 year proctologic service	11	≥1 cm:3 <1 cm:7	2	7	exclusion	74		
Udezue, 1989 [59]	N=500 7-75 year frank bleeding surgical outpatients	neoplasm lesions:5				10	79	infection:2 prolaps:1	3
Hixson, 1989 [60]	N=75 non-massive bleeding referred patients	1	≥1 cm:14				75	7	3
Peillon, 1989 [61]	N=38 referred patients	21			8			21	8
Krishnan, 1989 [62]	N=70 surgical outpatients	5	7	10	20	5	21	11	21
Brenna, 1990 [63] *	N=194 gastroenterologic outpatients	12	18	13				13	49
Bhargava, 1990 [64]	N=144 gastroenterologic outpatients	6	13	1	1			others:53	26

Table 4 continued

		Primary diagnoses							
Studies first author	population	malignancy %	polyps %	IBD+ %	diverticulosis/ -itis %	fissura ani abscess %	haemorrhoids %	other %	unknown cause %
Church, 1990 [65]	N=269 surgical outpatients	14	adenoma ≥1cm:7	6	8			4	41
Wang, 1991 [66]	N=205 5-90 year acute and severe	23	adenoma:3 juv.polyps:7	21	2			18 angiodys- plasia:15	26

* Total sum of diagnoses exceeds 100%; more than one diagnosis per patient
\# Those with an obvious diagnosis of malignancy were excluded
\+ Inflammatory Bowel Disease

A colorectal tumour was found to be the cause of blood loss significantly more frequently in cases of "blood mixed with the faeces" (35%), and less frequently in cases with anal protusion noticed by the patient (10%) or haemorrhoids identified by general practitioner (10%).
The results of the Australian study relate to a referred but less selected population than the other studies presented in Table 4.[22] In these latter studies, often higher percentages of malignant tumours (up to 39%) and adenomas (up to 32%) were found.

Predictive value of rectal bleeding for colorectal cancer

The data presented can be used to obtain an estimate of the predictive value of overt rectal blood loss for the presence of a malignant colorectal tumour in the 3 situations described. For this we took the incidence figure of rectal blood loss as presented in the previous paragraphs, the incidence of colorectal cancer in the western world[67] and 2 estimations of the number of patients with colorectal cancer and overt blood loss as an initial symptom. These estimations of between 10% and 50% of the occurrence of overt rectal bleeding in colorectal malignancy are derived from frequencies reported by retrospective studies that have recorded signs and symptoms, including blood loss, in patients in whom a colorectal tumour was identified. In one study "blood with *stool" was an initial symptom in 10% of patients with a colorectal carcinoma.*[68]
In other studies different initial symptoms may have been leading to further investigation for colorectal cancer with overt rectal blood loss having appeared in the course of time (may be not an initial symptom) in 40-80%.[69-74]
Results are presented in Table 5. Within the limits of uncertainly inherent to this type of analysis it can be seen that the predictive value of rectal bleeding for colorectal malignancy increases from probably less than 1 in 1000 in the general population to around 2 in 100 in general practice and to up to 36 in 100 in the practice of the medical specialist.

Table 5. Estimation of predictive values of rectal blood loss for malignant colorectal tumours

	general population	general practice	referred patients
Incidence of rectal blood loss	20 per 100 per year	6 per 1000 per year	70 per 10^5 per year
Expected number of people with rectal blood loss per 10^5 people per year	20,000	600	70
Incidence colorectal malignant tumours per 10^5 per year [67]	50	50	50
Number of colorectal malignancy with rectal blood loss (in 50% or 10% of these) as a presenting symptom per 10^5 people per year	25 5	25 5	25 5
Predictive value of rectal blood loss for colorectal malignancy	0.12% 0.02%	4% 0.8%	36% 7%

Discussion

Studies on the occurrence of blood loss per rectum in the general population can yield percentages that are either higher or lower than in reality is the case. There are various reasons for an underestimation. Rarely do people inspect their stool; in none of the studies the patients' report was controlled by inspection (validity); and the percentages reported nearly always concern "healthy" or even "more healthy than average" populations (exclusion of known intestinal disorders). Furthermore, it is not always easy for people to think, let alone speak about, diseases. Wadsworth et al[32] offer three explanations for this: firstly, inadequate social acceptance (e.g. an interview about haemorrhoids is not readily accepted); secondly, fear or superstition that talking about a disease increases the likelihood of contracting it; and thirdly, a limited memory. The reported percentages can also be an overestimation.

Therefore it seems useful to perform a prospective study on the incidence of rectal blood loss in this setting and to identify signs, symptoms, and risk factors that may contribute to effective and efficient diagnosis.

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3. Diagnostic approach of patients with rectal bleeding in general practice. State of the Art

Fijten GH. Bloedverlies per anum. Diagnostiek in de huisartspraktijk. The Practitioner (Dutch ed.) 1992; 9: 509-12.

The current diagnostic approach of patients with rectal bleeding in general practice in the Netherlands is discussed in this chapter. The subject was previously published in Dutch and is translated in English with slightly adjustment for this thesis.

ABSTRACT

In an average general practitioner's population, yearly hundreds of people suffer from overt rectal blood loss and a dozen consult a doctor for this reason. General practitioners may be concerned overlooking cancer which does not present with an evident clinical picture. However, in the same patient population, colorectal cancer which results in rectal bleeding occurs probably less frequently than once every 2 years. A bleeding rectum carcinoma which can be palpated by means of a digital rectal examination only occurs approximately once every 10 years. Knowledge of the diagnostic value of other signs and symptoms in combination with rectal bleeding would be helpful to select patients for further diagnostic investigation. However, this knowledge is not yet available.

Introduction

What does overt rectal blood loss indicate? Is it a sign of cancer? Is it reason to perform a digital rectal examination and/or to perform more invasive diagnostic examinations?

Rectal bleeding is a very broad term which can be distinguished into massive blood loss, minor overt blood loss and occult blood loss. Massive blood loss and occult blood loss are of a different order. A patient with massive rectal blood loss will generally be referred to a specialist immediately. Occult blood loss is particularly of interest as a screening test. It will only be dealt with in this paper in its relation to minor overt blood loss.

Delay in treatment

Among general practitioners as well as the general public, rectal bleeding is known as a signal for malignant colorectal tumours. Yet, patients often do not consider rectal bleeding a reason to consult their general practitioner, nor is it always reason for the general practitioner to conduct further examinations.

Literature has shown that the delay in treating colorectal tumours can be shortened. Graffner and Olsson found that 66% of the patients with tumours in the rectum or sigmoid had complaints for more than 3 months before consulting their general practitioner (patient delay).[1] In general, these complaints are a change in bowel habit (70%) or blood loss (50%). A doctor's delay of more than 3 months between the first consultation and surgery occurs in 34% of the patients with rectal or sigmoid tumours. In many cases (61%), an initial diagnosis of haemorrhoids is made. Occasionally (4%), the delay results from a negative outcome for radiological examinations. Only 16% of the patients has a digital rectal examination during their first consultation, even though a tumour could be palpated in 44% of these patients.

According to Dixon et al. approximately one quarter of the patients with rectal tumours do not undergo a digital rectal examination before being referred to a specialist.[2] In Dixon's report, the average referral delay is 16 weeks for carcinoma in the left half of the colon and 27 weeks for carcinoma in the right half of the colon.

Following digital rectal examination, further examinations such as colonoscopy, sigmoidoscopy and double contrast radiological examinations are often propagated for patients suffering from rectal blood loss. It is assumed that early detection of colorectal tumours (i.e. before complaints manifest themselves) will lead to a better prognosis. However, it has not been unequivocally demonstrated that suffering a shorter period of blood loss has a positive effect on the duration of survival, or that waiting for further examinations is irresponsible.[3] Overt rectal blood loss is a common occurrence and generally, in more than 90% of the new cases, it is not associated with more serious clinical conditions. The dilemma general practitioners often face is deciding whether to expose their patients to possibly unnecessary anxiety and costs, or whether to risk diagnosing a potentially malignant tumour too late or not at all. Considering the low prevalence of malignant causes for blood loss, it seems appropriate to select only those patients with an increased risk for malignant tumours for further invasive examinations.

Symptoms and possible sources

The case history and the development of the symptoms often determine the probable diagnosis and the diagnostic approach (Table 1). Pain, blood loss, mucous discharge, a change in bowel habit, diarrhoea, weight loss, nausea, tiredness and the development of these symptoms can be important indicators of a serious disorder. The most frequent initial symptom in patients with tumours in the descending colon is a change in bowel habit. This is often followed by rectal blood loss and abdominal pain. It is important to know which groups of patients with these symptoms are known to have a higher risk for colorectal tumours (Table 2).

Table 1. Sources of rectal bleeding.

Most frequent

Haemorrhoids
Blood on the stool, after defaecation and on toilet paper. Feeling of prolaps, anal pain, anal itch are frequent. Trombose of haemorrhoids is painful. External haemorrhoids are seen by perianal inspection, internal haemorrhoids are seen by proctoscopy.

Fissura ani
Usually painful defaecation and bright red blood on the stool, after defaection and on toilet paper.
Seen by perianal inspection.

Unknown source
No source found even after follow-up.

Less frequent or rare sources

Fistula, abscess
Rarely rectal bleeding; seen by inspection.

Morbus Crohn, colitis ulcerosa
Recurrent rectal bleeding, abdominal pain, periods of diarrhoea, asthenia.

Colitis
After antibiotics, infections, ischaemia, irradiation.

Proctitis
After antibiotics, suppositoria, trauma, sexually transmitted infections, inflammatory; constipation, mucous discharge.

Vascular-malformations, angiodysplasia
Sometimes massive rectal bleeding.

Rectum prolaps
Inspection during straining.

Diverticulosis
Commonly present, rarely a source of bleeding, sometimes massive rectal bleeding.

Solitary rectum ulcus
Anal discharge, leakage of mucus, mucous discharge, constipation.

Table 1 continued

Polyps Polyps > 1 cm and localised in the rectum sigmoid may provoke complaints, little polyps in the rectum are usually hyperplastic (non-neoplastic) and without symptoms.
Malignant colorectal tumours Change in bowel habit, blood mixed with stool, abdominal pain, sometimes weight loss, tiredness.
Invagination Painful abdominal cramp in children.
Haemorrhagic disorders
Other than colorectal tumours
Endometriosis Cyclic cramping pains in the rectum and cyclic bleeding.

Table 2. Risk factors for colorectal tumour.

- Previous history of colorectal neoplasm - First degree family member(s) having colorectal malignant diseases - Cancer of ovaria, endometrium, mammae - Polyposis syndroms, families with polyposis - Colitis ulcerosa: distal colon longer than 15 years, entire colon longer than 7 years

The importance of digital rectal examination

For patients with rectal blood loss, perianal inspection is a must. A number of common causes, such as a fissure or a prolaps, can be diagnosed. When the cause of the blood loss is a fissure, the general practitioner must carefully consider whether or not to perform a painful digital rectal examination. On the whole, however, performing a digital rectal examination after a perianal inspection can be of great value in diagnosing tumours, even though tumours are rarely found. This examination is also important for determining if there is faeces in the rectum before performing a proctoscopy. Finally, it is possible to examine the faeces on the glove for overt or occult blood.

A proctoscopy can be a worthwhile additional procedure. Probable causes for blood loss such as haemorrhoids, proctitis and a rectum ulcus or tumour can be diagnosed with this procedure. In addition, it is possible to obtain samples for a culture or to treat haemorrhoids. Proctoscopy is not (yet) considered a basic skill for general practitioners.[4]

If haemorrhoids, fissurae ani or other non-serious disorders are diagnosed, more serious proximal pathology (tumours, colitis ulcerosa or Morbus Crohn) must still be taken into consideration. A negative diagnosis based on a digital rectal examination does not exclude a malignant disorder. Even if a diagnosis of haemorrhoids or proctitis is made with the help of proctoscopy, possible malignancies higher in the colon must not be excluded, especially in patients older than 40-45 years of age. However, if patients have haemorrhoids (preferably diagnosed by means of proctoscopy) but lack other signs of malignancy, a regimen and follow-up check-up will often suffice.

If there is reason to suspect a malignant cause for rectal bleeding, then a sigmoidoscopy or a double contrast radiological examination of the colon is recommended in addition to a digital rectal examination (and a proctoscopy). When sigmoidoscopy shows no abnormalities in the rectum, sigmoid and distal colon, additional radiological examinations are advised for patients older than 40-45 years of age.[5] Since these examinations do not provide a good image of the anal canal, digital rectal examination must still be performed.

There is insufficient scientific evidence to support the claim that digital rectal examinations must be performed on all patients suffering from rectal blood loss. Even though digital rectal examination is not a very demanding procedure, general practitioners are often reluctant to perform it. A study by Hennigan et al. names the following reasons:[6]

1. the reluctance and embarrassment of the patient;
2. the knowledge that the examination will be repeated after referral; and
3. the lack of time.

The general practitioner's embarrassment and doubts about the usefulness of the examination may also be reasons for not performing a digital rectal examination.

Epidemiological considerations

From screening studies it appears that approximately 1.5% of the people questioned report rectal blood loss in the previous 2 weeks and approximately 13%-16% report blood loss in the previous 6 months or 20% in the previous year.[7-11] Gill found that 19% of the people questioned never look at their own faeces.[8] Only a small fraction of the people suffering from rectal blood loss consult a general practitioner. If everyone were to consult a general practitioner as a result of rectal blood loss, the general practitioner would see approximately 40 patients with this complaint each month and 500 patients each year. At present, the average general practitioner annually sees an estimated 10-15 patients whose primary complaint is rectal blood loss. New malignant tumours in the colon occur on average once every 1.5 years. Malignant tumours in the anus, rectum or sigmoid occur once every 6.5 years in an average practice.[12] In approximately half of the cases of rectum carcinoma, rectal blood loss is the first symptom. Tumours located above the rectum or sigmoid result in overt blood loss less often (14%).[1]

It is estimated that general practitioners will come across a patient with a rectal tumour causing blood loss once every 13 years. Three quarters of these tumours can be reached with a finger during a digital rectal examination. With colon tumours, 55% is within reach of the rectoscope (25 cm). The incidence of malignant tumours increases with age. In people under 40 years of age, malignant tumours in the anal canal or rectum, recto-sigmoid junction occur very rarely-less than once per 100,000 people per year. The incidence of malignant tumours in people between 40 and 50 years of age is 6 per 100,000 people per year and between 50 and 60, 24 per 100,000. The incidence in people over 60 years of age is 100 per 100,000 people per year.[13]
Screening in Sweden has shown that for people between 60 and 65 years of age, the predictive value of bright red blood loss for a carcinoma is 1.3%, and for an adenomatous polyp it is 0.9%. It is remarkable that if there is a positive Haemoccult test as well as overt blood loss, the incidence of a carcinoma is 8.8% and the incidence of at least one adenomatous polyp is 27.5%.[9]

The data from this screening raises the question on which people in the age category 60-65 with bright red blood loss an examination of the colon should be performed, and for which people close observation of the development of the symptoms suffices. This question is even more relevant for younger people, in whom the incidence of malignancy is lower. Patients in a risk category (Table 2) should in any case be eligible for further examinations.

The importance of further examinations

When considering whether or not to perform one of the examinations (proctoscopy, rectosigmoidoscopy, colonoscopy, radiological examination), it is important to keep in mind that no examination offers a 100% assurance that a malignant disorder can be ruled out. Dealing with such uncertainty characterizes the work of the general practitioner. Knowing the patient, his/her background, the family, and the case history, and keeping an eye on the development of the symptoms are of great importance to an effective and efficient diagnosis. Knowing the limited value of an examination is as important as a competent performance of the examination.
When a patient suffers from rectal blood loss, a good case history must be made. In addition, a local examination, that is a perianal inspection and a digital rectal examination, must be performed. If there is an increased chance or suspicion of more serious pathology in the rectum or colon, further examinations should take place. Of course, the age of the patient plays an important role as well. An arbitrary, but generally accepted age limit is 45. Colorectal malignancy rarely occurs at a younger age.

The need for research

Which other signs and symptoms increase or decrease the probability of colorectal cancer in patients with rectal bleeding in general practice and to what extent they influence this probability is yet unknown.

We have initiated an empirical study to find the predictive value of signs and symptoms in combination with rectal bleeding. The study and the results will be presented in the following chapters.

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4. Methods of the empirical study

Introduction

This chapter gives a review of the general methodological aspects. The methodology sections in the following chapters give information on the specific methodology relevant for the subject of that chapter.
The study was carried out in cooperation with the Diagnostic Coordinating Centre (DCC) Maastricht, the Department of Internal Medicine at the University Hospital Maastricht and the Department of General Practice at the University of Limburg of Maastricht.
Patients were recruited from September 1988 to June 1990. Outcome data were gathered in 1991.

Questions

To answer the main question, "is it possible to discriminate effectively between patients with rectal bleeding who have colorectal cancer and those who do not?; or at least to discriminate between those who need invasive investigations and those who do not?", the following data are important.

1. The incidence of rectal bleeding, as an index of the inception cohort.
2. The prior probability of colorectal cancer and the other potential sources of bleeding, also as an index of the study population.
3. The predictive values of signs, symptoms and laboratory test results in general practice, providing the essential information for medical decision making. These data are used to construct a prediction model in general practice.
4. Determination of the predictive values in an outpatient clinic population. Since referred patients with rectal bleeding will almost always undergo further diagnostic investigations, including endoscopy or roentgenography, additional information compared to general practice might be gained.

Knowledge of the differences in predictive values between general practice and the internal medicine clinic may be of use in improving the communication between general practitioners (GPs) and internists regarding patients with rectal bleeding.

In both general practice and the outpatient clinic the operationalized question was: to what extent do other (combinations of) symptoms enable the physician to confirm or rule out serious disease?

In general practice the focus was on colorectal cancer, since the prediction of the presence or absence of colorectal cancer is the main decision problem.
In the outpatient clinic the focus was on serious disease requiring further diagnostic investigation. Inflammatory bowel disease (IBD) and colorectal neoplasm (cancer and polyps) were taken together as serious disease.

Design

The design of the study can be defined as 'pseudo-follow-up' study, investigating a cross-sectional relationship between particular factors (signs, symptoms and simple laboratory test results) and a particular outcome (colorectal cancer, neoplasm or IBD), while the outcome can be only detected by follow-up. All diagnostic data available after a follow-up period of at least 1 year were used to establish the gold standard for the diagnostic outcome.

Outcome

After the follow-up period of at least 1 year the final diagnostic conclusion was determined. Three researchers (G Fijten, J Muris and R Starmans), blinded for the initial complaints and symptoms, abstracted all available diagnostic information from the medical records and established the diagnoses. Additionally, the final conclusion was presented to the patient's general practitioner who was asked for additional, not recorded, information or confirmation.

The final diagnoses were classified in accordance with the International Classification of Primary Care (ICPC), defined on the basis of the criteria of the International Classification of Health Problems in Primary Care (ICHPPC-2).[1,2]

In many general practice situations it is impossible to find a hard 'gold' standard because not all patients undergo colonoscopy or surgery. It was considered unethical (and very expensive) to submit such a protocol including endoscopy without preselecting 'serious bleeding'. It was assumed that a potentially malignant source of rectal bleeding would have been discovered within the follow-up period.

Endoscopy or roentgenography in all patients with rectal bleeding could yield some diagnoses, like diverticulosis and polyps, which would not necessarily be the source of bleeding.

Diverticulosis and polyps were classified as the outcome when these disorders were regarded as the source of bleeding. For a diagnosis of haemorrhoids proctoscopy was generally desired. But in cases where the complaints had been considered typical for haemorrhoids this was also accepted as the outcome after at least 1 year. Typical haemorrhoid signs and symptoms were: bright red blood dripping into the pan after bowel action and prolaps or one or more visible bleeding haemorrhoids.

For a diagnosis of IBD (proctitis and colitis) at least sigmoidoscopy was necessary.

Consensus of the three researchers and the general practitioner enabled the reference diagnosis to be established.

Study populations

Consecutive patients with rectal bleeding were recruited in general practice and general internists' outpatient clinics. Since it was noticed during the course of the study in general practice (study A) that the number of patients included in the study was less than expected and very variable, it was decided to do a complementary study (study B) with a modified protocol as described further on in this chapter and in Chapter 5. The aim of the study B was to assess a

more accurate incidence rate. In summary there were three study populations.

Study A: Patients recruited by 83 GPs in Limburg, the southernmost province in the Netherlands. Initially 9 other GPs started with the study but they quit after some time without any of their patients included for the study.

Study B: Patients recruited by 10 GPs in the area of Maastricht during a three-month period. Patients from 1 GP had been excluded since it was uncertain if all eligible patients were included in the study.

Study C: Patients recruited in four general internists' outpatient clinics. There was no overlap of patients in study A, B and C.

Inclusion and exclusion criteria

Inclusion:
- All patients presenting to the doctor with overt blood loss per anum or rectum (rectal bleeding) seen by the patient within the previous three months. Rectal bleeding may be either the reason for encounter or be reported in the course of history taking.

Exclusion:
- younger than 18 years of age, since children have a different spectrum of diagnoses and completing an extensive questionnaire might be difficult;
- older than 75 years of age, because during a pilot study it had appeared that older people had difficulties in completing the questionnaire;
- if the patient was known to have colorectal cancer or IBD;
- if urgent admission to a hospital was indicated, for example in cases of massive rectal bleeding, acute intestinal obstruction or perforation;
- if the patient was pregnant, since signs, symptoms and laboratory test results may be influenced by pregnancy.

As far as the outcome was concerned, patients were excluded if they were lost to follow-up. Moving to an unknown destination was the only accepted reason for loss to follow-up. For calculation of the incidence rate of rectal bleeding these patients have been included.

Instruments

The data were collected through the following instruments.

1. A semi-structured questionnaire filled in by the doctor after the first consultation containing 70 variables: history, physical examination and initial management. This questionnaire is included in Appendix I (in Dutch). A complete physical examination was requested for all patients.
2. Low haemoglobin (Hb)(<8.4 mmol/l in males and <7.4 mmol/l in females) may be indicative for chronic bleeding. High erythrocyte sedimentation rate (ESR) has been found to have discriminating ability with respect to IBD and malignancies.[3] The optimal upper limit was 12 mm/1 hr in men and 28 mm/1 hr in women, with no correction for age needed. Several cut-off points, for example 30 mm/1 hr for men and women, were tried in the search for an optimal point for discrimination. Leucocyte count has been reported to be an independent predictor for cancer and bacterial infections[4], but it has also been shown that high white blood cell count (WBC) is not a clinically interesting alternative to ESR.[5] It was decided therefore to determine WBC ($>10^9$/l) in addition to ESR.

   Faecal occult blood (FOB) testing in cases with overt rectal bleeding may additionally contribute to the diagnosis of colorectal neoplasm (cancer or polyps) especially in patients who have seen blood loss only once. Furthermore for patients with haemorrhoids the presence of occult blood in a central sample of the faeces may be indicative for colorectal pathology. In a screening study it has been shown that in patients, aged 60-64 years, the probability of neoplasm increased from 5.6% to 36.3% if FOB was positive.[6] The discriminatory value of the FOB was found to have been studied only in screening and case control settings. The literature on the diagnostic value of FOB is large, but rather inconclusive about its usefulness.[7,8] It was decided to determine FOB with the Haemoccult test in three subsequent portions of stool after a peroxidase and red meat-free diet.

   Carcinoembryonic antigen test (CEA) was not included in this study. It has shown to be valuable in assessing prognosis and early detection of metastases in colorectal cancer, but not in the detection of an undiagnosed tumour.[7]

The simple laboratory tests, Hb, WBC, ESR and Haemoccult (included in Appendix II), were assessed in the nearest hospital laboratories (which function for GPs use also). This was done to reduce the interpractice variation in assessment of these tests.

The laboratories had been informed about the study. The desirability of an unequivocal assessment among the laboratories was respected. More extensive and invasive diagnostic investigation was not prescribed by the study protocol. This was only done when the doctor considered it to be indicated.

3. A self-completion patient questionnaire containing 150 questions. Signs and symptoms mentioned in literature as having discriminatory value for the diagnostic outcome were used.[9-13] A large section of the questionnaire contained questions relevant for patients with non-acute abdominal complaints. This section could be skipped when not applicable. The variables considered to be relevant for rectal bleeding are presented in Chapter 6 and 7.

   Psycho-social factors may have an impact on the consulting behaviour of patients. Therefore 3 psychological scales were included: the VOEG, the Dutch version of the "Inventory for Subjective Health" (psychobiological stress), the subscales Self-esteem and Social Inadequacy of the Dutch Personality Inventory and the ZUNG questionnaire for depression.[14-16]

   The patient questionnaire containing symptoms, (previous-)history, family history, medication consumption, social status and psychological scales is included in Appendix III (in Dutch).

Pilot studies

The instruments have been tested for rectal bleeding separately from non-acute abdominal complaints and for rectal bleeding combined with abdominal complaints. For rectal bleeding the pilot study was done in four practices during two months (18 patients).

For the combined study a pilot study was done in one general practice, one health centre (50 patients in general practice) and in an internist's outpatient clinic in one hospital (50 patients).
The latter pilot study had revealed that the content of some psychological items provoked some resistance. It was therefore decided to restrict the questionnaire regarding the psychological scales to:
- the abbreviated VOEG for psychobiological stress (13 items)
- the NPV subscale for self-esteem (19 items)
- the NPV subscale for social inadequacy (15 items)
- the ZUNG scale for depression (20 items).

Monitoring

During the period of data collection the GPs, the internists and the registrars were frequently visited to stimulate them to be on the alert for including patients, to give feedback about their yield and to discuss potential problems arising. Stress was laid on avoiding selective inclusion regarding serious or harmless disorders. Special attention was paid to motivating patients to complete the questionnaire. Completion of digital rectal examination was encouraged.
Repeatedly newsletters were sent to the participating physicians to give information about the course of the study and to pay special attention to the problems which had arisen.

Evaluation of potential inclusion

Since during the course of the study it was noticed that fewer patients than expected were included, with a very variable frequency among doctors, special efforts were taken to evaluate the underdetection rate, the reasons for underdetection and the possibility of selective underdetection.

General practice

Study B was initiated to find an accurate incidence rate of rectal bleeding. For this purpose daily controls of patient records were performed by practice assistants, who kept a notebook to gather data (age, gender, names) regarding all patients of whom rectal bleeding or abdominal complaints were recorded by the GP. Using this notebook, the doctors' questionnaires were checked for completeness of patients' recruitment.
The protocol was simplified by means of a single A4 format doctor's form (Appendix IV), by making the patient questionnaire not obligatory and by not prescribing laboratory tests. There was only one exclusion criterion, age less than 18 years.
The participation period was short (3 months, March till June 1990) and intensive.

In study A five GPs kept for a certain period a list with data and reasons for withdrawal (non-inclusion).

Outpatient clinic

An additional registration with epidemiologic data of referred patients with rectal bleeding derived from the University Hospital of Maastricht may serve as a map of the rectal bleeding presented in the general internist's outpatient clinic.

1. A retrospective analysis of patients' records of those who had been discharged from the hospital having a diagnosis of anal or colorectal malignancy in 1989 was done to find the frequency of patients with these malignancies and with rectal bleeding as a presenting symptom as well as the distribution of these patients among surgeons and internists.
2. Data from the Endoscopy Department at the University Hospital of Maastricht.

Results are presented in the general discussion, Chapter 8.

Data transport

The questionnaires and laboratory results were checked for errors and missing answers by the researchers after each visit to the participating physicians.
The initial data were coded and imported into the VAX/VMS mainframe by the Data-entry service of the Department of Automation at the University of Limburg. The missing values and incorrect coding were checked using the BMDP-2D program and as much as possible corrected. The data of the follow-up assessment were coded and imported into a Personal Computer in a dBase program. After controlling for missing data and incorrect coding conversion with the software Kermit, entry into the mainframe was carried out.
Both sets of data were then combined on the mainframe and analysed with BMDP software.[17]

Statistical analyses

The data were analysed univariately first to detect incorrect coding for correction.
Second, the distribution of the results for the several items was assessed. For continuous variables several cut-off points were assessed for an optimal discriminatory cut-off point. Age was divided into age groups. Diagnostic outcome was divided in 9 groups: colorectal malignancy, polyps, colitis, proctitis, diverticulosis, infection, haemorrhoid(s), fissura ani (including fistula and abscess) and "no source of rectal bleeding found".
Most variables were transformed into dichotomous variables, with a cut-off point optimal for discrimination.
Loss of weight reported on the patients' form was derived by subtraction of the reported actual weight and earlier mean weight.
The psychological scales and the VOEG were recoded and summed up according to accepted guidelines.

In bivariate analysis the association between each variable with several outcome groups was assessed (Appendix V). Chi-square statistics were used to test

statistical significance. From the cross tabulation (BMDP 4F) the sensitivity, the specificity, the positive predictive value (PV^+), the negative predictive value (PV^-) and the odds ratios of the (independent) variables for the (dependent) diagnostic outcome were derived.
In study A the analysis was performed mainly with respect to colorectal malignancies versus all other diagnoses and, additionally, with respect to colorectal neoplasm (malignancies and polyps). In Appendix V, the association with the other diagnostic groups is presented. In study C the diagnostic outcome concerned colorectal neoplasm and IBD (colitis and proctitis).
The association with the other diagnostic groups is presented in Appendix V. Because of the quantity of data (small number of patients and not obligatory patients' questionnaire) such analysis was not done in study B.

All signs and symptoms can be considered as diagnostic tests and evaluated according to the rules for assessment of diagnostic tests.[18]
Sensitivity and specificity are classically considered the discriminatory characteristics of diagnostic tests but for clinical practice predictive values are more appropriate. These diagnostic indices are especially informative in studying one test. In a more complex situation, such as clinical practice, the adjusted odds ratio (OR) or regression coefficient (coef) (which allows calculation of the odds ratio: $OR = e^{coef}$) are more suitable. OR = (true positive x true negative) : (false positive x false negative) or
$OR = (PV^+ \times PV^-) : (1 - PV^+)(1 - PV^-)$.[19]
If bivariate odds ratios are presented with 95% Confidence Intervals (CI), these have been calculated using Epi Info on a personal computer[20]; if logistic regression coefficients are presented, both coefficients and 95% CI were calculated by BMDP-LR on VAX/VMS mainframe.
The logistic regression coefficient determines the independent predictive value of a variable taking the other variables into account simultaneously.[19,21]

Forward stepwise multiple logistic regression analysis was used to obtain an adequate prediction model with a reduced number of variables. Variables which showed an association with the diagnostic outcome of choice with a p-value < 0.1 were entered into multiple logistic regression. Entry and remove limits

were applied for p-values < 0.05. So in the reduced model only variables which have independent statistically significant predictive values were included. The diagnostic value of the regression models were assessed by the goodness of fit test Hosmer Lemeshow[22], the PV^+ and PV^- for several cut-off points, the maximum sum of sensitivity and specificity and the Area Under the Curve (AUC) of a Receiver Operating Characteristic Curve (ROC).[23-27] The AUC permits an overall impression of the discriminating performance of a model. An AUC of 1 or 0 discriminates perfectly and an AUC of 0.5 does not discriminate at all. The AUC was calculated with the aid of a software program by EP Brummelkamp, H Straatman and ALM Verbeek at the Catholic University in Nijmegen based on an article by Harley and McNeal.[27]

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5. The incidence and outcome of rectal bleeding in general practice

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ABSTRACT

The objective of the studies reported in this paper was to determine the incidence as well as the final diagnostic outcome of rectal bleeding presenting in general practice. Because of the wide variety observed in incidence rates among 83 GPs in the first study (A) an additional study (B) was undertaken. In study B with 10 GPs special efforts were made to maximize the catchment rate. The mean 'consultation incidence rate' was 7 per 1000 people per year. A follow-up period of at least 1 year was applied to establish the final diagnostic conclusion. Occurrence of colorectal cancer was found in 3% of patients with rectal bleeding. This may represent an overestimation of the prior probability since there was a selection in favour of patients with clinically relevant rectal bleeding. In about 90% of the patients rectal bleeding was related to minor ailments or self-limiting disorders.

Further study on predictive values of (combinations of) others signs and symptoms is necessary to develop clinical recommendations.

Introduction

Overt rectal bleeding is a common symptom. A recent study reports a prevalence of 20% in the general population.[1] Only a small number of the people with rectal bleeding, however, consult a doctor. The incidence of rectal bleeding in patients presenting in general practice can be roughly estimated to be at between 4 and 16 per 1000 people per year.[2,3] Some of these patients will have colon or rectal cancer. The incidence of colorectal cancer is 44 per 100,000 inhabitants per year in The Netherlands and increases with age.[4] In less than half of the cases of colorectal cancer rectal bleeding is a presenting symptom.[5,6] Therefore the prior probability of cancer in people with rectal bleeding can be estimated to be around 0.1%. Empirically, there is little known about the prior probability of colorectal cancer in patients presenting with rectal bleeding to the general practitioner. A Medline search (CD ROM) in the literature, published between 1984 to 1992, with "rectal bleeding" as one of the keywords, yielded only one study, twice referred to (by Goulston et al in 1986[7] and by Mant et al in 1989[8]), in which patients were recruited in general practice. This Australian study gives a prior probability of 11% of cancer in patients presenting "rectal bleeding" as their clinical problem. In this study only patients older than 40 years of age were included. Furthermore, reports from study populations selected by referral to hospital are not useful for decision making in general practice.[9] Depending on the selection before referral, the prior probability may be as high as 39%.[10]
The study reported here deals with the incidence and outcome of rectal bleeding in general practice.

Methods

Design

Consecutive patients with rectal bleeding were recruited by General Practitioners (GPs) in Limburg, the most southern province in the Netherlands, in a period from September 1988 to April 1990.

The design of the study can be characterized 'pseudo follow-up': patients are followed, for at least one year, to establish a final diagnosis.
This study was part of a larger study on rectal bleeding and non-acute abdominal pain.

Patients

All patients presenting to the doctor with overt rectal bleeding or a history of recent (i.e. within the last 3 months) rectal blood loss visible for the patient had to be included in the study.
Patients were excluded from the study if they met one of the following criteria: age younger than 18 years or older than 75 years, pregnancy and urgent admission to a hospital (massive bleeding or acute abdomen).

Data collection

Data were collected through the following:

1. A self-reported patient questionnaire containing 150 questions (somatic, social and psychological). A large section of questions required for abdominal pain can be skipped if not applicable.
2. A semi-structured questionnaire filled in by the doctor at the first consultation containing 70 variables: history, physical examination and initial management.
3. Laboratory tests: haemoglobin, erythrocyte sedimentation rate, white blood cell count and the Haemoccult test (3x, with a diet low of peroxidase and free of red meat).

The diagnostic items selected were those mentioned in literature as being relevant to discriminate between several diagnoses. [8,11-13]
The instruments were tested in a pilot study (for rectal bleeding only) in 4 practices during 2 months (18 patients) and in a pilot for the larger study in a health centre (50 patients).

Final diagnosis

Outcome data were gathered in 1991. For this purpose the researchers (G Fijten, J Muris, R Starmans) reviewed the patient records in the practices after a follow-up period of at least one year. Any further diagnostic investigation (e.g. endoscopy) during this period was free to the decision of the GP. A final discussion with the GP completed the clinical follow-up. The follow-up procedure was blinded for the initial complaint(s) which could be rectal bleeding and/or non-acute abdominal complaints. The ICPC is used for the classification of diagnoses using the criteria of ICHPPC-2.[14,15]

Monitoring

Action was taken to reduce the number of dropouts. Attention was paid to the problem of underregistration through regular personal contacts with the GPs (once a month) and via a newsletter circulated twice a year. The researchers were responsible for the contacts with the participating practices and for follow-up, each about one-third of the geographical area.
During the study performed according to this protocol (study A) it was noticed that the number of patients included was less than expected and very variable between practices. Therefore, in order to estimate possible underregistration by minimizing the number of dropouts, special efforts were taken by another 10 GPs using a modified protocol: study B.

Study B

This modified protocol was as follows:
- daily controls of patient records by the practice assistant (a notebook was kept to register data (age, gender, names) regarding all patients with rectal bleeding who visited the practice that day);
- very frequent (weekly) practice visits to check the questionnaires with the assistant's notebook;
- short intensive period of participation: 3 months (March till June 1990);

- no exclusion criteria except < 18 years of age;
- a simplified (one A4 format) doctors' form;
- the patient questionnaire not obligatory (but desired);
- no laboratory tests prescribed;
- outcome data collected in the same way as in study A.

Data analysis

Data were analysed on VAX-VMS mainframe using BMDP and on personal computer using Info Epi.[16,17] The Chi-square test was used to assess the statistical significance of differences in contingency tables.

Results

Study A included 290 patients presenting with rectal bleeding in general practice according to the forms from 83 GPs. On average the duration of participation by the GPs was 11 months, with a range of 1 to 24 months. Standardized for participation time and part-time employment, the incidence of rectal bleeding in an average general practice (2200 persons per practice) was 2.15 per 1000 persons per year, with a inter-practice range of 1 to 8.
In study B 48 patients were collected by 10 doctors in 3 months. Since in study B special efforts have been taken to minimize the dropout rate (or, maximize the catchment rate) the incidence rate can be calculated more accurately, as is shown in Table 1.

The resulting incidence rate is 6.8 per 1000 per year, with an inter-practice range of 0 to 18.5. On average this is three times as high as in study A. Only 3 GPs in study A yielded an incidence rate as high as the mean in study B.

Table 1. Incidence rate of rectal bleeding presented in general practice, per 1000 per year.

Practice	number (N)	weeks of registration (W)	practice size (S)	number per 1000 per year
A	7	12	2800	10.8
B	3	12	2800	4.6
C	0	12	3100	0
D	3	11	2400	5.9
E	8	13	2500	12.8
F	4	13	2500	6.4
G	9	11	2300	18.5
H	9	13	3500	10.3
I	1	13	3200	1.25
J	4	11	2750	6.9
Total	48			6.8

Calculation of the mean of incidence rate = $\left(\sum_{A-J}\left(\frac{Nx52}{W}\right)x\left(\frac{1000}{S}\right)\right):10$

Mean = 6.8
Median = 6.6
Range = 0 - 18.5

Table 2 shows the age and gender distribution of patients in study A and B. In general no major difference was observed, although there were relatively more patients aged older than 55 years in study A ($p=0.07$). The gender differences were not statistically significant.

Table 3 shows the diagnostic outcome in the two studies.

In study A 21 patients (7%) were lost to follow-up, due to moving to an unknown destination. The mean follow-up period was 19.6 months, with a standard deviation of 4.9 and a range of 12 to 40 months.

In study B 4 patients (8%) were lost to follow-up. The follow-up period varied from 12 to 15 months.

Table 2. Age and gender distribution of patients in study A and in study B.

Age and gender	study A number	%	study B number	%
Age				
18 - 39 years	144	49	24	50
40 - 44 "	39	13	7	15
45 - 49 "	19	7	5	10
50 - 54 "	28	10	9	19
≥ 55 "	60	21	3	6
Gender (1 missing)				
female	163	56	22	46
male	126	44	26	54
Total	290	100	48	100

Table 3. Final diagnoses related to rectal bleeding in study A and study B.

Diagnosis	study A N = 269 %	study B N = 44 %
Unknown cause (but healthy)	61	52
Haemorrhoids	16	30
Fissura ani (fistel, abscess)	7	9
Infections	2	2
Diverticulosis	1	0
Proctitis	4	0
Colitis	5	7
Polyps	2	2
Cancer	3	0
Total	101*	102#

* 6 patients with 2 diagnoses
# 1 patient with 2 diagnoses

In both studies there was often (61% and 52%) no specific diagnosis related t rectal bleeding found. These patients remained healthy within the follow-u period. Minor ailments and selflimiting disorders like fissura ani an haemorrhoids were frequently diagnosed with preponderance in study B: i 39% of patients in study B and in 23 % in patients in study A.
Haemorrhoids occurred twice as often in study B as in study A, but otherwis the two studies showed no major differences. Causes which can be considere 'serious' (colitis, proctitis, polyps and cancer) occurred with a frequency o around 10% in both studies. The prior probability of cancer was 3% in stud A and 0 in study B.

Study A patients were divided into 2 groups in order to evaluate differences in outcome between (1) those practices which participated at least 6 months with an incidence rate of rectal bleeding above the mean incidence rate and (2) those which participated only briefly or had an incidence rate below the mean (Table 4).
Age and gender were not statistically different but minor ailments (haemorrhoids, fissura ani, infection and diverticulosis) occurred more in the group with a higher incidence rate ($p = 0.048$). Different cut-off points for participation intensity (length of period and number of patients recruitment), for example 5 or 9 patients per practice, were applied with similar results.

Discussion

The incidence rate of rectal bleeding in general practice was found to be around 7 per 1000 people per year and varied among practices with a maximum incidence rate of 18 per 1000 per year. Study A concerns patients selected for the study according to the initial protocol, including laboratory tests and a patient questionnaire. There is probably an underregistration of rectal bleeding in this group especially regarding younger patients due to non-compliance of the registrating doctor.

Table 4. Patients and outcome in two groups, related to the incidence rate of the practice and duration of participation of the GPs.
Group 1. GP participated > 6 months and incidence rate > 2.15 per 1000 per year.
Group 2. GP participated < 6 months or incidence rate < 2.15 per 1000 per year.

	group 1 N = 126		group 2 N = 164		total** N = 290	
	number	%	number	%	number	%
Age						
18 - 39		53		48		50
40 - 49		19		20		20
50 - 59		18		14		16
60 - 75		10		18		14
Gender (1 missing)						
female		57		56		56
male		43		44		44
Outcome*						
cancer	3	2	6	4	9	3
polyps	3	2	3	2	6	2
colitis	2	2	11	7	13	5
minor ailments	73	58#	70	43	143	49
unknown cause**	45	36	74	44	119	41
Total	126	100	164	100	290	100

* diagnoses ranked according to severity
** lost to follow-up included
# $p < 0.05$

GPs in study A mentioned several reasons for not recruiting all patients who met the inclusion criteria. Most frequently it was "too much fuss for a simple and harmless complaint", often "lack of time" and sometimes the study was considered harmful for the patient because the possibility of inducing fear. Furthermore, the longer patients' questionnaires in study A might have caused some resistance among the GPs to motivate the patients with minor rectal bleeding, although the questionnaires had proved to be acceptable in a pilot study. However, this was done by a selected group of highly motivated GPs.
In study B special efforts had been taken to reduce underregistration.

Laboratory test and patient questionnaires were not obligatory. At the same time there was a daily check of patient records. In study B the incidence of rectal bleeding was higher and there were relatively more younger patients. The incidence rate of around 7 per 1000 per year found in study B appears therefore to be the true incidence rate. This result is comparable to estimations that can be derived from Dutch registration projects. They have given an incidence rate of rectal bleeding of unknown cause of 4 per 1000 per year and of disorders which frequently result in rectal bleeding of 16 per 1000.[2,3]

In this study it has been assumed that the follow-up period of at least one year is sufficient as a gold standard for the diagnosis of cancer. Usually a malignant cause of bleeding will not be self-limiting. For colitis, proctitis, polyps and diverticulosis, endoscopic or radiologic confirmation was necessary. Not all patients had colorectal endoscopy nor radiologic investigation. For clinically important colitis it was assumed that this would be detected within the follow-up period. For the diagnosis of haemorrhoids proctoscopy was desired unless clinical symptoms and history were strongly indicative for haemorrhoids. If this was not the case the conclusion was: 'bleeding of unknown cause'. Although the gold standard is not 100% valid for all specific diagnoses, it is for clinically important diagnoses. It must be emphasized that the patients without a specific diagnosis were healthy after a follow-up period of at least one year. Taking this in mind it can be concluded that serious disorders occurred in around 10%. Malignant colorectal disease was diagnosed in 3% of patients in study A and in none in study B. The GPs of study A may have selected patients with respect to clinically relevant bleeding or age. This can result in a higher or overestimated prior probability of cancer. Although it should be noted that the size of study B and therefore the precision is smaller, the prior probability in a less preselected population is more likely to be less than 3%. The Australian study had found a probability of cancer of 11% in patients older than 40 years with 'rectal bleeding as a clinical problem'.[8] This different finding may be attributed to selection by age, but selection bias in favour of 'clinically relevant bleeding' cannot be excluded. These patients, of whom 42% were not available for analysis, were recruited in general practice but referred to a specialist for final diagnosis.

We conclude that the incidence of 'rectal bleeding presented in general practice' is about 7 per 1000 per year. The initial study protocol, study A, yields a lower rate, 2 per 1000, which is probably an underestimation of the real incidence but reflects rectal bleeding considered to be clinically relevant by the GPs. In patients with 'rectal bleeding presented in general practice' the prior probability of cancer is 3% or less. About 90% of the sources of bleeding are minor ailments or self-limiting disorders. In order to develop clinical recommendations for GPs for effective and efficient selection of patients (with a reasonably high prior probability of cancer) for invasive diagnostic workup, further study on predictive values of other signs and symptoms in combination with rectal bleeding is necessary.

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6. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice

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ABSTRACT

Objective : to determine the diagnostic value of (combinations of) signs, symptoms and simple laboratory test results for colorectal cancer in patients with rectal bleeding presenting in general practice.

Design : pseudo follow-up study; initial complaints and findings were compared with the final diagnoses which were independently assessed based on clinical follow-up established after at least 1 year.

Setting : General Practices (83 GPs) in the South of the Netherlands.

Subjects : 269 consecutive patients in the ages 18-75 years presenting overt rectal bleeding to the general practitioner.

Outcome measure: sensitivity, specificity, predictive values, odds ratios and a prediction model derived from multiple logistic regression analysis.

Results : age, change in bowel habit and blood mixed with or on stool show a statistically significant independent value in the discrimination between patients with a low and those with a high probability of colorectal cancer. The prediction model has a sensitivity of 100% and a specificity of 90% at a cut-off point (posterior probability) of 0.042.

Conclusion : although the number of patients with colorectal cancer is small (n=9) it was possible to identify three characteristics which can be helpful in the prediction of presence or absence of colorectal cancer in general practice. Application of the model presented might prevent 90% of 'unnecessary' invasive diagnostic procedures for patients with rectal bleeding who do not have colorectal cancer (true negative). Testing the performance of the model in other general practice populations is recommended.

Introduction

Overt blood loss per anum or per rectum (haematochezia) is common in general practice. The incidence of patients in the ages of 18 to 76 years presenting this symptom to their general practitioner (GP) is 7 per 1000 people per year.[1] Although its source is usually not serious it may also be the first symptom of a colorectal malignant disorder.[1] It is open to debate whether the prognosis of symptomatic colorectal malignant disease may be improved by earlier diagnosis,[2,3] but the finding of a carcinoma will often raise the question whether it would have been possible to detect it earlier. Partly because of this there is considerable disagreement as to the optimal diagnostic management. Some advocate a full examination of every patient with blood loss per rectum (sigmoidoscopy in combination with barium enema or colonoscopy) in order to rule out the possibility of a malignant tumour,[4-6] whereas others favour a more conservative approach.[7] The GP is faced with the task of selecting patients in such a way that the costs and benefits of ancillary tests are reasonably balanced.

Little is known about the diagnostic value of specific signs and symptoms useful in general practice.[8,9] An early discrimination between patients with a low and those with a reasonably high probability for colorectal cancer could reduce the number of invasive investigations and prevent 'unnecessary' alarm.

The aim of the present study was firstly to determine the predictive value of patient characteristics, signs and symptoms for the presence of colorectal malignancy and secondly to identify important predictor variables contributing to a multivariate prediction model. Such a model could be helpful for GPs in deciding whether to proceed with further assessment.

Methods

Design

The design of the study can be characterized as 'pseudo follow-up': a cross-sectional relationship between signs and symptoms and the diagnostic outcome is studied, while the outcome can be only detected by follow-up.

All diagnostic information (medical records and information of the GP) available after a follow-up period of at least one year was used by three of the authors (GF, JM, RS), blinded for the initial complaints, to establish the final diagnostic conclusion(s). Endoscopy or rontgenography was not obligatory and only performed when considered necessary by the GP. It was assumed that a potentially malignant source of rectal bleeding would have been discovered within the follow-up period. The International Classification of Primary Care[10] was used for diagnostic classification. In cases with more than one diagnosis the severest is used in the analysis.

Patients

From September 1988 to June 1990, 290 consecutive patients with rectal bleeding were recruited by 83 GPs in Limburg (the southernmost province of the Netherlands), with an average duration of participation of 11 months per doctor. Patients were included when overt rectal bleeding was the reason for encounter or when there was a history of recent (within the previous three months) rectal blood loss visible for the patient. Patients were excluded 1) if they were younger than 18 years or older than 75 years, 2) if they were pregnant, 3) if there was an urgent admission to a hospital (e.g. massive bleeding, acute abdominal pain or bowel obstruction) and 4) if follow-up data were not available.

Variables

The rectal bleeding study is part of a larger study on rectal bleeding and non-acute abdominal complaints. In compiling the questionnaires used in this study, items were selected which are reported in literature as being relevant for discrimination between the several diagnoses.[11-15]

The data were collected by the following means:

1. A semi-structured questionnaire filled in by the doctor after the first consultation, containing 70 variables; history, physical examination and initial management.

2. A questionnaire filled in by the patient, containing 150 (somatic and psychological) questions.
3. Laboratory tests: haemoglobin (Hb), erythrocyte sedimentation rate (ESR) (several cut-off points, including an optimal cut-off point according to Dinant et al[16]), white blood cell count (WBC) and occult blood in the faeces (FOB) (Haemoccult test, 3x, with a diet low of peroxidase and free of red meat).

Statistical analysis

Data were analysed on VAX-VMS mainframe and personal computer, using BMDP and Epi Info (for odds ratios and 95% Confidence Intervals (CI)[17,18] For significance testing the Chi-square test for independent proportions was used.[19] The diagnostic values of variables (patient characteristics, signs and symptoms derived from the doctors' form together with some additional symptoms derived from the patients' form) were evaluated subsequently with bivariate and multivariable techniques. For variables showing an association (p-value <0.1) with cancer in bivariate analysis, sensitivity, specificity, predictive values (PV^+, PV^-) and crude odds ratios were computed.

PV^+ = percentage of patients with the sign or symptom who have colorectal cancer.

100%-PV^- = percentage of patients without the sign or symptom who have colorectal cancer.

Except for age, (continuous) variables were dichotomized (no or absence=0, and yes or presence=1). All diagnostic variables, for which $p<0.1$, were entered into logistic regression analysis to find the 'independent' predictive value of each taking the other variables into account simultaneously. Forward stepwise logistic regression analysis was used to find a prediction model to predict the probability for colorectal cancer with a limited set of significantly contributing variables (reduced model).[20] Enter and remove limits were applied for p-values <0.05. From the regression coefficients odds ratios (OR) can be calculated, $OR=e^{coefficient}$. OR = (true positive x true negative) : (false positive x false negative) or OR = (PV^+ x PV^-) : (1 - PV^+)(1 - PV^-).

If the coefficient is positive, the odds ratio is greater than 1, which indicates that the variable is positively associated with cancer. If the coefficient is negative, the odds ratio is less than 1, which indicates that the variable is negatively associated with cancer.[21] The discriminatory power of the model was examined using the Area Under the Receiver Operating Characteristic (ROC) Curve (AUC). The AUC measures the discriminatory power of a test by simultaneously comparing its sensitivity and specificity at a range of cut-off points; a test that discriminates perfectly between disease and no disease has an AUC of 1 or 0, a test without discriminatory power has an AUC of 0.5.[22,23] In addition, the regression results were evaluated by determining the cut-off points (posterior probabilities) associated with the maximum sum of sensitivity and specificity.[24] In a second analysis the predictive values were determined after combining colorectal cancer and polyps into one group.

Results

Of 290 patients 21 were excluded since they were lost to follow-up (moved to an unknown destination). A total of 269 patients were studied, with a mean age of 42 years (range 18-75, standard deviation 15 years); 56% were females. Age and gender of the 21 excluded patients did not differ from the remaining 269 patients ($p \geq 0.1$). The mean of follow-up time was 20 months with a standard deviation 5 months.

For 51% of the patients rectal bleeding was the reason for encounter: 49% had another reason, for example abdominal complaints, but blood loss per rectum was seen and mentioned by the patient. Eight patients used anticoagulants.

At the end of the initial consultation 8% of patients were referred to a medical specialist (5% to an internist, 3% to a surgeon); endoscopy or roentgenography was requested for 14% and 10% of patients respectively. In the course of the follow-up period, after at least one year, a total of 24% of patients had been referred, 14% to an internist, 5% to a surgeon, 2% to another specialist and 3% to several specialists. A total of 31% had further investigations initiated by the GP by means of sigmoidoscopy (9%), colon roentgenography (9%), proctoscopy (8%), sonography (6%) and colonoscopy (2%) (some patients underwent more than 1 investigation).

Diagnostic outcome

The diagnostic outcome related to rectal bleeding of the study population of 269 patients is shown in Table 1 in relation to age and gender. The age distribution of the patients was not different for males and females (data not shown). The vast majority (95%) of patients had diagnoses not related to neoplastic transformation: 75% of the patients in fact had haemorrhoids, or no bleeding cause could be identified in the follow-up period. None of the patients using anticoagulants had colorectal cancer nor polyps. Colorectal cancer was present in 9 patients (3.3%, 95%CI 1.2%-5.4%) with a strong preponderance in males (7 out of 9) and older individuals (8 out of 9 older than 60). The odds ratio (gender x cancer) of males compared to females was 4.7 (p=0.04).

Table 1. Frequency of colorectal carcinoma, polyps and other diagnoses according to age and gender. Row percentages per age or gender category (numbers in brackets).

		Diagnoses related to rectal bleeding		
	total number N=269	cancer N=9	polyp N=6	others[1] N=254
	number	% 3	% 2	% 95
Age				
18-29 years	(62)	0	0	100
30-39 years	(71)	0	0	100
40-49 years	(55)	0	2	98
50-59 years	(41)	2	7	91
60-75 years	(40)	20	5	75
Gender				
female	(151)	1	1	98
male	(118)	6	3	91

gender $p < 0.05$ (Chi-square 2 df)
age $p < 0.01$ (Chi-square 8 df)

Cancer : rectumcarcinoma (6), sigmoidcarcinoma (1) and coloncarcinoma (2)
Polyp : adenomatous polyp (3) and benign polyps not specified (3)
[1]Others : no cause of bleeding found (162), haemorrhoid(s) (41), fissura ani (18), infection (6), diverticulosis (2), proctitis (12) and colitis (13)

Diagnostic value for colorectal cancer

We next determined the association between signs and symptoms (variables) and the diagnostic outcome, in particular colorectal cancer. Signs, symptoms and laboratory test results which did not have a statistically significant ($p \geq 0.1$) association with colorectal cancer neoplasm are shown in Table 2.

Table 2. Variables without a statistically significant association with colorectal cancer.

History:
diarrhoea at night,
anal pain, anal itch, feeling of anal protrusion,
painful motion, incomplete evacuation of stool,
flatulence, rumbles, vomiting,
feeling ill, fever, change in eating habit, decreased appetite,
length of history of bleeding, previous history of abdominal disease,
medication used,
frequency of blood loss, amount of blood seen,
color of blood seen,
blood seen on toilet paper only,
blood seen before defaecation, during, at the end, after,
or without defaecation,
mucous discharge, tenesmus,
patient worries about bleeding, worries because of the severity of the complaints, patient considers cancer to be the source of bleeding,
stressful period,
history of abdominal surgery,
visits abroad (tropical or Mediterranean countries),
alcohol consumption (> 2 glasses/day),
smoking.

Physical examination:
general impression, abdominal inspection,
abdominal auscultation, palpation, percussion.

Psychological tests:
psychobiological stress (VOEG)
self-esteem, social inadequacy (Dutch Personality Inventory)
signs of depression (ZUNG).

Variables with a significant association ($p<0.1$) are listed in Table 3 together with their sensitivity, specificity, predictive value and odds ratio. In general practice the diagnostic value of a variable is highly determined by its predictive value for the absence of having a colorectal malignancy. Therefore of particular interest are those variables that have a very low (close to 0) positive predictive value (PV^+) or a very low '100 minus negative predictive value (PV^-)'. The presence or absence of these respective variables indicates absence of colorectal cancer. In our analysis it appears that colorectal cancer is highly unlikely (1% or less) in patients who did not see blood on or mixed with stool, in patients who did see blood on the toilet paper and in patients without change in bowel habit, with pain at night, with a family history of abdominal disease or with a previous history of rectal bleeding. All other variables, although significantly associated with the outcome or having a reasonable sensitivity or specificity for the presence of colorectal cancer, were not useful for selection of patients with a very low probability of having malignant disease (that is for diagnosis by exclusion).

Rectal digital examination, although required by the protocol, was done only in 77% of patients. Results were generally negative and if positive mainly pointed to the presence of haemorrhoids. The association between abnormal prostate and colorectal cancer is an observation based on 2 patients (one with cancer).

Proctoscopy was carried out at the first consultation by the GP in only 17% of patients. This subpopulation included only 2 patients with cancer.

Abdominal inspection, auscultation, percussion and palpation were carried out in 80-90% of all patients. None of these examinations contributed substantially to the probability of cancer. Anal fissurae were diagnosed in 29 patients, all without colorectal cancer. However, this negative association of fissurae with cancer was not significant ($p>0.1$).

Results of laboratory tests in relation to colorectal cancer are shown in Table 4. These data were available for 225 patients with a prior probability of cancer of 2.2% (5/225). As far as the diagnostic value for excluding colorectal cancer is concerned, patients with an ESR lower than 30 mm/1 hr, a WBC below 10^9/l or Haemoccult negative (three times) have a probability of colorectal cancer of 1% or less.

Table 3. Diagnostic value of signs and symptoms for colorectal cancer in patients with rectal bleeding ($p<0.1$).
N = 269
Prevalence = 3.3%

Signs/symptoms	number	sensitivity %	specificity %	PV^+ %	100-PV^- %	odds ratio	p
Blood seen							
mixed with stool only	14	40	95	14	1.3	5.9	*
on stool or mixed with stool only	54	80	79	7	0.5	3.4	*
others or combinations	122	20	53	1	3	0.1	**
unknown	54	44	81	7	2	3.4	*
Abdominal pain	135	29	48	2	4	0.3	*
Change in bowel habit (more frequently or diarrhoea or variously but not obstipation)	78	88	72	9	0.5	18.4	***
Pain at night	50	0	76	0	3	0	**
Decreased appetite	42	11	84	2	4	0.7	**
Nausea	68	11	74	2	4	0.4	***
Weight loss	42	44	85	10	2	4.6	**
Family history of abdominal disease	83	0	62	0	6	0	*
Previous history of rectal bleeding	96	0	63	0	5	0	**
Pale sclerae	6	13	98	17	3	7	*

Table 3 continued

Signs/symptoms	number	sensitivity %	specificity %	PV^+ %	100-PV^- %	odds ratio	p
Perianal eczema	17	33	95	18	2	8.6	***
Rectal palpation (N=208)							
haemorrhoid	20	22	93	10	3	3.8	*
tumour	1	11	89	100	3	undefined	***
abnormal prostate	2	11	99.6	50	3	31.8	***
Proctoscopy (N=45) abnormal	30	0	30	0	13	0.2	**

* $0.1 > p \geq 0.05$
** $0.05 > p \geq 0.01$
*** $p < 0.01$

Table 4. Diagnostic value of laboratory test results for colorectal cancer in patients with rectal bleeding.
N = 225
Prevalence = 2.2%

Laboratory test results	number	sensitivity %	specificity %	PV^+ %	100-PV^- %	odds ratio	p
Haemoglobin							
low (♀ < 7.5 mmol/l, ♂ < 8.5 mmol/l)	14	33	95	14	2	8.8	***
ESR							
high (♀ > 28 mm/h, ♂ > 12 mm/h)	23	40	91	9	2	6.3	**
high ≥ 30 mm/h	12	40	96	17	1	14	***
White blood cell count (N=219)							
high (> 10^9/l)	25	75	90	12	0.5	26.3	***
Haemoccult ≥ 1 positive out of 3	41	50	82	5	1	4.6	*

* 0.1> p≥ 0.05
** 0.05> p≥ 0.01
*** p< 0.01

Multiple logistic regression for cancer

The diagnostic index resulting from forward stepwise logistic regression analysis is shown below Table 5.

Table 5. Predicted probability of colorectal cancer according to multiple logistic regression analysis in patients with rectal bleeding.
Prior probability = 0.03

Predicted (posterior) probability of colorectal cancer for patients with a changed bowel habit and/or blood mixed with or on stool in age categories.

Age in years	Change in bowel habit			
	+		-	
	blood "mixed with" or "on" stool		blood "mixed with" or "on" stool	
	+	-	+	-
30	0.002	0.0002	0.0002	$1x10^{-5}$
40	0.01	0.002	0.001	0.0001
50	*0.10*	0.01	0.01	0.001
55	*0.22*	0.03	0.03	0.003
60	*0.44*	*0.09*	*0.07*	0.009
65	*0.68*	*0.21*	*0.18*	0.03
70	*0.86*	*0.43*	*0.38*	*0.07*

Above the optimal cut-off point for exclusion (0.042) is in italic

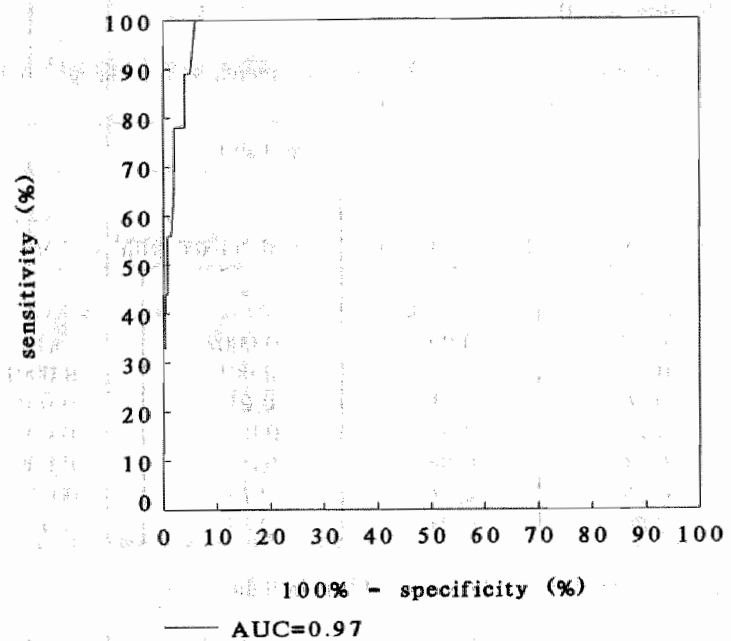
Diagnostic index: logit (p) = - 6.7 + 2.1 ((Age-50)/10) + 2.3 if change in bowel habit + 2.1 if blood mixed with or on stool
Log likelihood = - 17.86, Hosmer Lemeshow p = 0.51

Predicted (posterior) probability: $\frac{1}{1+e^{-logit(p)}}$

Entered in logistic regression were: all history and physical examination variables with $p<0.1$, age (for statistical reasons transformed to (age-50)/10, i.e. decades below and above 50 years) and gender. Three variables remained significantly predictive: age (OR = 8), change in bowel habit (OR = 10) and blood mixed with stool or on stool (OR = 8). The combination of these three could be assessed as a diagnostic test for the prediction of cancer.

The area under the ROC curve (AUC) was 0.97 (Figure 1), which means a high discriminatory power.

Figure 1
ROC curve illustrating the relation between sensitivity and specificity of the prediction model (diagnostic index) for colorectal cancer.



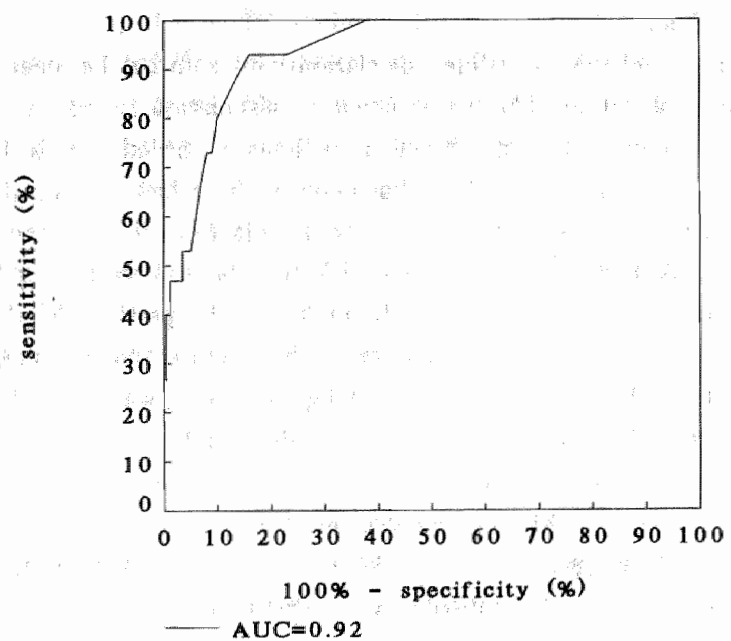
The maximum sum of sensitivity and specificity is achieved with a cut-off point of 0.042, corresponding to a sensitivity of 100% and a specificity of 90%. As stated before, we are particularly interested in accurately predicting the absence of malignancy.

Applying a posterior probability of 0.042 as the cut-off point, above which the test result is considered positive for cancer, results in 13% of patients (n=35) classified as positive. This cut-off point corresponds to a PV^+ of 26%. Below the cut-off point there were 87% of patients (n=234). Those were 'truly' classified negative (no 'false negatives') with a 100%-PV^- being 0%.

Polyps

In 6 patients in our population polyps were detected and related to rectal bleeding: none of these was younger than 40, but polyps occurred at somewhat younger age than cancer (Table 1). If polyps were added to cancer as the outcome parameter, the bivariate analysis showed fewer significant variables compared to cancer as the outcome (not significant: pain at night, decreased appetite, previous history of bleeding and Haemoccult) and did not show new significant variables. The logistic regression analysis resulted in a similar model, which can be described as follows: diagnostic index= -4.8 + 1.4 ((age-50)/10) + 1.9 if change in bowel habit + 2.1 if blood mixed with or on stool. (Hosmer Lemeshow p=0.49, log likelihood= -32.4). The AUC was 0.92 (Figure 2).

Figure 2
ROC curve illustrating the relation between sensitivity and specificity of the prediction model (diagnostic index) for cancer and polyps.



At a posterior probability of 0.058 the maximum sum of sensitivity (93%) and specificity (84%) was 177%. Applying this cut-off point 21% of patients were predicted positive for colorectal cancer or polyps with PV^+=25% and 79% predicted negative with 100%-PV^-=0.5%.

Discussion

This study showed a prior probability of rectal bleeding for colorectal cancer of 3.3% in general practice. For an effective selection of patients, resulting in either a very low probability or a reasonably high probability of cancer, knowledge of predictive values of other signs and symptoms in combination with rectal bleeding is desired.

Many single signs and symptoms did not show any discriminatory power. Some signs were statistically significantly associated with cancer but the discriminatory power was not strong, except for age and a palpable tumour. Patients above 60 years had a higher probability of cancer than younger patients. When a tumour is palpable, a very rare finding, there will not be a decision problem.

Some variables and their possible association with colorectal cancer need some comment or explanation. There was negative association found between family history of abdominal disease. Nineteen patients recorded that a first degree relative has an abdominal neoplasm but none of these had colorectal cancer (or polyps). This is remarkable since colorectal neoplasm in first degree relatives is known as a risk factor.[25] The relative risk (of about 2 to 3) is probably too small to be found in our population. It might also be partly related to the fact that this question, both in questionnaires of the doctors and patients, was open (unstructured) and not specifically asking for the presence of colorectal neoplasm (rather than abdominal disease) in the family. The inclusion of FOB testing in the study may raise questions whether this is useful in cases with overt rectal bleeding. FOB was included since it may additionally contribute to the diagnosis of neoplasm as was shown in a screening study, where the probability of neoplasm for patients with overt rectal bleeding increased from

5.6% to 36.3% when FOB was positive.[26] Furthermore, FOB could be useful for patients who had seen blood loss only once. Laboratory tests were not entered into logistic regression because of the missing data. These missing data may be due to the resistance of the doctor to confront the patient with "unnecessary" investigations for a research protocol, when the patient is either highly suspected of having serious disease or when there is obviously a harmless cause.

Forward stepwise logistic regression analysis resulted in three variables significantly contributing to the prediction of presence or absence of cancer. With an optimal cut-off point for exclusion of cancer (maximum of negatives but no false negatives) 87% of all patients with rectal bleeding were correctly predicted as being negative for cancer and 90% of patients without cancer were predicted as being negative (a specificity of 90%). Compared to recommendations for further assessment of all patients with rectal bleeding in order not miss cancer[27], application of the regression model in the study population reduced the number of indications for further assessment by 87%. Compared to a policy of further assessment of all patients aged older than 40 years (138 patients), the model reduced the number of cases of suspected cancer in all patients by 75% (for those without cancer by 80%).
It would be interesting to see what symptoms and signs are associated with the presence of polyps, since polyps are considered to be precursors of cancer. Our study, however, was not designed to find definitive answers in this respect, since we did not ask for full colonic examination in all patients presenting with rectal bleeding. Therefore, even with a follow-up time of at least 1 year it remains possible that some polyps have been missed. The discussion about the relevance of early detection (before symptoms occur) of polyps is beyond the purpose of the present study. Non-bleeding polyps or self-limiting bleeding polyps were not detected but the prediction model can be applied for overtly bleeding polyps.

There were fewer patients included in the study than expected on the basis of the incidence rate of rectal bleeding in general practice of 7 per 1000 people per year.[1]

According to this rate we could have expected in a period of 11 months about 1200 patients with rectal bleeding by 83 GPs (about 2350 people per full-time GP; 6 parttime GPs; population of 188,000). In the same period about 60 patients in the ages 18-75 should suffer from colorectal cancer.[28] Of these patients probably between 10% and 50% should present with rectal bleeding.[29,30] Taken into account that some of these would be urgently admitted to hospital (e.g. symptoms of bowel obstruction or perforation) and therefore not included in the study, our 9 patients with colorectal cancer are within the expected range. Information from the participating GPs confirmed our impression that patients with rectal bleeding who were not detected were especially those with minor ailments.[1] Although special efforts had been taken to reduce the numbers of non-detected rectal bleeding patients and missing data through regular practice visits and via a newsletter, it was not feasible to gather all the data requested. Reasons mentioned for not including a patient were: "it is too much fuss for a simple and harmless complaint", or "lack of time" and sometimes the study was considered harmful for the patient because the possibility of inducing fear. We consider this data collection the maximum of what is possible in general practice research. Furthermore, the possible missing cases on both extremes of the spectrum, from obviously not serious to obviously serious (acute admission to hospital), suggest that the findings are based on and applicable to patients in whom rectal bleeding is likely to be a decision problem for GPs. The prior probability of colorectal cancer in the total group of patients with rectal bleeding (covering the whole spectrum) is probably less than 3%. The 21 dropouts (lost to follow-up) were due to moving to an unknown destination without any reason to suspect selective dropout.

The small number of patients with cancer in the study may be a problem for statistical purposes, but in practice it means that the incidence and prevalence of some signs and symptoms in correlation with cancer is too low to be observed or to be shown statistically significant in about 83 'GP-years'. Although the number of colorectal cancer patients is small in our study, it must be recognized that this number will need three professional lifetimes of a GP to be diagnosed. Therefore, the clinical characteristics in our model deal with a large general practice population experience.

For the following reasons the results cannot be considered as definitive evidence of diagnostic value: 1) the statistical test (likelihood ratio test) is less valid in samples with few cancer cases, 2) in view of the total number of variables, a type I error (falsely significant) may have occurred. Therefore, it is useful to test our model in a different but comparable population. It is worthwhile doing so since such a simple model would aid in effective and efficient diagnostic strategies.

In a previous study Mant et al[31] concluded that signs and symptoms did not satisfactorily aid in deciding whether to proceed with full colonic investigation on the basis of a bivariate analysis. In their population, which was aged older than 40 years and derived from general practice but referred for diagnosis (according to study protocol), the only variables significantly associated with colorectal cancer and polyps were: blood mixed with faeces, anal protrusion noticed by the patient and the presence of haemorrhoids. The prior probability in their study was higher (11% for malignancy and 8% for adenomas) than in our study (3% and 2% respectively). For patients older than 40 years in our study the prior probability of together cancer and polyps was 11%, which is still somewhat less than the 19% in their study. The finding by Mant et al that the likelihood of colorectal cancer or polyps is higher among women contrasts with our findings. Logistic regression showed no significant additional contribution of gender to our model.
We did not find studies which present predictive values of combinations of signs and symptoms.

We conclude that in patients with rectal bleeding the predictive power of many signs and symptoms for colorectal cancer in general practice is low. The combination of age, change in bowel habit and blood seen mixed with or on stool can serve as a useful diagnostic tool for the prediction of colorectal carcinoma (or overtly bleeding polyps). This is the first reported model developed to discriminate between such patients with a very low (close to 0) probability of colorectal cancer (and overtly bleeding polyps) and those with a high probability. Although our model appears to do this quite successfully, testing its performance in other general practice populations is recommended.

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7. Predictive value of signs, symptoms and laboratory tests in patients with rectal bleeding in an outpatient clinic

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ABSTRACT

Background : Diagnostic value of (combinations of) signs, symptoms and simple laboratory test results for Inflammatory Bowel Disease (IBD) and colorectal neoplasm in patients with rectal bleeding was determined through predictive values, regression coefficients and probabilities.

Methods : Pseudo follow-up study; initial complaints and findings were compared with the final diagnoses based on clinical follow-up, established after at least 1 year. Consecutive patients presenting overt rectal bleeding in General Internists' outpatient clinics were included in the study.

Results : In the study population with a prevalence of IBD of 26% and of neoplasm of 6%, 18 variables have a statistically significant predictive value. Stepwise multiple logistic regression analysis showed 4 to 6 variables with an independent contribution to the discrimination between the presence and absence of IBD or neoplasm. The Receiver Operating Characteristic (ROC) of the regression model had an Area Under the Curve (AUC) of 0.92. A model based on variables derived from history taking was able to predict IBD or neoplasm with a sensitivity of 100% and a specificity of 64%.

Conclusions: Application of the model might prevent 43% of further invasive investigations in patients with rectal bleeding. Testing of the performance of the model in other outpatient clinic populations is recommended.

Introduction

Overt rectal bleeding is a well-known alarming signal, with colorectal cancer and inflammatory bowel disease (IBD) being potential sources. However, little is known about the predictive value of the combination of this symptom with other signs, symptoms and simple laboratory tests for the presence or absence of these conditions. Several clinical features have been reported to be of some predictive value enabling discrimination between patients with a self-limiting or harmless (anal) source of bleeding and those with serious colorectal disease.[1-4] Most reports do not give quantitative information regarding the predictive values, except the study published by Mant et al[4]. These investigators concluded, on the basis of bivariate analyses, that in patients with rectal bleeding who consulted a general practitioner, most bowel symptoms and clinical features are not helpful in deciding whether to proceed to full colorectal assessment. The question arises whether the combination of several clinical features, in a prediction model determined by multiple logistic regression analysis, could be more helpful.

We are interested in the predictive values in patients presenting with rectal bleeding to a general internists' outpatient clinic, as part of a larger study about the incidence and medical management of patients with rectal bleeding.

In this paper we focus on (1) the determination of the predictive value of the patients' history, some psychological phenomena, results from physical examination and some simple laboratory test results for colorectal IBD or neoplasm and (2) the determination of the predictive value of a combination of these signs and symptoms. The aim is to find a prediction model which discriminates sufficiently to withhold patients without these lesions from invasive investigations.

Methods

Patients

From September 1988 to April 1990 105 consecutive patients having overt rectal bleeding and referred to the Departments of Internal Medicine at four hospitals in Limburg, in the South of the Netherlands, were recruited for the study. Patients were included in case overt rectal bleeding was the reason for consultation or when there was a history of recent (within the last three months) rectal blood loss visible for the patient while the patient was not already known to have IBD or neoplasm. Patients were excluded if their age was less than 18 years or more than 75 years or if there was an urgent admission to hospital (e.g. massive bleeding, acute intestinal obstruction or perforation).

Data

All patients entered into the study were asked to fill in a standard questionnaire with items reported in literature as being relevant for the discrimination between several anal and colorectal diagnoses.[5-8] Patient's fear of cancer was reported to be an important predictor of a malignancy[9] and psycho-social factors may have impact on the consulting behaviour of patients. Therefore, questions regarding anxiety and three psychological scales were included: the VOEG, the Dutch version of the 'Inventory for Subjective Health' (psychobiological stress)[10], the subscales Self-esteem and Social Inadequacy of the Dutch Personality Inventory[11] and the Zung questionnaire for depression.[12] Results of history taking and physical examination were registered by the internists. Basic laboratory tests were included: Haemoglobin (HB), White blood cell count (WBC), Erythrocyte Sedimentation Rate (ESR) and Haemoccult test for faecal occult blood (FOB) (3 times, with a diet low of peroxidase and free of red meat).
Further diagnostic investigation was done according to the choice of the physician.

For ESR several cut-off points were evaluated.
In total 60 variables were analysed: age, gender, 4 laboratory tests, 32 variables derived from the doctor's questionnaire and 42 variables derived from the patient's form. Among variables represented both in the patient's and the doctor's questionnaire (n=20), those derived from the doctor were primarily chosen for further analysis.

Outcome

After a follow-up period of at least one year the final diagnostic conclusion was determined. Three of the authors (GF, JM, RS), blinded for the initial complaints, abstracted all available diagnostic information from the medical records and established the diagnoses. The final conclusion was presented to the patient's general practitioner (GP) who was asked for additional information or confirmation. The final diagnoses were classified according to the International Classification of Primary Care.[13] In cases with more than one possible diagnosis the most severe is used in the analysis.

Analysis

Data were analysed on VAX-VMS mainframe using BMDP.[14] Clinical data were initially analysed using bivariate techniques. The positive (PV^+) and negative (PV^-) predictive values were computed, for both IBD (colitis or proctitis) and colorectal neoplasms (adenomatous polyp or carcinoma) versus anal sources (haemorrhoids, fissura ani), infections, diverticulosis or no source found at all.
All variables were dichotomous. For age also an interval scale was used. Variables showing a statistically significant association (Chi-square test for independent proportions $p<0.1$) with a specific diagnosis group were entered into a forward stepwise logistic regression analysis to determine the 'independent' predictive value of each variable taking the other variables into account simultaneously.[15-17] Enter and remove limits were applied for p-values <0.05.

From the regression coefficients odds ratios (OR) can be calculated, OR = $e^{coefficient}$. OR = (true positive x true negative) : (false positive x false negative) or OR = (PV^+ x PV^-) : (1 - PV^+)(1 - PV^-). If the coefficient is positive, the odds ratio is greater than 1, which indicates that the variable is positively associated with IBD or neoplasm. If the coefficient is negative, the odds ratio is less than 1, which indicates that the variable is negatively associated with IBD or neoplasm.[16] The fit of resulting logistic models to the derived data set was assessed using the Hosmer Lemeshow test.[18]

The discriminatory power of the regression model (prediction model or diagnostic index) was examined using the Area Under the Receiver Operating Characteristic (ROC) curve (AUC). The AUC measures the discriminating power of a test by simultaneously plotting its sensitivity and specificity at a range of cut-off points (predicted or posterior probabilities). A test that discriminates perfectly between disease and non-disease has an AUC of 1 or 0; a test with an AUC of 0.5 does not discriminate at all.[19,20] In addition, the regression results were evaluated by determining the cut-off points (posterior probabilities) associated with the maximum sum of sensitivity and specificity.[21]

Results

General

A total of 104 patients were studied, with a mean age of 41 years (range 18-71, standard deviation 14 years); 52% were females. One patient was lost to follow-up. The mean of follow-up time was 25 months with a range of 12 to 36 months. Four patients in this population used anticoagulants, of whom one had IBD.

For 64% of the patients rectal bleeding was the reason for encounter: 36% had another reason, for example abdominal complaints, but blood loss per rectum was seen and mentioned by the patient.

During the follow-up period all patients were further investigated by endoscopy (84%; proctoscopy 2%, sigmoidoscopy 69%, colonoscopy 13%), or by roentgenography (21%).

Diagnostic outcome

The diagnostic outcome per age category is shown in Table 1.

Table 1. Frequencies of diagnoses related to rectal bleeding per age category, in 104 patients.

Age (years)	no colorectal source*		IBD		colorectal neoplasm#		other colorectal sources**		total	
	N	%	N	%	N	%	N	%	N	%
18-29	13	21	9	33	1	17	1	10	24	23
30-39	20	31	8	30	1	17	1	10	30	30
40-49	12	21	6	22	0	0	1	10	19	18
50-59	9	14	0	0	2	33	4	40	15	14
≥ 60	7	13	4	15	2	33	3	30	16	15
Total	61	100	27	100	6	100	10	100	104	100

* anal source (19), no source found (42)
\# cancer (3) and polyps (3)
** rectum ulcus (1), rectum prolaps (1), infection (4), diverticulosis (4)

Colorectal sources (rectum prolaps, rectum ulcus, infection, diverticulosis, proctitis, colitis, polyp or carcinoma), judged to be related to rectal bleeding, were found in 41% of patients. In this population IBD (proctitis (n=8) and colitis (n=19)) is the most frequent source. Three patients had an adenomatous polyp as the probable source of rectal bleeding. Three cancers were found: two in the rectum and one in the rectum/sigmoid. One patient with cancer was relatively young at 38 years of age. Among younger patients (<50 years) the prevalence of IBD was higher than among older patients, 32% versus 13% (p=0.05). Among older patients neoplasms were more prevalent, 13% versus 3% (p=0.04). There was a slight preponderance of females regarding colorectal sources, 44% compared to 38% for males (p=0.14). In 59% of cases (n=61) no colorectal source of rectal bleeding was found within the follow-up period. Anal sources were found in 18% (n=19) of cases; no source of bleeding was found in 40% (n=42). In the category "no bleeding source found" 45% fulfilled the criteria of the Irritable Bowel Syndrome (n=19).

Diagnostic value

Signs, symptoms and laboratory test results which did not have a statistically significant ($p \geq 0.1$) association with IBD or neoplasm are shown in Table 2.

Table 2. Variables without a statistically significant association with IBD or neoplasm.

Age, gender

History:
abdominal pain,
pain at night, diarrhoea at night,
anal pain, anal itch, feeling of anal protrusion,
painful motion, incomplete evacuation of stool,
flatulence, rumbles,
feeling ill, fever, change in eating habit,
weight loss,
length of history of bleeding, previous history of abdominal disease,
medication used,
amount of blood seen,
color of blood seen,
blood seen on toilet paper only, on stool only, mixed with stool only, or combinations,
blood seen before defaecation, during, after, or without defaecation,
patient worries because the severity of the complaints,
patient considers cancer to be the source of bleeding,
stressful period,
history of abdominal surgery,
first degree family member having abdominal neoplasm,
first degree family member having abdominal disease,
visits abroad (tropical or Mediterranean countries),
alcohol consumption (> 2 glasses/day).

Physical examination:
general impression, inspection of sclerae,
abdominal auscultation, palpation, percussion,
perianal inspection, rectal palpation.

Laboratory tests
haemoglobin (♀ < 7.5 mmol/l, ♂ < 8.5 mmol/l),
WBC (> 10^9 /l).

Psychological tests:
self-esteem, social inadequacy (Dutch Personality Inventory).

Significant associations were found for the variables shown in Table 3.

Table 3. Predictive values of signs, symptoms and laboratory test for IBD or neoplasm in 104 patients presenting rectal bleeding, with p-values <0.1. Prevalence = 32%.

Variables	frequency (%)	PV^+ (%)	PV^- (%)	p
History				
Abdominal pain > 2 weeks	70	25	52	0.03
Previous period with rectal bleeding > 1 year ago	31	55	75	0.004
Change in bowel habit	41	46	79	0.007
Bowel frequency				
a) ≥ 22/week	27	52	67	0.008
b) increase in bowel frequency	50	49	86	0.0002
Aspect of faeces: very hard	7	0	67	0.07
watery, diarrhoea	12	58	72	0.03
Blood seen more than once	67	45	90	0.007
Blood seen at the end of defaecation	32	47	73	0.06
Mucous discharge	51	43	77	0.04
Tenesmus	34	43	74	0.08
Decreased appetite	14	50	76	0.05
Nausea	55	20	53	0.004
Vomiting	8	0	66	0.05
Smoking	42	21	61	0.06
Anxiety because of bleeding	66	40	78	0.07
VOEG > 3 (psychobiological stress)	80	27	50	0.05
ZUNG > 40 (signs of depression)	22	11	64	0.03
Physical examination				
Abdominal inspection abnormalities (including distension and scars)	25	15	62	0.04
Laboratory tests				
ESR (♀ > 28, ♂ > 12 mm/hr)	16	56	71	0.03
Haemoccult ≥ 1 pos.result(s) out of 3	33	72	88	0.000

PV^+ = % pts with the sign, symptom or a positive test result who have IBD or neoplasm
PV^- = % of patients without the sign, symptom or positive test result who do not have IBD or neoplasm

Regarding the variable change in bowel habit (more frequent defaecation or diarrhoea or variously normal stool and diarrhoea, excluding constipation), the information derived from both the doctors' forms and the patients' forms (increased bowel frequency) was analysed. Since there may be a different perception of change in bowel habit between doctors and patients, both items are shown and entered into the multiple logistic regression analysis to find the strongest predictor.

Psychological variables, in particular the presence of psychobiological stress (VOEG) and signs of depression (ZUNG) were significantly related to the absence of neoplasm or IBD. Anxiety because of the bleeding was related to the presence of these diseases.
Except for abdominal inspection, physical examination did not show a significant association with a positive diagnosis. Neither did digital rectal examination, although in one patient a palpable tumour was diagnosed. It must be noted here that there were only 3 rectum/sigmoid tumours in the study population.

Data regarding laboratory test results were missing for WBC in 7 patients, for ESR and HB in 5 patients and for FOB in 16 patients. ESR with a cut-off point of 30 mm per hour did not show a significant association with a positive diagnosis, but with a cut-off point, reported to be optimal by Dinant et al[22], of 28mm for females and 12mm for males the ESR significantly correlated with serious disease.
For a meaningful clinical application of these variables, their ability to correctly identify patients with a very low probability of colorectal neoplasm or IBD is most important. The use of the variable should lead to the exclusion of patients without these diseases, in other words the PV^+ should be very low (e.g. $< 10\%$) or the PV^- should be very high (e.g. $> 90\%$). As can be seen in Table 3, very few variables appeared to be useful in this respect; the presence of very hard faeces or vomiting and the fact that blood was seen only once virtually exclude the presence of colorectal neoplasm or IBD.

Logistic regression

Results of logistic regression analysis are shown in Table 4.

Table 4. Prediction models, resulting from forward stepwise multiple logistic regression analysis, with IBD and neoplasm as the dependent variable.
Model 1: history taking
Model 2: history taking, physical examination and FOB test

Model	1		2	
Variables	coefficient	*se	coefficient	*se
Abdominal pain > 2 weeks			- 2.9	0.9
Change in bowel habit	+2.9	0.8	+2.1	0.7
Blood seen more than once	+3.9	1.0		
Blood seen at the end of defaecation	+2.5	1.8		
Tenesmus	+2.3	0.8		
Nausea	- 3.0	0.8		
Signs of depression (ZUNG)	- 2.7	1.0		
Inspection (distension, scar)			- 3.3	1.1
Haemoccult ≥ 1 pos. result(s) out of 3			+4.8	1.0
Constant	- 4.9	1.2	- 1.0	0.5
Log likelihood	- 33.4		- 32.2	
Hosmer Lemeshow p	0.8		0.8	
AUC	0.92		0.91	

*se: standard error

Model 1. Diagnostic index, logit (p) = - 4.9
- 2.7 if signs of depression
+2.5 if blood is seen at the end of defaecation
+3.9 if blood is seen more than once
+2.3 if tenesmus is reported
- 3.0 if nausea is reported
+2.9 if change in bowel habit is reported

Model 2. Diagnostic index, logit (p) = - 1.0
+4.8 if haemoccult is positive
- 3.3 if abdominal distension or scars by inspection
- 2.9 if abdominal pain of more than 2 weeks duration
+2.1 if change in bowel habit (except obstipation)

In model 1, 18 items derived from history taking were entered. Six items appeared to have an independent statistically significant contribution to the prediction of IBD or neoplasm.

If the patient had a changed bowel habit (OR = 18), if blood was seen more than once (OR = 49), if blood was seen at the end of defaecation (OR = 12) and if tenesmus was present (OR = 10), the probability of a positive test result (posterior probability of IBD or neoplasm) was very high. If the patient had signs of depression (OR = 0.07) or reported nausea (OR = 0.05), the posterior probability was very low. For the several combinations predicted probabilities can be calculated with the formula below Table 5. In model 2 three variables derived from physical examination and laboratory tests were added to model 1. Inspection (OR = 0.04) and FOB (OR = 121) were stronger predictors than most items from model 1. These items, in combination with abdominal pain of more than two weeks of duration (OR = 0.06) and change in bowel habit (OR = 8), resulted in a well-fitting prediction model.
Both models 1 and 2 scored satisfactorily for the goodness-of-fit test, the Hosmer Lemeshow test, as well as for the AUC. The diagnostic values of the models are shown in Table 5 and the ROC curves in Figures 1 and 2. The maximum sum of sensitivity and specificity is equal, 168%, for both models.

Figure 1
ROC curve of prediction model 1: history variables

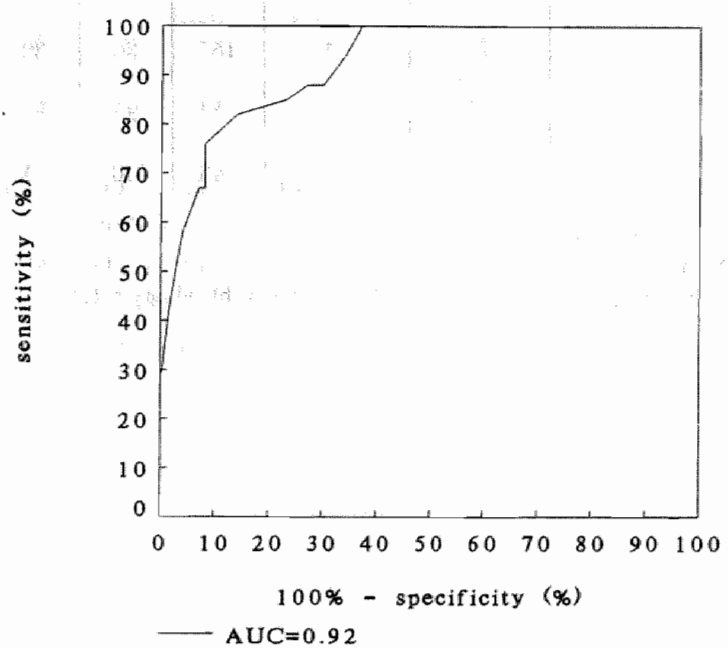


Table 5. Diagnostic value of the logistic regression model for IBD or neoplasm at different cut-off points (predicted probabilities).

Cut-off point for predicted probability	sensitivity %	specificity %	Σ %	PV^+ %	PV^- %	TN %
Model 1						
0.10	100	60	160	54	100	42
0.14	100	64	164	56	100	43
0.30	82	86	168*	73	91	59
0.50	76	92	168*	81	89	63
0.70	67	93	160	81	86	64
0.90	27	100	127	100	75	68
Model 2						
0.08	100	17	117	34	100	10
0.10	94	55	149	49	95	38
0.30	76	92	168*	81	89	63
0.50	73	94	167	86	88	64
0.70	64	99	163	95	85	67
0.90	48	100	148	100	81	68

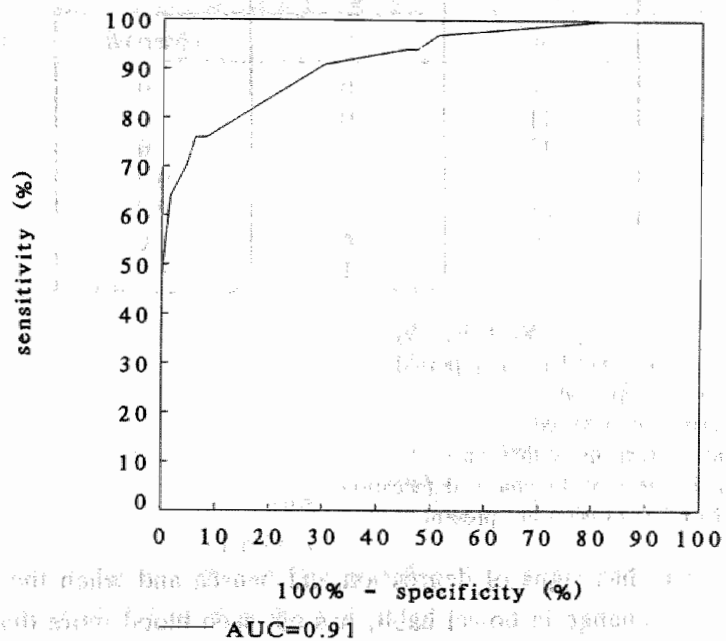
Σ = sum of sensitivity + specificity

* = maximal Σ

TN % = (number of true negative/104 patients with rectal bleeding) x 100

$$\text{Predicted probability} = \frac{1}{1+e^{-logit(p)}}$$

Figure 2
ROC curve of prediction model 2: history variables, abdominal inspection and FOB



Let us illustrate how such a model can be used in clinical practice with an example of a simplified sumscore. Regression model 1 is simplified to an additive score where the six characteristics, with comparable regression coefficients, are weighted as one point. The sumscore is the sum of the points for each patient. This sumscore (considered as an interval variable) is entered into logistic regression analysis to find the predicted probabilities at the several scores. The results are shown in Table 6.

Table 6. Observed and predicted probability of IBD or neoplasm for sumscores.

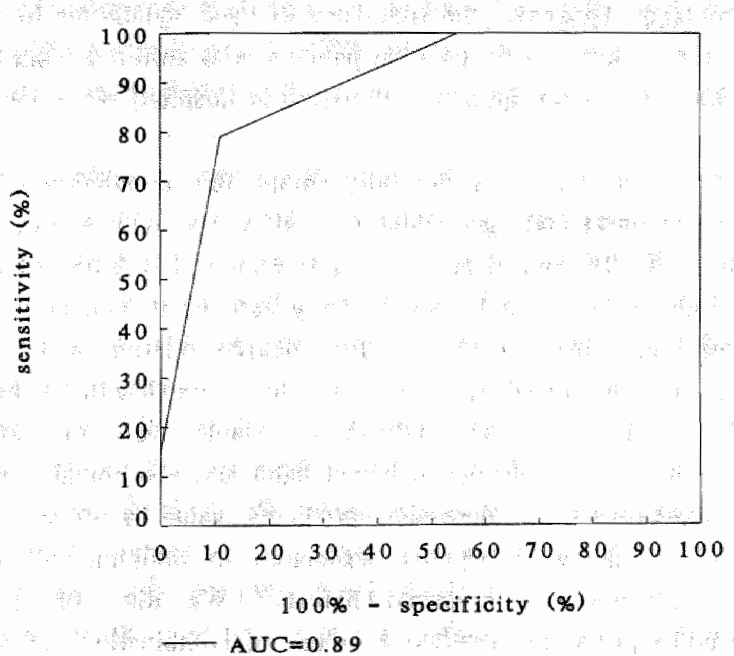
Model 1				
	total number with score	IBD or neoplasm	proportion of IBD or neoplasm	
Sumscore	n	n	observed	predicted
-2	2	0	0	0.0001
-1	11	0	0	0.001
0	19	0	0	0.014
1	38	7	0.2	0.167
2	29	21	0.7	0.741
3	4	4	1.0	0.976
4	1	1	1.0	0.998

sumscore = $V_1 - V_2 + V_3 + V_4 + V_5 - V_6$
V_1 = 1 if change in bowel habit is reported
V_2 = 1 if nausea is reported
V_3 = 1 if tenesmus is reported
V_4 = 1 if blood is seen more than once
V_5 = 1 if blood is seen at the end of defaecation
V_6 = 1 if signs of depression are present

When the patient has signs of depression and nausea and when the patient has no tenesmus, no change in bowel habit, has not seen blood more than once and has not seen it at the end of defaecation the sumscore is minus 2. In the study population none of these patients had IBD or a neoplasm. Applying a cut-off point of ≤ 0, for example, a patient with 2 symptoms scoring negative and with 2 or less than 2 other 'positive' items is considered as having a very low probability of IBD or neoplasm.

The predicted probabilities according to the sumscore are very close to the observed probabilities in the study population. The correlation between the predicted probability by the regression model and the sumscore was high, R = 0.97. The sumscore is a simplification of the model and is somewhat less accurate. The AUC is 0.89 (Figure 3) and the Hosmer Lemeshow p = 0.49.
With a similar optimal cut-off point, ≤ 0 (100% sensitivity), the sumscore results in 31% (n=32) true negatives, whereas model 1 results in 43% (n=45) true negatives.

Figure 3
ROC curve of sumscore: history variables



Discussion

A patient with rectal bleeding may confront physicians with a decision problem: invasive investigation (endoscopy or roentgenography) for further assessment or not. For this clinical reason IBD and neoplasm together were chosen as the dependent variable.

In decision analytic terms, the clinical problem in this patient population can be defined as 'exclusion diagnosis': to find a subpopulation that almost certainly does not have IBD or cancer and can be spared from further more invasive tests. This means that only variables with a PV^+ of close to zero or a PV^- of close to 100% are clinically relevant. One of the main findings of our analysis is that many of the numerous items regularly used in clinical practice for their presumed importance in predicting the presence or absence of colorectal disease did not have statistically significant predictive values in our bivariate analysis. For those which showed a predictive value this was almost never

sufficient to exclude the probability of IBD or neoplasm; only the presence of hard faeces, vomiting and having seen blood loss only once allowed exclusion of IBD or neoplasm. However, the frequency of these symptoms in the study population was very low, partly because patients who suffered from vomiting caused by bowel obstruction (an acute admission to hospital) were not included in this study.
In the study by Mant et al, in a not fully comparable population with rectal bleeding of recent onset and aged older than 40 years, with a probability of colorectal cancer of 19% and of any colorectal source of bleeding of 29%, the investigators found some variables significantly associated with any colorectal source of bleeding: female gender, a first degree relative with colorectal cancer, anal protrusion noticed by the patient, blood mixed with faeces and the presence of haemorrhoids.[4] In our study these variables were not significantly discriminatory. In contrast, change in bowel habit and abdominal pain lasting longer than 2 weeks were of independent predictive value in our study but not predictive in Mant's study. A negative association of smoking with IBD is a widely known phenomenon reviewed before.[23] We did not find other comparable studies presenting predictive values of combinations of signs and symptoms in patients with rectal bleeding.

Studying the influence of the diagnostic variables simultaneously in a stepwise multiple logistic regression analysis, only 6 of the 16 variables entered in model 1 (history variables) were found to contribute independently to the prediction of IBD or neoplasm. Nausea and signs of depression were independent predictors for the absence of IBD or neoplasm. It is important to make a critical decision regarding invasive diagnostic investigations, especially for patients without serious disease but with psychosomatic complaints or psychological problems, in order to prevent somatic fixation.
Of the 19 variables entered into model 2 (including history, abdominal inspection and FOB) only 4 were found to contribute independently to the prediction of IBD or neoplasm. Model 1 and model 2 are equally good regarding the measured discriminatory power (AUC), the goodness of fit and the maximum sensitivity and specificity.

However, regarding clinically important parameters model 1 is better. Applying the model with an optimal cut-off point for exclusion of serious disease (maximum negative rate but without false negatives, i.e. an optimal specificity and a sensitivity of 100%), model 1 leads to a negative rate of 43% (n=45) and consequently 43% of invasive investigations could be avoided, while all IBD and neoplasm were identified. Sixty-four percent of patients without these diseases were predicted negative (specificity). With model 2, for the same purpose (exclusion of true negatives), the specificity was 17%, and only 10% (n=12) patients could possibly profit from applying the model. It can therefore be accepted, with some reserve, because of the missing data, that the laboratory tests did not provide additional contribution to the diagnosis of absence of IBD or neoplasm.

The inclusion of FOB testing in the study may raise questions whether this is useful in cases with overt rectal bleeding. FOB was included since it may additionally contribute to the diagnosis of neoplasm as was shown in a screening study, where the probability of neoplasm for patients with overt rectal bleeding increased from 5.6% to 36.3% when FOB was positive.[24] Furthermore, FOB could be useful for patients who had seen blood loss only once.

Interpretation of the results is not possible without consideration of the study population. The incidence rates of colorectal diseases may be different in other clinical situations.

Furthermore selection before referral can influence the diagnostic values.[25-27] In the Netherlands before consulting a specialist patients have to be seen by the GP. Many GPs have a service for proctosigmoidoscopy and roentgenography at their disposal without referring the patient to an outpatient clinic. For colonoscopy patients usually are referred either to a Surgery Department or to an Internal Medicine Department. Patients obviously having, or very likely to have, haemorrhoids or colorectal cancer are more often referred to surgeons. Patients with rectal bleeding of unknown origin are more often referred to internists.

The model here presented indicates that some variables are important and others unimportant predictors in the study population. It was not considered

useful to split our study population at random, into a 'study population' and a 'test population'. This would not provide information about the external clinical validity, but only about the random sample variability.[27] Moreover, splitting the limited study population would decrease the statistical precision considerably. Replication of our study and testing the performance of the model independently in another, comparable, population seems useful. Preferably the study size should be large in order to decrease the standard errors and, consequently, to find more precise estimations.

We conclude that a prediction model based on variables resulting from history taking can be useful in selecting patients who really do not need sigmoidoscopy or colonoscopy and to prevent 'unnecessary' investigations and alarm. It is recommended to test the performance of the model based on history taking in other populations.

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8. General discussion

Introduction

In this chapter, the main findings of the study will be reviewed and some practical aspects, the strengths and limitations of the methodology will be discussed. After a short review of our findings in relation to the literature, practical implications and recommendations with regard to research will be given.

Main findings

In general practice it appears possible to discriminate effectively between rectal bleeding patients who do not have cancer and those who have a reasonably high probability of colorectal cancer (who need invasive diagnostic investigation). In the study population it is possible to identify 87% of patients as truly negative for colorectal cancer (those who do not need invasive diagnostic investigation for colorectal cancer).
Also in the internists' outpatient population it appears possible to discriminate effectively between patients who do not have serious bowel disease and those who have a reasonably high probability. In this population 43% are truly classified negative.

1. The incidence of patients consulting the general practitioner (GP) with overt ano-rectal blood loss (rectal bleeding) in the ages 18-75 years is about 7 per 1000 people per year. The initial study protocol, study A, yielded a lower rate, 2 per 1000, which is probably an underestimation of the real incidence but may reflect the incidence of rectal bleeding considered to be clinically relevant (likely to be a decision problem) by the GPs.
2. In rectal bleeding patients in the ages 18-75 years presenting in general practice the prior probability of colorectal cancer is 3% or less. The prior probability increases with age. About 90% of the sources of bleeding are minor ailments or self-limiting disorders.

3. In general practice as well as in the internist outpatient clinic, many signs, symptoms, results of physical examination and simple diagnostic tests usually considered to be of diagnostic value (60 variables are analysed), do not contribute significantly in the discrimination between the presence and absence of serious disease (in general practice colorectal cancer (and polyps), in the outpatient clinic colorectal neoplasm and IBD). Variables which have shown to be statistically significant associated with the diagnostic outcome in bivariate analysis, often do not show a statistically significant association in multivariable analysis.

Forward stepwise logistic regression analysis was used to obtain a prediction model with a reduced number of significant variables. The logistic regression coeffient determines the independent predictive value of a variable taking the other variables into account simultaniously. From the regression coefficients odds ratios (OR) can be calculated, $OR = e^{coefficient}$. OR = (true positive x true negative) : (false positive x false negative) or
$OR = (PV^+ \times PV^-) : (1 - PV^+)(1 - PV^-)$. If the coefficient is positive, the odds ratio is greater than 1, which indicates that the variable is positively associated with the diagnostic outcome. If the coefficient is negative, the odds ratio is less than 1, which indicates that the variable is negatively associated with the diagnostic outcome.

4. For the general practice population, forward stepwise logistic regression analysis resulted in three variables significantly contributing to the prediction of presence or absence of colorectal cancer: age ([age - 50]: 10) (OR = 8), change in bowel habit (more frequent, diarrhoea or variously normal stool and diarrhoea but not obstipation) (OR = 10) and blood seen mixed with or on stool (OR = 8). With a cut-off point optimal for exclusion of cancer (with a sensitivity of 100% no false negatives, so $PV^- = 100\%$) a maximum of specificity of 90% was reached. This means that 87% of all patients with rectal bleeding were predicted (correctly) negative and 90% of those without cancer were predicted negative.
   According to the presented prediction model (Chapter 6, Table 5) a rectal bleeding patient is suspected for colorectal cancer in the following cases: if

the patient is older than 70 years; if the patient is older than 60 years and suffers from at least one of the two symptoms: a changed bowel habit (with exclusion of constipation) and blood mixed with or on stool; if the patient is older than 50 years and has both the above mentioned symptoms. Patients younger than 50 years have a very low probability of colorectal cancer (close to 0%). This probability decreases in absence of the mentioned symptoms and with younger age. It must be remembered that colorectal cancer although relatively rarely does occur at younger age.

If overtly bleeding polyps were added to cancer as the outcome parameter, the logistic regression analysis resulted in a similar model. However, the maximum sensitivity was not 100% but 93% (1 patient had an undetected polyp).

5. In an internists' outpatient clinic population the analysis was done regarding colorectal neoplasm (cancer and polyps) taken together with Inflammatory Bowel Disease (IBD), including proctitis and colitis. The prior probability of these 'serious bowel diseases' is 32% in the study population.

   Forward stepwise logistic regression analysis found a set of six signs and symptoms, derived from history taking, significantly predicting serious disease, namely: change in bowel habit (with exclusion of constipation) (OR = 18), blood seen more than once (OR = 49), blood seen at the end of defaecation (OR = 12), tenesmus (OR = 10), nausea (OR = 0.05), signs of depression (OR =0.07). A set of four variables was found when physical examination and laboratory test results were also taken into account: change in bowel habit (OR = 8), abdominal pain less of than 2 weeks of duration (OR = 0.06), abnormal findings with abdominal inspection (OR = 0.04), and at least one positive Haemoccult test out of three tests (OR = 121). The regression model derived from only history findings was more useful for diagnosis by exclusion. Application of this model might spare 43% of all patients with rectal bleeding and 64% of those patients without IBD and neoplasm from invasive diagnostic procedures.

Methodology

Practical aspects

Practical problems and the study protocol

Research in general practice and especially a multipractice study has some pitfalls.[1,2] "It is always important to be aware that individual GPs differ in the way they interpret the definitions used in a research project and in the way the research record will be completed. Also, in the hurly-burly of general practice it can be very difficult to ensure that all patients available for the study are included. When under pressure, the doctor may wish to excuse himself from undertaking extra work or may simply forget to include the patient in the study."[1] Morrell relates some pitfalls to the fact that few GPs have been taught how to undertake a research project. Other pitfalls are related to the fact that GPs have a very special relationship with their patients, often spanning years of repeated contact which offers unique opportunities but carries with it serious responsibilities. The fact that the average consultation in general practice lasts just a few minutes and collecting complex research data is difficult in this setting is yet another pifall.[1] Dambsbo and Olsen concluded that the quality of multipractice studies depends crucially on whether the recording period is not too long, whether the forms to be filled in are as simple as possible, and whether the participating doctors are motivated for the study.[2] Aware of these practical problems we have tried to optimalize the participation of the doctors. They were informed about the expected practical consequences before they agreed to participate in our study. Those who agreed can be considered as motivated. Action was taken to keep them motivated and involved in the study, for example, through regular personal contacts and via a newsletter. The workload per patient varied between doctors from 10 to 20 minutes and seemed quite acceptable (doctor's questionnaire and laboratory test are enclosed in Appendices I and II). However, one of the problems the participating GPs most frequently mentioned regarding the compliance to the study was lack of time. Other reasons were "too much fuss for a simple and harmless complaint" and "a possibility of inducing fear and harm for the patient". Furthermore, the long

patient's questionnaires (Appendix III) might have caused some resistance among the GPs to motivate the patients with minor rectal bleeding, although the questionnaires had proved to be acceptable in a pilot study.
Because general practice is an unexplored field regarding our questions it was not possible to design a short and simple form. Because of the very low prior probability of colorectal cancer a quite long recording period was necessary.
In evaluating the experience with studies A (initial protocol) and B (modified protocol) there are advantages and disadvantages in both. Study B with a simplified doctor's questionnaire (Appendix IV) and a short registration period was more reliable regarding the incidence rate of rectal bleeding than study A. But the availability of other data of interest in order to determine predictive values of signs and symptoms, i.e. answers to questions in doctors' forms and answers in patients' forms, is less. The simplified doctor's form was completed less accurately and answers to open questions were sometimes hardly readable or not clearly interpretable. Patients' questionnaires were not obligatory (but desired) and therefore only available for 66% of the patients with rectal bleeding in study B (in study A for 90%). Moreover, the available patient questionnaires in study B were often not completed satisfactorily resulting in much missing data. Patients with minor ailments and complaints of only short duration may have been less motivated to fill in the questionnaire. Laboratory tests were not available (not included in the study protocol).
Because of the small number of patients, the absence of patients with colorectal cancer and the large amount of missing data, we did not analyse the study B data. For GPs in study B the workload per patient was less than in study A, but study B yielded a larger number of patients per unit of time counterbalancing the first advantage.
The variation in incidence rates did not influence the prior probabilities of the several diagnoses very much while cancer did not occur in study B. The conclusion that cancer is a relatively rare cause of rectal bleeding remains, for the 'selected' and even more for the 'unselected' general practice population. The prior probability of colorectal cancer in an 'unselected' general practice population will probably be even lower than we found in our study population.

Combined study

The cooperation with a study on non-acute abdominal complaints in general practice and outpatient clinics, initiated by the Department of General Practice at the University of Limburg, made it possible to find and manage a large number of physicians ready to participate. However, a complicating factor might have resulted from the combination of two entry complaints, 'rectal bleeding' or 'non-acute abdominal complaints', for three possible reasons. First, the inclusion criteria might not have been quite clear in the beginning. The 'non-acute abdominal complaints' should have been lasting longer than two weeks while this restriction was not desired regarding rectal bleeding. Second, the long patients' questionnaires might have caused some resistance among the GPs regarding the patients with minor rectal bleeding, although many questions could be skipped in cases without abdominal pain and although the questionnaires had been demonstrated to be acceptable in a pilot study. Finally, some doctors may have been more interested in and focused on chronic abdominal complaints and less alert to including patients with rectal bleeding, while the reverse may have been also true.

Strength of the methodology

This study encompasses the general practice experience of 83 GPs with an average duration of participation of 11 months (study A) and 10 GPs with 3 months' participation (study B). To find a similar database about three professional lifetimes of GPs are needed.

Study B was initiated to function as a reference group with an optimal incidence rate. Comparing the two studies confirmed that in study A patients with 'minor ailments' were more likely not to be included in the study. We consider this data collection about the maximum of what is possible in general practice research. The possible missing cases on both extremes of the spectrum, from obviously not serious to obviously serious (acute admission to hospital), means that our findings are based on and applicable to patients in whom rectal bleeding is likely to be a decision problem for GPs.

The gold standard of diagnoses is described in Chapter 4. It was assumed that clinically relevant and potentially serious sources of rectal bleeding would have been discovered within the follow-up period of at least 1 year. Endoscopy or roentgenography of all patients could have yielded some diagnoses, like diverticulosis and polyps, which were not necessarily the source of bleeding. Diverticulosis and polyps were classified as the outcome only when these disorders were regarded as the source of bleeding.

A hospital outpatient population may provide more detailed information regarding some diagnostic outcomes because of a generally more extensive investigation. Therefore, we did an analysis in internist outpatients clinics similar to that in general practice. These patients were comparable to the general practice population regarding age and gender (Table 1).

Table 1. Age and gender distribution of patients with rectal bleeding in internists' outpatient clinics (OP) and in general practice (GP)

Age (years)	OP		GP	
	number	(%)	number	(%)
18-39	55	(53)	144	(50)
40-49	19	(18)	58	(20)
50-59	15	(14)	46	(16)
≥ 60	16	(15)	42	(14)
Gender				
Female	55	(52)	164	(56)
Male	50	(48)	126	(44)
Total	105	(100)	290	(100)

In the outpatient population all patients had further diagnostic investigation during the follow-up period, while in the general practice population only 48% had any further colorectal examinations by means of endoscopy or roentgenography initiated by the GP (31%) and/or by referral (25%) (Table 2).

However, rates of colorectal cancer and polyps were equal in the two populations (Table 3). This supports the assumption that the length of the follow-up period and therefore our gold standard could be regarded as appropriate for our purpose.

Table 2. Further diagnostic investigations in the internists' outpatient population (OP) and general practice population (GP) through the time of follow-up

	OP N=104	(%)	GP N=269	(%)
Endoscopy				
proctoscopy	2	(2)	21	(8)
sigmoidoscopy	72	(69)	23	(9)
colonoscopy	14	(13)	6	(2)
Roentgenogram of lower bowel	22	(21)	23	(9)
Ultrasound scan of upper or lower abdomen	10	(10)	15	(6)
No further investigation initiated by the doctor participating in the study	0		186	(69)
Referral total	11	(11)	67	(25)
surgery	8	(8)	41	(15)
internal medicine (other internist)	3	(3)	14	(5)
gynaecology	0		3	(1)
psychology	0		2	(1)
more than 1 discipline	0		7	(3)
No referral nor further investigation	0		140	(52)

Table 3. Diagnoses related to rectal bleeding in the outpatient population (OP) and general practice (GP)

	OP N=104	(%)	GP N=269	(%)
Unknown cause	44	(42)	162	(61)
Haemorrhoid(s)	14	(13)	43	(16)
Fissura ani, abscess	8	(8)	19	(7)
Infection	4	(4)	6	(2)
Diverticulosis/itis	4	(4)	2	(1)
Proctitis	8	(8)	12	(4)
Colitis	19	(18)	13	(5)
Polyps	3	(3)	6	(2)
Colorectal carcinoma	3	(3)	9	(3)
Total	107*	(103)*	272*	(101)*

* 3 patients had 2 diagnoses

Limitations of the methodology

Representativeness of the population

The specific Dutch Health Care situation with open access to general practice for all patients, with a fixed list of patients per GP and a 'gate-keeper' function of GPs will have a positive influence the representativeness of our findings.
Of course, the local situation within the Netherlands may vary. Some practices will have access to endoscopy facilities while others have to refer the patient to an internist or surgeon for this.
Rectal bleeding was recorded and included in the study without systematically all consulting asking patients whether they had seen blood loss per rectum. Inter-doctor variation in alertness for rectal bleeding and selection of inclusion of patients in the study was not measured.

General practice results

Although special efforts had been taken to reduce the numbers of 'not-included' (undetected) rectal bleeding patients in the study through regular practice visits and via a newsletter, it was not possible to gather all the data requested. Information from the participating GPs indicated that patients with rectal bleeding who were not included in the study were especially those with minor ailments. This was supported by the results of study B (Chapter 5). In order to evaluate the extent of underregistration and the extent of selective underregistration with its possible influence on the prior probability of colorectal cancer, the following figures of expected numbers of patients can be given. On the basis of the results of study B, in study A about 1200 patients had to be included by 80 full-time GPs (77 full-time GPs and 6 part-time GPs, and a population of $\pm$ 80 x 2350 = 188,000 people) in a period of 11 months. In study A, however, only 290 patients with rectal bleeding (269 analysed) were accrued. In this population and among the expected 1200 patients with rectal bleeding, between 5 and 25 patients would be expected to suffer from colorectal cancer as illustrated in Chapter 2*.Of these a proportion would have been urgently referred to hospital and would therefore not be included in our study. So, the number of not-included cancer patients is probably very small.
This conclusion is confirmed by the following deduction. According to data of a recent Dutch retrospective study of patients with colorectal cancer, GPs

* The incidence rates as described in Chapter 2 were corrected for the fact that 75 years was the upper age limit for inclusion in our study. According to registrations in England 42% of patients with colorectal cancer are aged older than 75 years.[3]

referred 43% of these patients to hospital within one week after presentation because of a palpable tumour, acute abdominal complaints or massive bleeding.[4] Since these patients are probably urgently referred, they would have been excluded from our study. In 35% of the remaining patients in the retrospective study the GP reported that the patient had overt rectal bleeding. On the basis of the data in this latter study and assuming that about 30% of patients with colorectal cancer are older than 75 years[5], we could expect 9 patients to be suffering from colorectal cancer in our study population. In fact 9 patients in our study did have colorectal cancer. So, the number of 'not-included cancer patients', in contrast to the number of 'not-included rectal bleeding patients with minor ailments', is probably very low.
Combining the results of studies A and B, the prior probability of colorectal cancer in patients with rectal bleeding in general practice, younger than 76 years of age, would be 0.8% (9 (study A) per 1200 (expected number in study A)). We found a prior probability of 3.3%. Even if some patients with colorectal cancer were missed in study A, which is not very likely as shown above, the maximum prior probability according to the above mentioned maximum expectation of 25 patients, would be 2.1%. This illustrates that GPs have selected patients with rectal bleeding having a slighty increased probability of cancer for inclusion in the study. It has to be remembered that this study population represents those patients that confront GPs with a decision problem.

Outpatient clinic

The study population recruited in the internists' outpatient clinic is a selected population, of which the preselection is determined by regional circumstances. The findings are therefore not generally representative for patients referred for rectal bleeding in general. In other areas and other countries the prevalences of the several diagnoses related to rectal bleeding may be different. The prior probability of colorectal cancer in our population was remarkably low. Two additional registrations, with linked epidemiologic data of rectal bleeding patients referred to the University Hospital of Maastricht, may serve as a map of the diagnostic route of those patients, via internists' outpatient clinics, via acute admissions or via surgeons. The internist of this hospital delivered a major part of outpatients for our study (50% versus 50% by the other three hospitals).

1. A retrospective analysis of patient records of those who had been discharged from the hospital having a diagnosis of anal or colorectal malignancy in 1989 was done to find the expected number of patients with these malignancies for inclusion in our study (Table 4). We found only 3 such patients presenting with rectal bleeding who were not urgently admitted and had initially consulted an internist.

Table 4. A retrospective analysis of patients with colorectal carcinoma diagnosed in 1989.

Aim	Mapping out the internist catchment of colorectal cancer presenting with rectal bleeding as compared to that of surgeons.
Objective	1. To determine the frequency of overt rectal bleeding seen by the patients and reported by the physician in patients with colorectal cancer. 2. To determine the proportion of patients seen first by internist or first by surgeons. 3. To find the proportion of urgent admission to the hospital.
Setting	University Hospital of Maastricht, the only hospital in an area of 150,000 inhabitants.
Subjects	All patients in the ages between 18 and 75 years, hospitalized for anal or colorectal carcinoma, diagnosed in 1989. Patients from outside the area of Maastricht were excluded.
Results	45 patients fulfilled the inclusion criteria. One patient was lost to analysis. 14 patients (32%) had a rectum carcinoma. 19 patients (43%) had a sigmoid carcinoma. 11 patients (25%) had a more proximal colon carcinoma. 1. 24 patients (55%) reported rectal bleeding. Overt rectal bleeding occurred in 86% of rectum carcinoma, in 63% of sigmoid carcinoma and in none of the colon carcinoma. 2. 25 patients first consulted a surgeon (57%). 3. 8 patients were urgently admitted to the hospital (18%). Only 3 patients presenting with rectal bleeding and who were not urgently admitted consulted an internist first.
Conclusion	Patients with a colorectal carcinoma presenting with rectal bleeding are mostly referred to surgeons.

2. Data regarding patients referred for proctoscopy, sigmoidoscopy or colonoscopy to the Endoscopy Department in University Hospital of Maastricht (Table 5) were checked. These data also support the conclusion that patients with colorectal carcinoma presenting with rectal bleeding were more frequently referred to surgeons.

Table 5. Endoscopy unit data, RP Adang et al., January 1989 - October 1990: 22 months

Total number of endoscopies of the lower gastrointestinal tract: 2270*

on the indication of rectal bleeding: 1052 (47%)

Endoscopic diagnosis of Neoplasm (without histologic confirmation) N=440
adenomatous polyp (n = 326), with rectal bleeding: 156 (48%)
rectumcarcinoma (n = 48), " " " : 27 (56%)
coloncarcinoma (n = 66), " " " : 29 (44%)

Rectal bleeding N = 1052
adenomatous polyp 15%
rectumcarcinoma 3%
coloncarcinoma 3%

Neoplasm N = 440
referred by general practitioner 25%
referred by surgeon 46%
referred by internist 29%

Expected number of patients with a neoplasm and rectal bleeding referred for endoscopy per year by internists:

adenomatous polyp: 12/22 x 0.29 (proportion internist) x 156 = 25 /year
rectumcarcinoma: 12/22 x 0.29 (proportion internist) x 27 = 4 /year
coloncarcinoma: 12/22 x 0.29 (proportion internist) x 29 = 5 /year

Included are patients older than 75 years of age and acute admissions (exclusion criterion for the study).

* Repeated investigations not included

The data in Table 5 include patients older than 75 and also acute admissions (both exclusion criteria in our study). When this is taken into account, internists in our area are shown to have relatively few patients with a colorectal carcinoma available to include in the study.

Regarding the predictive values of signs and symptoms in patients referred to internists' outpatient clinics, it is shown that even in this referred population it was possible to identify a subpopulation, on the basis of history findings, with a very low probability of serious disease.

Instruments

The signs and symptoms are 'soft' data. To validate these data it would be necessary for all patients to be seen by several doctors in a comparable situation (reproducibility) and that a gold standard for all symptoms was applied. This was, of course, not feasible.
We have selected the doctors' registration as the starting-point for analysis. The patient's questionnaire was used for additional information. Some questions and answers were only available in the patient's form, for example, the detailed questions about the manifestation of the blood seen and the extensive psychosocial questions, including the Zung self-rating scale.
When patients' questionnaires are compared to doctors' questionnaires it appears that some symptoms are more frequently reported in the patients' questionnaires than in the doctors' questionnaires. Remarkable examples are: nausea being reported in 105 patients' forms and only present in 68 patients according to the doctors' forms; tenesmus in 93 and 59 patients respectively; and abdominal pain in 152 and 135 respectively (Appendix V). Although in the patients' forms more missing data occur regarding these symptoms (28 for nausea and 40 for tenesmus) than in the doctors' forms (3 and 4 respectively) the occurrence is higher according these patients forms. Since it was beyond the scope of our research, we did not determine the agreement between patients and doctors. Although there may be differences in the interpretation of the questions between doctors and patients, among doctors (inter-doctor variation) and among patients (inter-patient variation), this database is considered to reflect usual daily general practice very well.

Statistics

The exact predicted probabilities derived from logistic regression may be not fully reliable due to the small number of patients with cancer (and polyps), N=9 (+6), in the study population. Fewer than 10 outcome events per independent variable in the model may result in "overfitting" the data.[6,7] For statistical purposes this is a problem but in practice it means that the incidence and prevalence of some signs and symptoms in correlation with cancer is too low to be observed or to be shown statistically significant in about 83 'GP-years'.

Interpretation of signs of depression

Signs of depression, in our study defined as a Zung score of >40, were present in 22% of outpatients and in 28% of patients with rectal bleeding in the general practice population. The Zung Self-Rating Depression Scale is accepted as a useful screening instrument for depression.[8] With application of a frequently used cut-off point for depression of >50, depression was present in 8% in the outpatient population and in 6% in general practice. This is comparable to the prevalence of depression in the primary care setting which has been reported in the range from 6% to 17%.[9]

Only in the outpatient population were signs of depression significantly predictive for the absence of 'IBD or neoplasm'. This may support the presence of a phenomenon described by Zung that patients with depression are frequently referred to specialists for additional medical workups; they are subjected to unnecessary, potentially harmful and costly diagnostic tests.[9]

Three symptoms which indicate depression are included both in the Zung questionnaire and in our gastroenterologic questions: decreased appetite, weight loss and constipation. These symptoms frequently occur in patients with gastroenterologic complaints. Constipation was present in 7% of our outpatients and was significantly associated with the absence of 'IBD or neoplasm', but decreased appetite (present in 14% of patients) was associated with the presence of 'IBD or neoplasm'. Weight loss (present in 27%) did not show a

significantly association with these diagnoses in this population.
Further study is necessary to evaluate the validity of the Zung questionnaire for diagnosing depression in patients with gastroenterologic complaints. In the outpatient population constipation may falsely increase an association between signs of depression and the absence of serious disease, whereas decreased appetite and weight loss tend to decrease such an association.

Findings in relation to the literature

Compared to the findings reported by Lamberts[10], the incidence of rectal bleeding in general practice of 4 per 1000 per year, the percentages of further diagnostic investigation (radiology/imaging: 1%) and referral to a medical specialist linked to rectal bleeding as a reason for encounter (14%), our findings in study A show a lower incidence (2 per 1000) and higher percentages of further diagnostic investigation (31%) and referral (25%). This may confirm our earlier illustrated conclusion that the general practitioners in study A have selected patients that are more likely to confront GPs with a diagnostic decision problem.
Our data represent a first analysis of the predictive value of rectal bleeding in combination with other signs and symptoms. It is only partially possible to compare our results with reports of common symptoms of serious disease or predictive values on the basis of bivariate analyses.
Holtedahl has shown that a single symptom known as a warning signal of cancer, with bleeding as one of the seven warning signals, is rarely a sufficient basis for decisions related to the diagnosis of cancer in general practice.[11] The quantitative data in the booklet by Holtedahl, aiming at early diagnosis of cancer in general practice, do not provide all the required diagnostic values of symptoms for clinical decision making.[12] He summarized some common symptoms of colorectal cancer in addition to rectal bleeding: change in bowel habit (that included constipation), mucous discharge from the rectum and anaemia. In our study mucous discharge is not significantly associated with cancer and none of our cancer patients had constipation.

Nylenna reported that no single symptom recorded in his study seems to be a very useful guide for an increased awareness of cancer.[13] The most important indicator was fear of cancer. "The chance of having a cancer reported within two years was four times as high in patients expressing fear of cancer as in those who did not." Change in bowel habit was also mentioned in this study as having predictive value for cancer (PV^+ of 7%) but without a more detailed risk quantification.

Mant et al reported significant associations with colorectal cancer and polyps of blood mixed with stool (positive association), of anal protrusion and of haemorrhoids identified by the general practitioner (both negative associations).[14]

None of these reports provided information sufficient to exclude the probability of colorectal cancer in general practice.

Three studies reported common reasons for suspecting serious disorders in outpatients. These are the occurrence of at least one of the following on presentation: blood mixed with stool, tenesmus, change in bowel habit and a positive family history of colorectal neoplasm.[15-17] In addition, each study reported other distinctive characteristics. Firstly, a neoplasm is, in addition to the above symptoms, considered by Cheung et al when there is leakage of mucous per rectum, weight loss, abdominal pain, and a palpable tumour.[15] In the study by Church, other suspected symptoms are: dark red blood and leakage of mucous.[16] Non-suspect symptoms in this study are: bright red blood during or after defaecation, on the paper or in the toilet. Finally, Newstead considered abdominal pain and age above 40 years to be additional reasons to perform colonoscopy in patients with rectal bleeding.[17] Most of these reported symptoms showed more or less diagnostic value either in our general practice population or in the outpatient population. However, according to our findings, abdominal pain and dark red blood are, on the contrary, associated with the absence of serious disease.

Practical implications

One of the main purposes of this study was to find ways to improve the diagnostic practice in relation to patients with rectal bleeding in general practice. Therefore, at the end of this work, we may try to answer the question: is improvement really necessary and how can this be accomplished? As far as the early diagnosis of patients with colorectal cancer concerns we did not find a reason to change the current diagnostic strategies. A profile of the patients with colorectal cancer is given in Table 6. Doctors' delay was defined as the period between the first consultation for rectal bleeding and action taken by the GP in order to confirm or rule out colorectal cancer, by either referral or further investigation. From this table it appears that most patients with colorectal cancer were referred or investigated further within 4 weeks, with one patient having a doctor's delay of 8 weeks.

In contrast, the diagnostic strategies of the GPs leave room for further improvement regarding the selection of patients who do not benefit from further diagnostic investigation. Of the 269 patients presenting with rectal bleeding only 18% had a diagnosis requiring further investigation (cancer, polyp, colitis, proctitis, infection, diverticulosis) whereas 48% in actual practice underwent further diagnostic investigation.

Neoplasms are the most difficult diagnoses for GPs because they usually do not present with an evident clinical picture and because GPs are concerned about the possibility of overlooking cancer. Polyps although in general being more prevalent than colorectal cancer seem to be less frequently related to rectal bleeding than cancer. The discussion about the relevance of early detection of polyps (before symptoms occur) is beyond the purpose of the present study. Diverticulosis is not an important differential diagnosis. It is a frequent finding when, especially in older patients, endoscopy or roentgenography is performed but it is rarely a cause for blood loss.[18] Patients with bleeding caused by diverticular disease are characterized by a sudden urge to defaecate followed by the passage of a large bloody stool.[19] Colitis, proctitis and infections are usually easier to diagnose.

Table 6. Patients with colorectal cancer in study A, N=9.

no.	age	♂/♀	†	doctors'delay in weeks	initial diagnoses	length of bleeding history	abdominal pain	ESR mm/h	WBC	localization tumour
434	71	♂	-	1	?	2-4 week	-	7	N	rectum
746	59	♂	+	1	haemorrhoid	?	-	31	↑	rectum
687	64	♂	+	0	?	<2 week	-	33	↑	colon, metas
567	68	♀	+	2	?	2-4 week	+	?	?	sigmoid, T_2N_0 DukesB
1217	63	♂	-	3	tumour	½-1 year	-	5	?	rectum
716	68	♂	-	8	haemorrhoid	?	-	?	?	rectum
254	63	♂	+	0	tumour	?	+	18	?	rectum
204	75	♂	-	0	tumour	2-4 week	-	?	↑	colon
553	75	♀	-	2	diverticulosis	>1 year	-	?	?	rectum

For patients nr. 746 and 716 there is no patient form available.
WBC=White Blood Cell Count, ↑ $>10^9$/l, N=Normal, ? unknown.

Our results indicate that with the use of a limited set of data from medical history, a considerable number of patients with rectal bleeding can be identified as not needing further investigation for exclusion or confirmation of cancer.
Goulston et al have presented data regarding the usefulness of clinical assessments (before further investigation) of doctors in this respect.[20] It appears that of the patients without cancer GPs were able to identify 64% (specificity) correctly by clinical assessment and gastroenterologists to do so in 80% of cases. The sensitivity of clinical assessment was 75% and 87% respectively. With the application of our model the specificity is 90% with the maintenance of a 100% sensitivity, indicating that this approach may be useful to overcome the problem of overdiagnosis.

Future research

General recommendations for further research can be made. Firstly, it seems useful to test the performance of our prediction model in another comparable and even larger general practice population. Also, it would be interesting to analyse differences in predictive values of signs and symptoms in patients with rectal bleeding in other different populations, other countries and other health care systems with different thresholds for consultation.
It is recommended to evaluate the diagnostic value of proctoscopy in general practice. Demonstration by proctoscopy of anal and rectal bleeding causes in combination with other signs may contribute to effective and efficient diagnostic strategies.
For a better understanding of differences in occurrence and significance of rectal bleeding and of the predictive values of signs and symptoms in general practice compared to referred patients it is recommended to perform a similar study in a referred population which include all referred patients within a given area. This could be feasible in an Endoscopy Department, perhaps in combination with a Roentgenography Department, where all patients within a certain area who need further diagnostic workup because of rectal bleeding could be identified.

It is further recommended to analyse differences in interpretations of symptoms between healthy people, patients and doctors in order to provide adequate and more focused public, patient and medical education.

Finally, our findings may contribute to the development of criteria for diagnostic investigation including referral and criteria for the extent of investigation (rectal examination, blood sample, proctoscopy, sigmoidoscopy, colonoscopy or roentgenography). Such criteria may be useful in daily practice in order to improve the effectiveness and efficiency of the diagnostic process and to improve the communication between GPs and patients and between GPs and specialists as well.

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9. Summary

1. Introduction

Overt ano-rectal bleeding is known as a danger signal. Knowledge of the predictive value of this sign in combination with other signs and symptoms is hardly available but desired for rational clinical practice. The main purpose of the present study was to collect quantitative data for the use in general practice. The main question in this study was whether it is possible to discriminate effectively between patients with rectal bleeding who have colorectal cancer and those who do not; or at least to discriminate between those who need invasive investigations and those who do not.

We tried to answer the following questions:

1. What is the incidence of rectal bleeding in general practice?
2. What is the prior probability of malignant disease in patients presenting with rectal bleeding in general practice? What are the frequencies of other sources of rectal bleeding?
3. What is the predictive value of (combinations of) signs, symptoms and simple laboratory tests a. for colorectal cancer in general practice?
   b. for serious bowel disease in outpatients?

2. Literature

To determine the occurrence and significance of overt blood loss per ano-rectum a Medline literature search was undertaken. The incidence of this symptom in the general population is reported in literature to be about 20 per 100 people per year, the 'consultation incidence' in general practice is reported to be about 6 per 1000 per year and the incidence of referral to a medical specialist is estimated to be about 7 per 10,000 per year. The clinical significance of the symptom varies within different populations: the predictive value of overt rectal blood loss for colorectal malignancy was estimated to be about 1 in 1000 or even less in the general population, around 2 in 100 in general practice and up to 36 in 100 in the referred patients. It is unknown how the manifestation of the bleeding (and other signs and symptoms) influence the care seeking and referral behaviour, leading to increased prior probabilities.

3. Current Dutch situation

The current diagnostic approach of patients with rectal bleeding in general practice in the Netherlands is discussed in Chapter 3. General practitioners often face a dilemma: deciding whether to expose the patient to possibly unnecessary anxiety and costs, or whether to risk diagnosing a potentially malignant tumour too late or not at all. General practitioners are concerned about the possibility of overlooking cancer which does not present with an evident clinical picture. Knowledge of the diagnostic value of other signs and symptoms in combination with rectal bleeding could be helpful.

4. Research protocol

Chapter 4 gives a review of the general methodological aspects of our empirical study. In both general practice and the outpatient clinic the question was operationalized as: to what extent do other (combinations of) symptoms enable the physician to confirm or rule out serious disease?

In general practice the focus is on colorectal cancer, since the prediction of the presence or absence of colorectal cancer is the main decision problem. In the outpatient clinic the focus is on serious disease requiring further diagnostic investigation. Inflammatory bowel disease (IBD) and colorectal neoplasm (cancer and polyps) were taken together as serious disease.

The design of the study can be defined as 'pseudo-follow-up' study, investigating a cross-sectional relationship between particular factors (signs, symptoms and simple laboratory test results) and a particular outcome (colorectal cancer, neoplasm or IBD), while the outcome can be only detected by follow-up. All diagnostic data available after a follow-up period of at least 1 year were used to establish the final diagnostic outcome (gold standard). It was assumed that a potentially malignant source of rectal bleeding would have been discovered within the follow-up period. Since referred patients with rectal bleeding will almost always undergo further diagnostic investigations, including endoscopy or roentgenography, additional information regarding the frequencies of possibly missed diagnoses of polyps and malignancies in the general practice population could be gained by analysing outcome data in a outpatient population.

Population

Consecutive patients in the ages 18-75 years with rectal bleeding were recruited in general practice (study A and B) and general internists' outpatient clinics (study C). Since it was noticed during the course of the study in general practice (study A) that the number of patients included in the study was less than expected and very variable, it was decided to conduct a complementary study (study B) with a modified protocol and special efforts to maximize the catchment rate. The aim of the study B was to assess a more accurate incidence rate. For this there were during a three months' period daily controls of patient records by practice assistants.

Data

The data were collected through a semi-structured questionnaire filled in by the doctor after the first consultation (history, physical examination and initial management); some simple laboratory tests: erythrocyte sedimentation rate, haemoglobin, white blood cell count and faecal occult blood; and a self-completion patient questionnaire (history, signs and symptoms).

5. Results

The incidence as well as the final diagnostic outcome of rectal bleeding presenting in general practice both in the initial study A (83 GPs, 11 months, N=290) and in study B with a modified protocol (10 GPs, 3 months, N=48) are presented in Chapter 5. In study **B** the mean **'consultation incidence rate' (of patients in the ages 18-75 years) is 7 per 1000 per year**, in study **A** this is **2 per 1000**. The study A data are further analysed. Follow-up data were available for 269 patients, with a mean follow-up period of 20 months (standard deviation 5 months).

Occurrence of colorectal cancer was found in 9 patients with rectal bleeding in study A (3.3%, 95%CI 1.2%-5.4%). In about 90% of the patients rectal bleeding was related to minor ailments or self-limiting disorders. A prior probability of 3.3% may represent an overestimation of the real prior probability since there was a selection in favour of patients who are more likely to be a decision problem for the GP.

Patients with obviously harmless rectal bleeding were less likely to be included in the study than patients which are more likely to confront the GP with a decision problem.

6. Predictive values in general practice

In Chapter 6 the predictive values of signs and symptoms in rectal bleeding patients for colorectal cancer are presented. In bivariate analysis most variables did not show statistically significant predictive value (chi-square $p \geq 0{,}10$) (Table 2). The diagnostic value of signs, symptoms and simple laboratory test results is determined by the sensitivity, specificity, predictive values and odds ratios. The diagnostic values regarding bivariately significant variables are given in Tables 3 and 4. All significant variables were entered into forward stepwise logistic regression analysis to find the 'independent' predictive value of each variable taking the other variables into account simultaneously. Although the number of patients with colorectal cancer is small ($n=9$) it was possible to identify three characteristics significantly and independently contributing to the diagnosis: **age, change in bowel habit (with exclusion of constipation) and blood only mixed with or on stool**. Constipation, blood on toilet paper, blood in lavatory bowl, other or unknown presentations and combinations of presentations did not show predictive value. For statistical reasons age is transformed into decades above and below 50 years ((age - 50): 10). The prior probability of cancer increases with age above 50 years and equally decreases with age below 50 years.

According to **the prediction model** (Table 5) with the application of a cut-off point optimal for exclusion (no false negatives and a minimal number of false positives) in the study population, a rectal bleeding patient is suspected for colorectal cancer in the following cases: if the patient is older than 70 years; if the patient is older than 60 years and suffers from at least one of the two symptoms: a changed bowel habit and blood mixed with or on stool; if the patient is older than 50 years and has both the above mentioned symptoms. Patients younger than 50 years have a very low probability of colorectal cancer (close to 0%). It must be remembered that colorectal cancer although relatively rarely does occur at younger age.

A prediction model containing the combination of these three signs can be assessed as a diagnostic test for the prediction of cancer.
The Area Under the Receiver Operating Characteristic (ROC) curve (AUC) is 0.97, which means a high discriminatory power. The maximum sum of sensitivity and specificity is achieved with a cut-off point of 0.042 (posterior probability), corresponding to a sensitivity of 100% and a specificity of 90%. For accurately predicting the absence of malignancy in our study population, application of this cut-off point is suitable. At this point 13% of patients (n=35) are classified as positive for cancer with a **positive predictive value (PV^+) of 26%**, while 87% of patients (n=234) are truly classified as negative **(PV^- = 100%)**. Application of the prediction model presented might prevent 90% of 'unnecessary' invasive diagnostic procedures for patients with rectal bleeding who do not have colorectal cancer.
If polyps, which were detected and related to rectal bleeding in 6 patients in our population, are added to cancer as the outcome parameter the logistic regression analysis results in a similar model. However, the discriminatory power is slightly less with an AUC of 0.92. The maximum sum of sensitivity (93%) and specificity (84%) is 177%. Applying the model in our study population with a cut-off point optimal for exclusion of cancer and polyps, 21% of patients are predicted positive for colorectal cancer or polyps with a PV^+ of 25% and a PV^- of 99.5%. It is concluded that in patients with rectal bleeding **the predictive power of many signs and symptoms for colorectal cancer in general practice is low.**
The answer on our main question in the study is: yes, **it appears possible to discriminate in rectal bleeding patients between those who do not have colorectal cancer and those who have a rather high probability of cancer. Therefore, it appears possible to discriminate effectively and efficiently patients for invasive diagnostic investigations.**
This is the first reported model developed to discriminate between such patients with a very low (close to 0) probability of colorectal cancer (and overtly bleeding polyps) and those with a high probability. Although our model appears to do this quite successfully, testing its performance in other general practice populations is recommended.

7. Predictive values in the outpatient population

In the study outpatient population the **prior probability** (prevalence) **of serious bowel disease is 32%**: 26% inflammatory bowel disease (IBD: colitis or proctitis) and 6% neoplasm (colorectal cancer or polyps). The 18 variables with a statistically significant predictive value on the basis of a bivariate analysis are given in Chapter 7.

Forward stepwise multiple logistic regression analysis shows 4 to 6 variables with an independent contribution to the discrimination between the presence and absence of IBD or neoplasm. The AUC of the two models is 0.92 and 0.91. Model 1 is based on variables derived from history taking and contains six items: **a changed bowel habit (except constipation), blood seen more than once, blood seen at the end of defaecation, tenesmus, (absence of) nausea and (absence of) signs of depression**. Model 2 is based on history: **change in bowel habit (except constipation) and (absence of) abdominal pain of more than two weeks of duration;** physical examination: **(absence of) abnormalities (scars and distension) by abdominal inspection;** and laboratory tests results: **at least one positive result of three faecal occult blood tests**.

Model 1 is more useful regarding exclusion of serious disease than model 2. Applying model 1 in the study population with a cut-off point optimal for exclusion, 43% of patients are truly classified negative for IBD or neoplasm, with a sensitivity of 100% and a specificity of 64%, $\mathbf{PV^+ = 56\%}$ and $\mathbf{PV^- = 100\%}$. With model 2, only 10% of patients can profit by being classified negative (sensitivity = 100%, specificity = 17%, PV^+ = 34%, PV^- = 100%). Testing of the performance of the model in other outpatient clinic populations is recommended. It can be accepted with some reserve because of the missing data, that the laboratory tests do not provide additional contribution to the diagnosis of absence of IBD or neoplasm.

8. Study yield

Although research in general practice and especially a multipractice study has some pitfalls (described in Chapter 8), this is the only possible way to find predictive values of signs and symptoms in combination with rectal bleeding

for colorectal cancer in general practice. It appears possible to discriminate effectively and efficiently between patients who need invasive diagnostic investigation because of a reasonably high probability of colorectal cancer and those for whom this is not indicated because of a very low probability.
To find a similar database about three professional lifetimes of GPs would be needed.
Combining the results of studies A and B in general practice, the prior probability of colorectal cancer in rectal bleeding patients in the ages 18-75 years is 0.8% (9 per 1200). In our study population, however, which is representing patients that may be more likely to confront GPs with a decision problem, the prior probability is 3.3%. It is illustrated that GPs have selected patients with rectal bleeding and a somewhat higher than average probability of cancer for inclusion in the study.
The study population recruited in the internists' outpatient clinic is a selected population, of which the preselection is determined by regional circumstances. The findings are therefore not generally representative for patients referred for rectal bleeding in general. The prior probability of colorectal cancer in our outpatient population is remarkably low. Two additional registrations, with linked epidemiologic data of rectal bleeding patients referred to the University Hospital of Maastricht, serving as a map of the diagnostic route of those patients, via internists' outpatient clinics, via acute admissions or via surgeons show that internists in our area have see relatively few patients with colorectal carcinoma available who meet the inclusion criteria of the study. It is shown that even in this referred population it is possible to identify a subpopulation, on the basis of history findings, with a very low probability of serious bowel disease. It is recommended for the future to test the performance of our prediction models in another comparable general practice population and in another comparable outpatient population.
Studying a population older than 75 years can provide additional information regarding predictive values in these patients who probably have a high prior probability of cancer (,polyps and diverticulosis). It would also be interesting to analyse differences in predictive values of signs and symptoms in patients with rectal bleeding in both other different general practice populations and referred populations.

Furthermore, it is recommended to evaluate the diagnostic value of proctoscopy in general practice. Demonstration of anal and rectal bleeding causes in combination with other signs may contribute to more effective and efficient diagnostic strategies.

It is further recommended to analyse differences in interpretations of symptoms between healthy people, patients and doctors in order to provide adequate and more focused public, patient and medical education.

Finally, our findings may contribute to the development of criteria for diagnostic investigation including referral and criteria for the extent of investigation.

Samenvatting

1. Inleiding, vraagstelling

Zichtbaar bloedverlies per anum wordt gezien als waarschuwingssignaal voor darmkanker. Een belangrijke taak van de huisarts bij een patiënt met bloedverlies per anum is om deze patiënt weloverwogen onder te brengen bij de groep met een minimale kans op darmkanker (en de patiënt daarmee onnodig onderzoek te besparen) of wel bij de groep met een redelijk grote kans (en daarmee een procedure met invasief onderzoek in gang te zetten).
Kennis van de predictieve waarde van bloedverlies per anum in combinatie met andere symptomen en bevindingen bij lichamelijk onderzoek ten aanzien van darmkanker en andere ziektenbeelden is nauwelijks beschikbaar maar wel noodzakelijk om rationele diagnostiek te bevorderen.
Het beschreven onderzoek beoogt deze kennis te vermeerderen en uiteindelijk een antwoord te zoeken op de volgende vraag: "is het mogelijk in een gedefiniëerde groep patiënten met bloedverlies per anum effectief en efficiënt onderscheid te maken tussen degene die wel en degene die geen darmkanker hebben?; ofwel is het mogelijk onderscheid te maken tussen patiënten bij wie al dan niet invasieve onderzoeken geïndiceerd zijn?" Getracht is de volgende vragen te beantwoorden:

1. Wat is de incidentie van bloedverlies per anum in de huisartspraktijk?
2. Wat is in deze populatie met bloedverlies per anum de a priori kans voor darmkanker? In welke frequentie komen andere oorzaken van bloedverlies voor?
3. Wat is de voorspellende waarde van (de combinatie van) andere symptomen en bevindingen in a. de huisartsenpopulatie voor darmkanker;
   b. een poliklinische populatie voor ernstige darmaandoeningen.

2. Literatuur gegevens

Om een beeld te krijgen van het vóórkomen en de betekenis van zichtbaar bloedverlies per anum werd een literatuurstudie via Medline verricht.
De incidentie van dit symptoom in de algemene bevolking is ongeveer 20 per 100 volwassenen per jaar. De "consultatie-incidentie" in de huisartspraktijk

ongeveer 6 per 1000 mensen per jaar en de incidentie van "verwezen" naar een medisch specialist wordt geschat op ongeveer 7 per 10.000 mensen per jaar.
De klinische (diagnostische en prognostische) betekenis van bloedverlies per anum varieert binnen verschillende populaties: de voorspellende waarde voor darmkanker wordt geschat rond 1 per 1000 of minder in de algemene populatie, rond 2 per 100 of minder in de huisartspraktijk en tot 36 per 100 in de verwezen patiëntenpopulatie. Het is niet bekend, in hoeverre de presentatie (de aard) van het bloedverlies en van andere bijkomende symptomen van invloed is op het om hulp vragen van mensen en op het verwijsgedrag van huisartsen, en daarmee op een toename van a priori kansen.

3. Huidige nederlandse situatie

De huidige diagnostische benadering van patiënten met bloedverlies per anum in de huisartspraktijk wordt in hoofdstuk 3 beschreven.
Er bestaat vaak een dilemma voor de huisarts: aanvullend onderzoek met mogelijk onnodige angst, ongemak en onkosten voor de patiënt, of geen onderzoek met het risico een mogelijke kwaadaardige tumor (te)laat op te sporen. Huisartsen zijn terecht bevreesd om kanker over het hoofd te zien te meer in situaties waarin een duidelijk klinisch beeld ontbreekt. Kennis van de diagnostische waarde van bloedverlies in combinatie met andere symptomen is nodig om het diagnostisch handelen van huisartsen beter te onderbouwen dan nu het geval is.

4. Onderzoeksopzet

In hoofdstuk 4 wordt een overzicht gegeven van de methodologische aspecten van de empirische studie. Zowel in de huisartspraktijk als in de algemeen internistische polikliniek was de vraagstelling: "in welke mate maken andere (combinaties van) symptomen het mogelijk om ernstige ziekten te bevestigen of uit te sluiten?"
In de huisartspraktijken beperken we ons tot darmkanker omdat hier het voorspellen van aan- of afwezigheid van deze ziekte het belangrijkste besliskundige probleem vormt.
In de internistische polikliniek richten we ons op een aantal mogelijke ernstige aandoeningen die om invasief onderzoek vragen: inflammatoire aandoeningen

(IBD: colitis en proctitis) en colorectale neoplasmata (kanker en poliepen).
Het design van de studie zou men "pseudo follow-up" kunnen noemen. Een cross-sectionele relatie tussen bepaalde factoren (symptomen, bevindingen bij lichamelijk onderzoek en uitslagen van eenvoudige laboratoriumtests) en een bepaalde uitkomst (diagnose) wordt onderzocht terwijl die uitkomst slechts via een follow-up vastgesteld kan worden. Alle klinische en diagnostische gegevens die beschikbaar zijn na een follow-up periode van minstens één jaar dragen bij aan het vaststellen van de uiteindelijke diagnose (gouden standaard). Er wordt vanuitgegaan dat ernstige ziekten die het bloedverlies veroorzaken niet self-limiting zijn en met een hoge mate van waarschijnlijkheid binnen één jaar manifest zijn.
Omdat verwezen (poliklinische) patiënten vrijwel altijd invasieve diagnostische onderzoeken, zoals endoscopie of röntgenonderzoek ondergaan, is het te verwachten dat de analyse van de diagnostische resultaten in deze populatie enige informatie zal kunnen verschaffen ten aanzien de mate waarin belangrijke diagnosen (zoals maligniteiten en poliepen) gemist zouden kunnen zijn in de huisartsenpopulatie (waar deze onderzoeken vaak niet plaats vinden).

Onderzoekspopulatie

Patiënten in de leeftijdscategorie 18-75 jaar bij wie sprake is van zichtbaar bloedverlies per anum, als reden van komst of gemeld tijdens een anamnese, werden in de studie opgenomen. Patiënten die acuut verwezen werden (bijv. wegens massaal bloedverlies of klachten verdacht voor darmobstructie of perforatie) evenals zwangeren werden uitgesloten. Omdat gedurende het verloop van de oorspronkelijke studie in de huisartspraktijk (studie A) bleek dat het aantal in het onderzoek opgenomen patiënten lager was dan verwacht en het aantal tevens sterk varieerde tussen de huisartsen onderling, werd besloten om een complementaire studie (studie B) met een aangepast protocol uit te voeren. Het hoofddoel van studie B was het vinden van de werkelijke incidentie van bloedverlies per anum in de huisartspraktijk. Hiertoe werden ondermeer gedurende 3 maanden dagelijks de patientenkaarten door de praktijkassistentes gecontroleerd op aanwijzingen voor bloedverlies per anum.
Studie C betreft de patiënten van de polikliniek Interne Geneeskunde.

Data

Gegevens werden verzameld met behulp van:

- een semi-gestructureerd vragenformulier dat door de arts na het eerst consult werd ingevuld (anamnese, lichamelijk onderzoek en beleid);
- enkele eenvoudige laboratoriumtests: bezinkingssnelheid der erytrocyte (ESR), hemoglobine-gehalte (Hb), aantal leucocyten (WBC) en een test voo occult bloed in de faeces (FOB);
- een uitgebreide door de patiënt zelf in te vullen vragenlijst (uitgebreider anamnese en psychologische tests).

In totaal werden 60 variabelen geanalyseerd. De vragenlijsten zijn als bijlag toegevoegd. De percentages van voorkomen van diverse diagnosen pe variabele zijn eveneens in de bijlagen vermeld.

5. Resultaten

De incidentie van bloedverlies per anum en de uiteindelijke diagnosen in d huisartsenpopulatie zijn weergegeven in hoofdstuk 5. In studie **A** (8 huisartsen, gemiddelde registratieduur 11 maanden, N=290) werd ee **incidentie** vastgesteld van **2** patiënten (in de leeftijd van 18-75 jaar) **per 100 per jaar** en in studie **B** (10 huisartsen, 3 maanden, N=48) van **7 per 1000 pe jaar**. In studie A was follow-up mogelijk bij 269 patiënten met een gemiddelde follow-up duur van 20 maanden (standaard deviatie 5 maanden). De gegevens van de studie A patiënten zijn verder geanalyseerd.

Bij 9 patiënten (3,3%, 95%CI 1,2%-5,4%) werd darmkanker vastgesteld. In ongeveer 90% van de patiënten was het bloedverlies gerelateerd aan onschuldige aandoeningen. De gevonden a priori kans van darmkanker van 3,3% is mogelijk een overschatting van de werkelijke a priori kans omdat er een selectie bestond ten gunste van patiënten bij wie het bloedverlies vaker een besliskundig probleem vormt ten aanzien van eventueel te verrichten aanvullende diagnostiek. Patiënten bij wie vrijwel zeker sprake is van een onschuldige aandoening werden minder vaak in het onderzoek betrokken.

6. Predictieve waarden in de huisartspraktijk

In hoofdstuk 6 worden de voorspellende waarden van symptomen en bevindingen bij patiënten met bloedverlies per anum voor darmkanker gepresenteerd. In de bivariate analyse bleken de meeste variabelen bleken geen statistisch significante (chi kwadraat, $p \geq 0{,}10$) voorspellende waarde te hebben (tabel 2).

De diagnostische waarde van symptomen en bevindingen wordt evenals die van laboratoriumtests bepaald door de sensitiviteit, de specificiteit, de voorspellende waarde en odds ratio. Van de variabelen die in de bivariate analyse statistisch significant discriminerend bleken, zijn de genoemde diagnostische waarden gegeven (tabel 3 en 4). Al deze variabelen werden ingebracht in een logistische regressie analyse (forward stepwise) om de "onafhankelijke" predictieve waarde van elke van deze variabelen te bepalen waarbij gelijktijdig rekening werd gehouden met de overige variabelen.

Hoewel het aantal patiënten met darmkanker klein is (N=9) bleek het mogelijk drie factoren te identificeren die **onafhankelijk en statistisch significant bijdragen aan de diagnose: leeftijd, een veranderd defaecatie patroon (behalve obstipatie) en bloed alleen of vermengd met of op de ontlasting.** Aan obstipatie, bloed op het toiletpapier, bloed in de pot, bloed anderszins of met een onbekende presentatie evenals van de diverse combinaties van presentaties van bloedverlies kon geen onafhankelijke predictieve waarde worden toegekend. Om statistische redenen werd leeftijd getransformeerd tot decades onder en boven 50 jaar ((leeftijd-50):10). Boven de 50 jaar neemt de kans op darmkanker toe met het stijgen van de leeftijd (in decaden) en beneden de 50 jaar neemt deze kans in gelijke mate af met het dalen van de leeftijd.

Bij toepassing van het gepresenteerde predictiemodel (tabel 5) in de studiepopulatie met een gekozen afkappunt welk optimaal is voor uitsluitingsdiagnostiek (geen fout-negatieven en een minimaal aantal fout-positieven), wordt een patiënt in de volgende gevallen als positief (verhoogde kans op kanker) geclassificeerd: indien deze ouder is dan 70 jaar; indien deze ouder is dan 60 jaar en minstens één van de twee symptomen ('veranderd defaecatiepatroon' en 'bloed vermengd met of op de ontlasting') heeft; of indien de patiënt ouder is dan 50 jaar en beide eerder genoemde symptomen

heeft. Patiënten jonger dan 50 jaar hebben een erg kleine a priori kans op kanker. Opgemerkt moet echter worden dat ook bij jongere patiënten, hoewel relatief zeldzaam, darmkanker voorkomt.
Het **predictiemodel** kan beoordeeld worden als een diagnostische test voor kanker. Deze test heeft een hoog onderscheidend vermogen (oppervlakte onder ROC curve (AUC) is 0,97). Bij het optimale afkappunt voor uitsluiting van kanker is de sensitiviteit 100% en de specificiteit 90%. In de studiepopulatie wordt dan 13% als positief geclassificeerd met een **positief voorspellende waarde (PV^+) van 26%** en 87% als negatief met een **negatief voorspellende waarde (PV^-) van 100%**. Toepassing van dit model zou aldus 87% "onnodige" invasieve diagnostische procedures kunnen besparen (bij patiënten zonder kanker in 90% van de gevallen). Indien poliepen, welke gerelateerd werden aan het bloedverlies (N=6), toegevoegd worden aan kanker als de uitkomstparameter dan resulteert de logistische regressie-analyse in nagenoeg hetzelfde model. Het onderscheidend vermogen is iets minder met een AUC van 0,92. De maximale sensitiviteit is 93% bij een specificiteit van 84%. Bij een afkappunt optimaal voor exclusie van 'bloedende poliepen en kanker' wordt 79% als negatief geclassificeerd met $PV^+ = 25\%$ en $PV^- = 99{,}5\%$. Er kan geconcludeerd worden dat de predictieve waarden van de overige gebruikelijke en diagnostisch belangrijk geachte symptomen en bevindingen erg beperkt zijn. De uiteindelijke onderzoeksvraag kan grotendeels bevestigend worden beantwoord. **Het is mogelijk gebleken te onderscheiden tussen patiënten die geen darmkanker hebben en degene die een verhoogde kans hebben. Daarmee is het mogelijk effectief en efficiënt onderscheid te maken tussen patiënten bij wie invasiefonderzoek geïndiceerd is vanwege een hoge kans op darmkanker en patiënten bij wie dit niet het geval is vanwege een zeer lage kans op kanker (vrijwel 0%).**
Hoewel deze eerste beschrijving van een predictiemodel voor het onderscheiden tussen patiënten met een zeer lage kans op kanker en een nogal hoge kans bruikbaar lijkt wordt aanbevolen om de uitkomsten in een identieke onderzoekspopulatie in andere huisartspraktijken te toetsen.

7. Predictieve waarden in poliklinische populatie

In de internistische polikliniekpopulatie (study C) is de **a priori kans** (prevalentie) van **ernstige aandoeningen 32%**: IBD 26% en colorectale neoplasmata 6% (hoofdstuk 7).

Een bivariate analyse levert 18 variabelen op die statistisch significante predictieve waarde hebben voor deze aandoeningen.

Logistische regressie analyse (forward stepwise) resulteert in twee modellen met 4 tot 6 variabelen welke een onafhankelijke bijdrage leveren aan het onderscheiden van de aan- of afwezigheid van IBD of neoplasmata. Beide modellen hebben een goed onderscheidend vermogen met een AUC van 0,92 en 0,91.

Het eerste model is gebaseerd op 6 variabelen, afgeleid van alleen anamnestische gegevens: **een veranderd defaecatie patroon (behalve obstipatie), bloed per anum frequenter aanwezig dan slechts éénmaal, bloed waargenomen op het einde van de defaecatie, loze aandrang, (afwezigheid van) misselijkheid en (afwezigheid van) tekenen van depressie.** Bij het tweede model zijn tevens het lichamelijk onderzoek en de laboratoriumtests betrokken: **een veranderd defaecatiepatroon, (afwezigheid van) buikpijn die langer dan twee weken bestaat, (afwezigheid van) abnormale bevindingen (littekens, opgezette buik) bij inspectie van het abdomen en ten minste één positieve van drie hemocculttests.** Het eerste model is beter in het uitsluiten van ernstige ziekte dan het tweede. Bij toepassing van het eerste model met een afkappunt optimaal voor exclusie is de sensitiviteit 100%, de specificiteit 64% en wordt 43% terecht als negatief geclassificeerd, met **PV^+ = 56% en PV^- = 100%**. Bij toepassing van het tweede model voor eenzelfde doel wordt slechts 10% terecht als negatief geclassificeerd (sensitiviteit 100%, specificiteit 17%, PV^+ = 34%, PV^- = 100%) waardoor dus minder patiënten "onnodige" invasieve diagnostische procedures bespaard blijven dan bij het eerste model. Ook de resultaten met deze modellen moeten in een identieke populatie uit andere praktijken getoetst worden. Met enige reserve, vanwege een aantal gemiste testuitslagen, kan geconcludeerd worden dat eenvoudige laboratoriumtests geen predictieve waarde toevoegen aan de anamnese voor het uitsluiten van IBD of neoplasmata.

8. Opbrengst van het onderzoek

Onderzoek in de huisartspraktijk en vooral in een "multipraktijk-setting" hee beperkingen en valkuilen (beschreven in hoofdstuk 8). Desalniettemin is dit d enige manier om voor de huisarts bruikbare informatie te verkrijge betreffende predictieve waarden van symptomen in combinatie met bloedverlie per anum. Het bleek mogelijk om effectief en efficiënt onderscheid te make tussen patiënten bij wie invasief onderzoek geïndiceerd is vanwege een hog kans op darmkanker en patiënten bij wie dit niet geïndiceerd is. Or vergelijkbare gegevens te verzamelen zijn ongeveer drie professionel loopbanen van huisartsen nodig.

Uit de combinatie van de resultaten van studie A en B kan afgeleid worden da in de huisartspraktijk de a priori kans op darmkanker voor patiënten me bloedverlies per anum in de leeftijd van 18-75 jaar en zonder reden voor acut verwijzing 0,8% (9 per 1200) zal zijn.

In studie A is deze kans 3,3% en betreft een groep patiënten die waarschijnlijl vaker een beslissingsprobleem voor de huisarts vormt. Patiënten met eviden onschuldige aandoeningen werden immers vaak niet in de studie opgenomer terwijl dit waarschijnlijk nauwelijks het geval was voor patiënten me darmkanker.

De internistische polikliniekpopulatie is een geselecteerde populatie waarbij de preselectie mede door regionale omstandigheden bepaald is. De bevindingen zijn daarom niet representatief voor verwezen patiënten met bloedverlies per anum in het algemeen. Opvallend is dat in de verwezen populatie van deze studie de a priori kans op darmkanker (3%) erg laag is. De evaluatie van additionele gegevens verzameld in het Academisch Ziekenhuis Maastricht (de grootste leverancier voor studie C: 50% van de totale studiepopulatie), bestaande uit een retrospectieve analyse van patiënten met maligne colorectale tumoren en een analyse van endoscopiegegevens, leidt tot de conclusie dat in onze regio internisten relatief weinig patiënten zien met darmkanker die voldoen aan de studiecriteria. Er werd aangetoond dat het zelfs in de verwezen populatie mogelijk is op basis van anamnestische gegevens een subpopulatie te identificeren die een zeer kleine kans heeft op een ernstige darmaandoening.

Aanbevolen wordt om in de toekomst het onderscheidend vermogen van de gepresenteerde modellen in identieke populaties uit andere praktijken te toetsen.

Onderzoek binnen een populatie ouder dan 75 jaar zal waarschijnlijk resulteren in een hogere a priori kans op darmkanker (en tevens op poliepen en diverticulose) dan in onze populatie en informatie kunnen verschaffen over de voorspellende waarden van de diverse variabelen in de oudere populatie. Verder zou het interessant zijn om verschillen in predictieve waarde van symptomen en bevindingen tussen een huisartsenpopulatie en een omvangrijkere 'verwezen populatie' te evalueren.

Ook wordt aanbevolen de diagnostische waarde van proctoscopie voor gebruik in de huisartspraktijk verder te onderzoeken. Het aantonen van anale en rectale oorzaken van bloedverlies in combinatie met andere symptomen en bevindingen kan bijdragen aan meer effectieve en efficiënte diagnostische strategieën.

Evenzeer is het aanbevelingswaardig verschillen in interpretaties van symptomen tussen gezonde mensen, patiënten en artsen te analyseren ter bevordering van zowel adequate en gerichte bevolkings- en patiëntenvoorlichting als het onderwijs aan medici.

Tenslotte zouden de resultaten van ons onderzoek kunnen bijdragen aan de ontwikkeling van criteria voor de aanvraag van (al dan niet uitgebreid) diagnostisch onderzoek en criteria voor verwijzing van patienten met bloedverlies per anum.

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De volgende huisartspraktijken hebben deelgenomen: *Baarlo:* J Hoefnagels, G Stemkens; *Bocholtz:* E Mom; *Born:* P van Galen, J Flos; *Brunssum:* H Drost, D van Geel, C Hoogervorst, W Nieuwdorp, A de Nooy, A Roos, J Tullens, J van Wanrooy; *Bunde:* J Swaans; *Eindhoven:* M Klomp, S van Rijn; *Eijsden:* H Ausems; *Elsloo:* J Boesten, H Jochems, J Koppes; *St. Geertruid:* H Habets; *Geleen:* M Dirckx, T Hellemons; *Gronsveld:* W Boersma; *Gulpen:* M Hendrickx; *Heerlen:* P van Aubel, P Bots, E Campman, J Dolhain, A Haas, M Hundscheid, H Logister †, J Luger †, A Nurmohamed, A Schlösser, A Sijstermans, B van der Werf, F Zwanikken; *Hoensbroek:* R Brouwers, P van de Voort, F Willemsen; *Horn:* G Saes; *Hulsberg:* C Kroes, J Nijhof; *Kerkrade:* E Hubbers, F Soomers; *Maastricht:* R Croughs, J Dejong, R Heijnen, R de Jong, Th Krebber, R Lauw, A Leenen, J Meijers, P Muyrers, L Nicolaï, C Phaff, H Reinink, J van Rooij, J Theunissen, P Vaissier, F Verhaegh, R van Well, P Wielders, G Wolfs, R Zonneveld, J Zuidweg, V Zwietering; *Mechelen:* H Huyben; *Mheer:* G van Buchem; *Neerbeek:* M Muris, Y van Leeuwen; *Nuth:* F Donders, G Wagenaar; *Obbicht:* M Link; *Roermond:* P van Esser, A de Vries, G Sampers; *Schin op Geul:* M Huyts; *Schimmert:* P Aarts; *Sittard:* M Brassee, P Freens, E Pustjens, P Ruers; *Stein:* A van den Berg, C Vincentie; *Tegelen:* W Beurskens, K Bloemen, T Mangnus, P Nijskens; *Vaals:* S Gerbers, P Heynen, J Meindersma; *Valkenburg:* P van der Ploeg, C Straus; *Venlo:* H Crebolder, H van Dam, R van der Grinten, R Heida, A van Kessel, G de Koning, J Muris, J Vlek; *Voerendaal:* R Panhuysen, P Hulshof.

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Het medisch archief van het azM heeft extra diensten verleend ter verkrijging van gegevens betreffende patiënten met "maligne colorectale tumoren" van zowel internisten als chirurgen.

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Sommige mensen hielpen in meer praktische zin: Mevr. G Wijnands en medewerkers van de afdeling Data-entry van het MEMIC; mevr. P Lemaire, de VAX-operator; Trudie Seegers en Paula Rinkens hebben beiden, in noodgevallen, geholpen bij de dataverwerking; Yvonne Daemen en Anjes Schreurs, boden kortdurend secretariële hulp; Mariëlle van Rijn, Caroline Gortemakers en Hilda Grooters, waren ijverige wetenschapsstagiaires; David Warndorff en Brenda Swaak hielpen bij de vertaling van twee hoofdstukken in het engels; Bob Wilkinson heeft uiteindelijk correcties op het engels taalgebruik van het hele manuscript verzorgd.

De medewerkers van het Diagnostisch Coördinerend Centrum (DCC) Maastricht leverden op velerlei wijze steun en werkplezier.
Isi Vos-Loverix, secretaresse DCC, heeft in momenten van nood en tijdens de laatste afwerkingsfase hand en span diensten verleend. Dankzij haar ijver en nauwgezetheid is de lay-out van de inhoud van dit manuscript tot stand gekomen.
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De projectgroep "Bloedverlies per anum": Geert Blijham (hoogleraar Oncologie), André Knottnerus (hoogleraar Huisartsgeneeskunde), Jean Muris (huisarts-onderzoeker), Peter Pop (hoogleraar Transmurale Geneeskundige Zorg, coördinator DCC), Richard Starmans (huisarts-onderzoeker), Hubert Schouten (statisticus), dank ik voor de goede samenwerking.
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Peter Pop, jouw inzet ter verbetering van rationele diagnostiek en samenwerking tussen huisartsen en specialisten zijn voor mij steeds een inspirerend voorbeeld geweest.
André Knottnerus, je was een stimulerende leermeester en tevens een sublieme begeleider.
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Het is een bekend gegeven dat de vrouw van een promovendus offers brengt. Jan, ik had je eenzelfde lot als partner van een promovenda willen besparen. Te vaak ging dit werk ten koste van onze spaarzame tijd samen. De manier waarop je me steunde waardeer ik zeer.

Curriculum vitae

Gerda Fijten was born on November 1st, 1957 in Maasbracht, the Netherlands. A miller's daughter and the third child of five, she grew up in the village Born. She finished her secondary education, Gymnasium beta, at the Serviam Lyceum in Sittard in 1976. In 1977 she matriculated ("propaedeuse") in Psychology in Tilburg. She studied Medicine at the University of Limburg in Maastricht, where she graduated in 1983. In 1984 she completed her general practitioner training at the University of Limburg. From 1985 to 1986 she attended the one-year Research Training for General Practitioners at the same University.

From September 1986 until September 1992 she worked as a general practitioner investigator at the Diagnostic Coordinating Centre Maastricht, where she carried out the study presented here. Since 1992 she has participated in the SGO (Stimuleringsprogramma Gezondheidszorg Onderzoek/ Health Services Research) Core Training for General Practitioners at the Department of General Practice of the University of Limburg.

In the period from 1983 to 1992 she was also part-time general practitioner in several practices, rural and urban, in the Netherlands. Since 1987 she has been involved in postgraduate education for general practitioners as a member of the WDH (Werkgroep Deskundigheidsbevordering Huisartsen). Since 1991 she has been a member of the Board of the European General Practice Research Workshop (EGPRW).

Appendix

I. Doctor's form, study A and study C

II. Laboratory tests

III. Patient's form

IV. Doctor's form, study B

V. Variables in relation to the several diagnoses

Appendix I. Doctor's form, study A

Diagnostisch Centrum
Rijksuniversiteit Limburg

Onderzoek
BUIKKLACHTEN

Artsenformulier **Artsnr.:**

PERSONALIA:

NAAM : _____ **VOORLETTERS:** _____

GEBOORTEDATUM : _____

	Pat.nr.	
	|_|_|_|_|	1- 4
	Kaartnr.	
	|_|_|	5- 6
	Artsnr.	
	|_|_|	7- 8
BUIKPIJN nee*/ja (* ga door met TRACTUS)	|_|	9
BEGIN pijn/andere symptomen:	|_|_|_|	10-12
(deze klachten periode):		
sinds: _____		
RELATIE MET MAALTIJDEN:		
- hongerpijn nee/ja	|_|	13
- na het eten erger nee/ja	|_|	14
- anders nee/ja, nl. _____	|_|_|	15-16
NACHTELIJKE PIJNEN: nee/ja	|_|	17
UITSTRALING: nee/ja flank/rug/bovenbeen	|_|_|	18-19
PLAATS van pijn: ☐ n.v.t.		
☐ rond navel		
☐ rechts boven		
☐ midden boven		
☐ links boven		
☐ rechts onder		
☐ links onder		
☐ midden onder	|_|_|	20-21
VERERGERENDE FACTOREN:		
- voorover bukken nee/ja	|_|	22
- liggen nee/ja	|_|	23
- andere nee/ja nl. _____	|_|_|	24-25

TRACTUS (deze klachtenperiode)

Eetlust	normaal/afgenomen			|_| 26	
Misselijk	nee/ja	**Braken**	nee/ja	|_| 27	|_| 28
Bloed braken	nee/ja	**Zuurbranden**	nee/ja	|_| 29	|_| 30
Opboeren	nee/ja	**Slikproblemen**	nee/ja	|_| 31	|_| 32
Geelzucht	nee/ja	**Anale pijn**	nee/ja	|_| 33	|_| 34
GEWICHT:	constant/afgevallen/aangekomen			|_| 35	

ONTLASTING:

☐ gewijzigd defaecatiepatroon, nl. _____	|_|_|	36-37
☐ bloed per anum	|_|	38
☐ slijm per anum	|_|	39
☐ loze aandrang	|_|	40
MICTIE AFWIJKEND: nee/ja, nl. _____	|_|_|	41-42

voor vrouwen:

- verergering tijdens/voor menstruatie nee/ja |_| 43
- dyspareunie nee/ja nl. oppervlakkig/diep |_|_| 44-45
- witvloed nee/ja |_| 46

VOORGESCHIEDENIS/FAMILIE

- bekend met buikaandoening nee/ja, nl. _____ |_|_| 47-48
- buikoperaties nee/ja, nl. _____ |_|_| 49-50
- buikaandoeningen in familie nee/ja, nl. _____ |_|_| 51-52
- eerder bloedverlies per anum nee/ja |_| 53
- andere relevante gegevens _____ |_| 54

PSYCHO SOCIALE ANAMNESE

- verkproblemen onbekend/nee/ja |_| 55
- relatieproblemen onbekend/nee/ja |_| 56
- andere relevante problemen nee/ja, nl. _____ |_|_| 57-58

MEDICAMENTEN nee/ja nl. _____ |_|_| 59-60

ROKEN nee/ja nl. _____ per dag |_|_| 61-62

ALCOHOL nee/ja nl. _____ per dag |_|_| 63-64

LICHAMELIJK ONDERZOEK

Sclerae, conjunctivae : normaal / bleek / rood / geel |_| 65

Stemming : normaal / angstig / depressief |_| 66

BUIKONDERZOEK:

- inspectie
  - ☐ opgezet |_| 67
  - ☐ littekens nl. _____ |_|_| 68-69
  - ☐ andere, nl. _____ |_|_| 70-71
  - ☐ geen afvijkingen
  - ☐ niet verricht

- auscultatie
  - ☐ rustige peristaltiek |_| 72
  - ☐ hyper peristaltiek
  - ☐ andere, nl. _____ |_|_| 73-74
  - ☐ niet verricht

- percussie
  - ☐ dempingen (abn.) nl. localisatie: _____ |_| 75
  - ☐ vergrote lever |_|_| 76-77
  - ☐ percussie pijn
  - ☐ geen afwijkingen
  - ☐ niet verricht

		Pat. nr.	
		|_|_|_|_|	1- 4
		Kaartnr.	
		|_|_|	5- 6
		Artsnr.	
		|_|_|	7- 8
- palpatie	☐ aktief spierverzet	|_|	9
	☐ abnormale weerstanden		
	☐ drukpijn nl. lokalisatie: _____	|_|_|	10-11
	☐ andere, nl. _____	|_|_|	12-13
	☐ geen afwijkingen		
	☐ niet verricht		
RECTAAL ONDERZOEK:			
- peri-anale inspectie	☐ haemorroïden ☐ gethromboseerd	|_|_|	14-15
	☐ niet gethromboseerd		
	☐ fissuur		
	☐ fistel		
	☐ eczeem		
	☐ geen afwijkingen		
	☐ niet verricht		
- rectaal toucher	☐ pijnlijke anaalring	|_|_|	16-17
	☐ haemorroïden		
	☐ tumor		
	☐ prostaatafwijkingen ja, nl. _____	|_|_|	18-19
	☐ volle ampula		
	☐ harde ontlasting		
	☐ bloed aan handschoen		
	☐ andere afwijkingen: _____	|_|_|	20-21
	☐ geen afwijkingen		
	☐ niet verricht		
- proctoscopie	☐ haemorroïden bloedend nee/ja	|_|_|	22-23
	☐ proctitis bloedend nee/ja	|_|	24
	☐ tumor bloedend nee/ja	|_|	25
	☐ poliep bloedend nee/ja	|_|	26
	☐ fistel	|_|	27
	☐ andere, nl. _____	|_|_|	28-29
	☐ geen afwijkingen		
	☐ niet verricht		

Voor vrouwen:

VAGINAAL TOUCHER	☐ niet verricht	|_|	30
- uterus	☐ vergroot nl. _____	|_|_|	31-32
	☐ drukpijn herkend nee/ja	|_|	33
	☐ andere afwijkingen _____	|_|_|	34-35
	☐ geen afwijkingen		
	Rechts / Links		
- adnexa	☐ palpabel nee/ja / nee/ja	|_|_|	36-37
VOORLOPIGE DIAGNOSE _____		|_|_|	38-39

BELEID (desgevenst meer dan één antwoord aankruisen)

☐ gerustgesteld	|_|_|	40-41
☐ terugkomen als de klachten niet afnemen		
☐ controle-consult, op welk termijn? _____	|_|_|	42-43
☐ nadere diagnostiek (buiten het voor dit onderzoek "standaard" laboratorium-onderzoek), te weten:		
☐ bloed nl. _____	|_|_|	44-45
☐ röntgen nl. _____	|_|_|	46-47
☐ endoscopie	|_|	48
☐ faeceskweek	|_|	49
☐ andere nl. _____	|_|_|	50-51
☐ geneesmiddelen nl. _____	|_|_|	52-53
☐ verwijzing, specialisme _____	|_|_|	54-55
☐ anders, nl. _____	|_|_|	56-57

VERZEKERINGSVORM: ZF / P \|_\| 58

Appendix II. Laboratory test

```
**************************************************************
*                                                            *
*       PROJECT : NIET-ACUTE BUIKKLACHTEN & BLOEDVERLIES     *
*                                                            *
**************************************************************
```

		Pat. nr. |_|_|_|_|	1- 4
Patiënt	.....	Kaartnr. |_|_|	5- 6
Arts	.....	Artsnr. |_|_|	7- 8
Geboortedatum	.....	9 |_|_|_|_|_|_|	14
Geslacht	.....	|_|	15
Datum consult	.....	16 |_|_|_|_|_|_|	21
Laboratorium te	.....	|_|	22
Datum laboratorium onderzoek	.....	23 |_|_|_|_|_|_|	28
BSE	|__|__|__| mm/uur	|_|_|_|	29-31
Aspect	1. g.b. 2. gesluierd 3. ..... (o.a. geel)	|_|	32
Hb	|__|__.__| mmol/l	|_|_|_|	33-35
Ht	|__.__|__| l/l	|_|_|_|	36-38
Ery's	|__|__.__| pl^{-1}	|_|_|_|	39-41
MCV	|__|__|__| fl	|_|_|_|	42-44
MCH	|__.__|__| fmol	|_|_|_|	45-47
MCHC	|__|__.__| mmol/l	|_|_|_|	48-50
Leuco's	|__|__.__| nl^{-1}	|_|_|_|	51-53
Occultbloed	1e keer neg. - pos. 2e keer neg. - pos. 3e keer neg. - pos.	|_| |_| |_|	54 55 56

Appendix III. Patient's form

Diagnostisch Centrum
Rijksuniversiteit Limburg

Onderzoek
BUIKKLACHTEN

Vragenlijst

Stempel arts:

PERSONALIA:

NAAM : _____ VOORLETTERS: _____

GEBOORTEDATUM: _____

ADRES : _____

POSTCODE : _____

WOONPLAATS : _____

Geachte Mevrouw, Mijnheer,

Bij Uw zojuist afgelegde bezoek aan de arts kwam o.a. ter sprake, dat U last had van buikklachten of bloed bij de ontlasting.

Aan de Rijksuniversiteit Limburg en het Diagnostisch Centrum Maastricht wordt wetenschappelijk onderzoek gedaan naar deze klachten. Ook Uw arts doet mee aan dit onderzoek.

Het doel van dit onderzoek is Uw arts in de toekomst te helpen bij het behandelen van deze klachten. Wij vragen daarvoor Uw medewerking.

U zult merken dat onze vragenlijst lang is. Vele vragen stellen wij om wetenschappelijke redenen, niet omdat we verwachten dat iemand daarvan nu extra veel last heeft. Sommige vragen zullen al door Uw arts gesteld zijn. Toch vragen wij U om ze nog een keer schriftelijk te beantwoorden. Mocht U het moeilijk vinden deze vragen te beantwoorden, dan kunt U aan Uw arts of de assistente vragen om U hierbij te helpen.

Van Uw arts krijgen we, nadat U Uw toestemming voor deelname aan het onderzoek gegeven hebt, de resultaten van het lichamelijk onderzoek, het laboratorium-onderzoek en de uiteindelijke diagnose.
Uw gegevens vallen onder het medisch geheim.
Wij zullen ze zorgvuldig verwerken, waarbij Uw naam en andere persoonlijke gegevens geheim blijven voor buitenstaanders.

Om het verloop van Uw klachten te vervolgen willen wij over één jaar nog eens contact met U opnemen.

Met vriendelijke groet, mede namens Uw arts.

Diagnostisch Centrum Maastricht,
Rijksuniversiteit Limburg
Mevr. Drs. G. Fijten, huisarts
Drs. J. Muris, huisarts
Drs. R. Starmans, arts

TOELICHTING:

- Schrijf alleen in het gedeelte **links** van de vertikale lijn. De kolom rechts van de pagina is nodig voor de verwerking. Wilt U hier niet schrijven.

- Probeer alle vragen te beantwoorden, behalve wanneer is aangegeven dat U een aantal vragen moet overslaan met **bijvoorbeeld** "ga door naar vraag 20".

- Beantwoord de vragen in de aangegeven volgorde, dan kunt U geen vragen vergeten.

- U kunt kiezen uit de voorgedrukte antwoorden; slechts één keuze is mogelijk, tenzij anders aangegeven wordt.

- Geef het door U gekozen antwoord aan door het erbij behorende hokje met cijfer aan te kruisen.

Voorbeeld: [X] 1 ja

[ ] 2 nee

- Indien er een lijn achter een door U gekozen antwoord staat kunt U daarop Uw antwoord toelichten.

Voorbeeld: [X] 1 ja, namelijk brandende pijn

[ ] 2 nee

- Uw informatie wordt strikt vertrouwelijk behandeld.

HARTELIJK DANK VOOR UW MEDEWERKING

VRAGENLIJST VOOR DE PATIËNT MET "NIET-ACUTE" BUIKKLACHTEN EN/OF BLOEDVERLIES UIT DE ANUS

Pat. nr. |_|_|_|_| 1- 4
Kaartnr. |_|_| 5- 6
Artsnr. |_|_| 7- 8

I Algemene gegevens.

1. **Wat is uw geboortedatum?** 9 14
   Dag: _____ maand: _____ jaar: _____ |_|_|_|_|_|_|

2. **Op welke datum vult U deze vragenlijst in?** 15 20
   Dag: _____ maand: _____ jaar: _____ |_|_|_|_|_|_|

3. **Wat is Uw geslacht?**
   [1] vrouw [2] man |_| 21

4. **Bent U:**
   [1] gehuwd of samenvonend |_| 22
   [2] alleenstaand nl.: [ ] nooit gehuwd of samenvonend geweest |_| 23
   [ ] gescheiden
   [ ] veduve/veduvnaar
   [ ] anders: _____ |_|_| 24-25

5. **WERKSITUATIE: wilt U aangeven wat op U van toepassing is.**
   (U kunt desgevenst meer dan één antvoord aankruisen)
   [1] ik heb nu een volledige baan. |_|_| 26-27
   [2] ik heb nu een part-time baan voor .. uren per week. |_|_| 28-29
   [3] ik ben nu verkloos
   [4] ik ben met pensioen/VUT
   [5] ik ben nu arbeidsongeschikt
   [6] ik volg een opleiding
   [7] ik ben huisman, huisvrouw
   [8] anders, namelijk: _____ |_|_| 30-31

6. **Wat was de reden van dit bezoek aan de arts?**
   (omschrijf Uw klachten)
   _____ |_|_| 32-33
   _____
   _____

Indien U géén bloedverlies uit de anus heeft gehad, doorgaan bij III vraag 19.

II **Dit gedeelte gaat over bloedverlies uit de anus.**

7. Hoelang heeft U nu bloedverlies uit de anus? sinds _____ |_|_|_| 34-36

8. Is dit de eerste keer (of eerste periode) in Uw leven dat U bloedverlies uit de anus heeft?

[1] ja |_| 37

[2] nee, hoelang geleden voor de allereerste keer: _____ |_|_|_| 38-40

[3] weet ik niet meer

9. Maakte U zich ongerust over het bloedverlies voordat U naar de huisarts kwam?

[1] ja, omdat _____ |_| 41

[2] nee |_|_| 42-43

10. Aan welke oorzaak dacht U zelf toen U naar de arts ging?
(U kunt desgevenst meer mogelijkheden aankruisen)

[1] aambeien |_|_| 44-45

[2] scheurtje in de anus (bv. kloofje)

[3] ontsteking, darminfectie

[4] uitstulpingen in de darmwand (bv. divertikels)

[5] darmpoliep

[6] darmkanker

[7] andere dan bovengenoemde, namelijk: _____ |_|_| 46-47

11. Hoe vaak is er de laatste weken bloedverlies uit de anus geweest?
(slechts één vakje invullen)

[ ] slechts één keer of zelden |_|_|_| 48-50

[...] keer per dag (aantal invullen) |_|_|_| 51-53

[...] keer per week (aantal invullen) |_|_|_| 54-56

[...] keer per maand (aantal invullen) |_|_|_| 57-59

12. Komt er wel eens bloed zonder ontlasting?

[1] ja |_| 60

[2] nee

13. Hoe is het bloed bij de ontlasting aanvezig?
(meer dan één antvoord aankruisen mag)

- [1] het bloed zit op of rondom de ontlasting — |_| 61
- [2] het bloed is vermengd met de ontlasting
- [3] het bloed zit op het toiletpapier
- [4] weet ik niet
- [5] anders, namelijk: _____ — |_|_| 62-63

14. Wanneer komt het bloed?
(meer dan één antvoord aankruisen mag)

- [1] vóór de ontlasting — |_|_| 64-65
- [2] tijdens de ontlasting
- [3] op het einde van de ontlasting
- [4] na de ontlasting
- [5] zonder ontlasting
- [6] weet ik niet

15. Hoeveel bloedverlies is er meestal per keer?
(het best passende antvoord aankruisen)

- [1] een streepje — |_| 66
- [2] enkele druppeltjes
- [3] een vingerhoedje
- [4] een kopje
- [5] meer dan een kopje

16. Wat is de kleur van het bloed?

- [1] helder rood — |_| 67
- [2] donker rood
- [3] wisselend helder/donker rood

17. Heeft U de laatste weken rommelingen in de buik gehad?

- [1] doorlopend — |_| 68
- [2] iedere dag, maar niet doorlopend
- [3] vaak (1-5 dagen per week)
- [4] af en toe (minder dan één dag per week)
- [5] nooit

18. Is Uw buik de laatste weken opgezet?

- [1] doorlopend — |_| 69
- [2] iedere dag, maar niet doorlopend
- [3] vaak (1-5 dagen per week)
- [4] af en toe (minder dan één dag per week)
- [5] nooit

29. **Wordt U 's nachts wakker van de pijn?**

- [1] ja, (bijna) elke nacht — |_| 42
- [2] ja, soms
- [3] nee

30. **Neemt de pijn toe of ontstaat de pijn als U op Uw rug ligt?**

- [1] ja — |_| 43
- [2] nee

31. **Neemt de pijn toe of ontstaat de pijn als U op Uw linkerzij ligt?**

- [1] ja — |_| 44
- [2] nee

32. **Neemt de pijn toe of ontstaat de pijn als U op Uw rechterzij ligt?**

- [1] ja — |_| 45
- [2] nee

33. **Neemt de pijn toe of ontstaat de pijn vlak vóór het eten?**

- [1] ja, ongeveer .. minuten vóór het eten — |_| 46
- [2] nee — |_|_|_| 47-49

34. **Neemt de pijn toe of ontstaat de pijn na het eten?**

- [1] ja, ongeveer .. minuten na het eten — |_| 50
- [2] nee — |_|_|_| 51-53

35. **Is koffie van invloed op de pijn?**

- [1] de pijn ontstaat of neemt toe na koffie — |_| 54
- [2] de pijn wordt minder of verdwijnt na koffie
- [3] koffie heeft geen invloed op de pijn
- [4] ik drink geen koffie

36. **Zijn frisdranken met "prik" van invloed op de pijn?**

- [1] de pijn ontstaat of neemt toe na frisdranken met prik — |_| 55
- [2] de pijn wordt minder of verdwijnt na frisdranken met prik
- [3] frisdranken met prik hebben geen invloed op de pijn
- [4] ik drink geen frisdranken met prik

37. **Zijn alcoholhoudende dranken van invloed op de pijn?**

- [1] de pijn ontstaat of neemt toe na alcoholhoudende dranken — |_| 56
- [2] de pijn wordt minder of verdwijnt na alcoholhoudende dranken
- [3] alcoholhoudende dranken hebben geen invloed op de pijn
- [4] ik drink geen alcoholhoudende dranken

38. Zijn melk of andere melkprodukten van invloed op de pijn? |_| 57

- [1] de pijn ontstaat of neemt toe na het drinken van melk
- [2] de pijn vordt minder of verdwijnt na het drinken van melk
- [3] melk heeft geen invloed op de pijn
- [4] ik drink geen melk

39. Is sterk gekruid eten van invloed op de pijn? |_| 58

- [1] de pijn ontstaat of neemt toe na sterk gekruid eten
- [2] de pijn neemt af of verdwijnt na sterk gekruid eten
- [3] sterk gekruid eten heeft geen invloed op de pijn
- [4] ik eet geen sterk gekruid eten

40. Is vet eten van invloed op de pijn? |_| 59

- [1] de pijn ontstaat of neemt toe na vet eten
- [2] de pijn vordt minder of verdwijnt na vet eten
- [3] vet eten heeft geen invloed op de pijn
- [4] ik eet geen vet eten

41. Zijn koolsoorten (bv. spruitjes, witte kool) van invloed op de pijn? |_| 60

- [1] de pijn ontstaat of neemt toe na het eten van bepaalde koolsoorten
- [2] de pijn vordt minder of verdwijnt na het eten van bepaalde koolsoorten
- [3] het eten van koolsoorten heeft geen invloed op de pijn
- [4] ik eet geen koolsoorten

42. Is "rauwkost" (bv. groenten, fruit) van invloed op de pijn? |_| 61

- [1] de pijn ontstaat of neemt toe na het eten van *bepaalde rauwkost*
- [2] de pijn vordt minder of verdwijnt na het eten van bepaalde rauwkost
- [3] het eten van rauwkost heeft geen invloed op de pijn
- [4] ik eet geen rauwkost

43. Zijn er andere voedingsmiddelen waardoor de pijn in de buik ontstaat of toeneemt?

- [1] ja, namelijk: _____ |_| 62
- [2] nee |_|_| 63-64

44. Zijn er andere voedingsmiddelen waardoor de pijn vermindert of verdwijnt?

- [1] ja, namelijk: _____ |_| 65
- [2] nee |_|_| 66-67

45. **Heeft U nadat U ontlasting heeft geproduceerd minder pijn in Uw buik?**

- [1] ja, meestal
- [2] ja, soms
- [3] nee, nooit

|_| 68

46. **Heeft U bij het begin van de pijn last van dunne ontlasting?**

- [1] ja, meestal
- [2] ja, soms
- [3] nee, nooit

|_| 69

47. **Moet U bij het begin van de pijn vaker ontlasting produceren?**

- [1] ja, meestal
- [2] ja, soms
- [3] nee, nooit

|_| 70

48. **Heeft U als kind buikpijn gehad?**

- [1] ja, vaak
- [2] ja, zelden
- [3] nee, nooit

|_| 71

IV **Nu volgen nog enkele vragen over Uw ontlasting. Het gaat er daarbij om onderscheid te maken tussen de periode dat U pijn of andere klachten (bv. bloedverlies, veranderde ontlasting) had en de periode dat U géén klachten had.**
Wilt U daarom beide kolommen invullen

Pat. nr. |_|_|_|_| 1- 4
Kaartnr. |_|_| 5- 6
Artsnr. |_|_| 7- 8

	KLACHTEN PERIODE	PERIODE ZONDER KLACHTEN		
49.	**Hoe vaak heeft U dan gemiddeld ontlasting?**	**Hoe vaak heeft U dan gemiddeld ontlasting?**		
	[1] ik heb ... keer per dag ontlasting	[1] ik heb ... keer per dag ontlasting	9 |_|	10 |_|
	[2] ik heb ... keer per week ontlasting	[2] ik heb ... keer per week ontlasting	11-12 |_|_|	13-14 |_|_|
50.	**Mijn ontlasting is dan:**	**Mijn ontlasting is dan:**	15-16	17-18
	[1] normaal, gevormd	[1] normaal, gevormd	|_|_|	|_|_|
	[2] erg hard, keutels	[2] erg hard, keutels		
	[3] zacht, breiig	[3] zacht, breiig		
	[4] waterdun, diarree	[4] waterdun, diarree		
	[5] sterk wisselend (soms hard, soms zacht)	[5] sterk wisselend (soms hard, soms zacht)		
	[6] anders namelijk: _____	[6] anders namelijk: _____	19-20 |_|_|	21-22 |_|_|

De volgende vragen gaan veer over de periode dat U pijn of andere klachten heeft.

51. Aankruisen wat bij U voorkomt
(U mag desgevenst meer mogelijkheden aankruisen)

- [1] slijm bij de ontlasting |_|_|_| 23-25
- [2] slijm uit de anus zonder ontlasting
- [3] duidelijk herkenbare voedselresten bij de ontlasting
- [4] pijn bij het produceren van ontlasting
- [5] rommelingen in de buik
- [6] veel last van winden laten
- [7] een gevoel dat nog niet alle ontlasting weg is als U naar het toilet bent geweest
- [8] 's nachts last van diarree
- [9] het gevoel naar het toilet te moeten zonder dat er ontlasting komt

52. Heeft U de laatste veken teerzvarte ontlasting gehad?

- [1] ja, de laatste maal is .. dagen geleden |_| 26
- [2] nee (ga door met punt V, vraag 54) |_|_| 27-28

53. Had U die teerzvarte ontlasting na het nemen van een bepaald geneesmiddel?

- [1] ja, namelijk: _____ |_| 29
- [2] nee |_|_| 30-31

V In dit gedeelte komen een aantal andere klachten aan de orde. Antvoordt svp met een kruisje in het betreffende vakje.

54. Is Uv eetlust de laatste veken afgenomen?

- [1] ja, ik heb geen zin in eten |_| 32
- [2] ja, ik heb minder zin in eten
- [3] nee

55. Ik heb de laatste veken een afkeer van:
(U kunt desgevenst meer mogelijkheden aankruisen)

- [1] groenten |_|_| 33-34
- [2] vlees
- [3] koffie
- [4] alcoholhoudende dranken
- [5] andere voedingsmiddelen, namelijk: _____ |_|_| 35-36
- [6] ik heb geen afkeer van voedsel

56. **Heeft U de laatste weken een vol gevoel na een kleine portie eten?**

[1] ja |_| 37
[2] ja, soms
[3] nee

57. **Heeft U de laatste weken last van misselijkheid gehad?**

[1] ja, daar heb ik vaak last van |_| 38
[2] ja, daar heb ik af en toe last van
[3] nee

58. **Heeft U de laatste weken moeten overgeven (braken)?**

[1] ja, daar heb ik vaak last van |_| 39
[2] ja, daar heb ik af en toe last van
[3] nee

59. **Heeft U ooit een zuur gevoel (of zure vloeistof) dat omhoog komt in Uw mond na het eten of drinken?**

[1] ja, vaak |_| 40
[2] ja, soms
[3] nee

60. **Heeft U problemen met het doorslikken van eten of drinken?**
(U kunt desgevenst meer antwoorden aankruisen)

[1] ja, eten blijft steken |_|_| 41-42
[2] ja, drinken blijft steken
[3] ja, doet pijn
[4] nee, helemaal niet
[5] anders namelijk: _____ |_|_| 43-44

61. **Heeft U regelmatig een brandend gevoel in de borst, achter het borstbeen?**

[1] ja, bij het eten |_|_| 45-46
[2] ja, bij bukken/liggen
[3] ja, bij _____ |_|_| 47-48
[4] nee, zelden of nooit

62. **Heeft U de laatste weken last van opboeren?**

[1] ja, vaak |_| 49
[2] ja, soms
[3] nee, nooit

63. Heeft U de laatste weken een gevoel of Uw buik opgezet is?

[1]	ja, vaak	|_|	50
[2]	ja, soms		
[3]	nee, nooit		

64. Heeft U de laatste weken last van:

(meer dan één antwoord invullen mag)

[1]	pijn bij de anus	|_|_|	51-52
[2]	jeuk bij de anus		
[3]	een gevoel dat er iets uit de anus puilt		
[4]	nee, ik heb geen van deze klachten		

65. Voelt U zich ziek?

[1]	ja	|_|	53
[2]	nee		

66. Heeft U zelf Uw eetgewoontes veranderd vanwege Uw klachten?

[1]	ja, namelijk: _____	|_|	54
[2]	nee	|_|_|	55-56

67. Wat was Uw gewicht 4 weken geleden en hoeveel weegt U op dit moment?

[ ]	4 weken geleden woog ik ongeveer .... kilo	|_|_|_|	57-59
[ ]	nu weeg ik .... kilo	|_|_|_|	60-62

68. Heeft U temperatuurverhoging gehad gedurende de laatste weken?

[1]	ja - hoeveel bedroeg de temperatuur? ....°C	|_|	63
[2]	nee	|_|_|_|	64-66
[3]	weet ik niet of temperatuur niet gemeten		

69. Gebruikt U geneesmiddelen (ook zetpillen)?

(U kunt desgevenst meer antwoorden aankruisen) \|_\|_\| 67-68

[1]	ja, middelen voor maag of darmen, naam _____	|_|_|	69-70
[2]	ja, laxeermiddelen, laxeerthee, naam _____	|_|_|	71-72
[3]	ja, antistolling (bloedverdunner) naam _____	|_|_|	73-74
[4]	andere middelen, naam _____	|_|_|	75-76
[5]	nee		

Pat. nr. |_|_|_|_| 1- 4
Kaartnr. |_|_| 5- 6
Artsnr. |_|_| 7- 8

70. Rookt U sigaretten, shag, pijp of sigaren?
(U kunt desgevenst meer antwoorden aankruisen) |_|_| 9-10
☐ 1 ja, ongeveer .... sigaretten per dag |_|_| 11-12
☐ 2 ja, ongeveer .... sigaren per dag |_|_| 13-14
☐ 3 ja, ongeveer .... pijpen per dag |_|_| 15-16
☐ 4 nee

71. Drinkt U alcoholhoudende dranken?
(U kunt desgevenst meer antwoorden aankruisen) |_| 17
☐ 1 ja, gemiddeld ongeveer .... glazen per dag |_|_| 18-19
gemiddeld ongeveer .... glazen per week |_|_| 20-21
gemiddeld ongeveer .... glazen per maand |_|_| 22-23
☐ 2 nee, of minder dan 1 glas per maand

72. Heeft U het de laatste weken drukker gehad dan anders?
☐ 1 ja |_| 24
☐ 2 nee

73. Heeft U de laatste weken een moeilijke periode doorgemaakt (afgezien van Uw klachten) of waren er situaties die "zwaar op de maag lagen"?
☐ 1 ja |_| 25
☐ 2 nee

74. Nemen de klachten toe bij stress of spanningen?
☐ 1 ja, namelijk bij _____ |_| 26
☐ 2 nee |_|_| 27-28

75. Heeft U met Uw huidige klachten de laatste weken niet kunnen werken?
☐ 1 ja, ... werkdagen niet kunnen werken in de laatste 3 weken |_| 29
☐ 2 nee |_|_| 30-31
☐ 3 ik werk niet

76. Heeft U buikoperaties ondergaan?
☐ 1 ja, namelijk: (hier operaties vermelden) |_| 32
_____ jaar: _____ |_|_||_|_| 33-36
_____ jaar: _____ |_|_||_|_| 37-40
☐ 2 nee

77. **Heeft één van Uw ouders vaak "buikklachten" gehad?**

[1] ja |_| 41
[2] nee
[3] weet ik niet

78. **Is bij één van Uw ouders ooit bij een onderzoek van buik of darmen een afwijking gevonden?**

[1] ja, namelijk: _____ |_| 42
[2] nee |_|_| 43-44
[3] weet ik niet

79. **Heeft één of meer van Uw broers of zussen vaak buikklachten gehad?**

[1] ja |_| 45
[2] nee
[3] weet ik niet
[4] ik heb geen broers of zussen (ga door met vraag 81)

80. **Is bij één of meer van Uw broers of zussen ooit bij een onderzoek van buik of darmen een afwijking gevonden?**

[1] ja, namelijk: _____ |_| 46
[2] nee |_|_| 47-48
[3] weet ik niet

81. **Heeft U kinderen?**

[1] ja, hoeveel .... |_| 49
[2] nee, (ga door met vraag 83) |_|_| 50-51

82. **Is bij één of meer van Uw kinderen ooit bij onderzoek van buik of darmen een afwijking gevonden?**

[1] ja, namelijk: _____ |_| 52
[2] nee |_|_| 53-54
[3] weet ik niet

83. **Bent U in het afgelopen jaar buiten Europa of in landen aan de Middellandse Zee geweest?**

[1] ja, welke(e) land(en) _____ |_| 55
[2] nee |_|_| 56-57

111. Ik houd van aktie.	juist	?	onjuist	|_| 23
112. Ik kan mijn gewoonten gemakkelijk veranderen.	juist	?	onjuist	|_| 24
113. Tot nu toe is me bijna alles gelukt wat ik wilde.	juist	?	onjuist	|_| 25
114. In een groep mensen houd ik me liever op de achtergrond.	juist	?	onjuist	|_| 26
115. Veranderingen in het weer hebben weinig invloed op mij.	juist	?	onjuist	|_| 27
116. Wanneer ik mijn leven nog eens zou moeten doen, zou ik het net zo doen.	juist	?	onjuist	|_| 28
117. Alleen bij mensen die ik goed ken, voel ik mij op mijn gemak.	juist	?	onjuist	|_| 29
118. Ik kan in korte tijd veel werk doen.	juist	?	onjuist	|_| 30
119. Op andere mensen heb ik weinig invloed.	juist	?	onjuist	|_| 31
120. Ik werk liever alleen dan met een aantal mensen samen.	juist	?	onjuist	|_| 32
121. Als ik op reis zal gaan, voel ik me ontspannen.	juist	?	onjuist	|_| 33
122. Ik werk graag snel.	juist	?	onjuist	|_| 34
123. Ik heb voor veel dingen belangstelling.	juist	?	onjuist	|_| 35
124. Ik kan goed tegen een grapje.	juist	?	onjuist	|_| 36
125. Als ik iets wil bereiken, zet ik meestal door.	juist	?	onjuist	|_| 37
126. Ik ben meestal ergens mee bezig.	juist	?	onjuist	|_| 38
127. Ik heb weinig behoefte aan kontakt met andere mensen.	juist	?	onjuist	|_| 39
128. Als de mensen naar mij kijken, word ik verlegen.	juist	?	onjuist	|_| 40
129. Ik doe mijn werk meestal met plezier.	juist	?	onjuist	|_| 41
130. Ik kan mijn problemen zelf wel aan.	juist	?	onjuist	|_| 42

VIII Bij de volgende vragen zijn vier antwoorden mogelijk. Wilt U een kruisje zetten in het hokje dat op U van toepassing is.

	nooit of een enkele keer	soms	dikwijls	meestal of altijd		
131. Ik voel me neerslachtig en somber.					_|	43
132. 's Morgens voel ik me het best.					_|	44
133. Ik heb huilbuien of het gevoel dat ik ieder moment wel in huilen kan uitbarsten.					_|	45
134. Ik heb moeite met slapen.					_|	46
135. Ik heb evenveel eetlust als een tijdje geleden.					_|	47
136. Ik vind kijken naar, samen zijn of praten met een aantrekkelijke man of vrouw leuk.					_|	48
137. Ik heb het gevoel dat ik magerder word.					_|	49
138. Ik heb last van verstopping.					_|	50
139. Mijn hart klopt sneller dan normaal.					_|	51
140. Ik raak van het minste vermoeid.					_|	52
141. Mijn gedachten zijn even helder als vroeger.					_|	53
142. Ik vind het gemakkelijk om alles te doen wat ik vroeger ook deed.					_|	54
143. Ik ben rusteloos en ongedurig.					_|	55
144. Ik ben hoopvol gestemd over de toekomst.					_|	56
145. Ik ben prikkelbaarder dan gewoonlijk.					_|	57
146. Ik neem gemakkelijk besluiten.					_|	58
147. Ik geloof dat ik nuttig en nodig ben.					_|	59
148. Ik vind mijn leven boeiend.					_|	60
149. Ik denk dat het beter zou zijn als ik dood was.					_|	61
150. Ik doe alle gebruikelijke dingen nog met plezier.					_|	62

Dit was de laatste vraag.

Heeft U alle vragen beantwoord?

Zijn Uw naam en adres, op de voorpagina correct ingevuld?

Vindt U het goed als met U contact wordt opgenomen indien we nog belangrijke vragen hebben n.a.v. het invullen van de vragenlijst? |_| 63

[1] ja
zo ja, wat is Uw telefoonnummer? _____
[2] nee

Geeft U deze vragenlijst af bij Uw arts (of zijn/haar assistente).

HARTELIJK DANK.

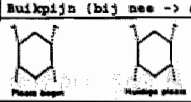
Ruimte voor opmerkingen
(vermeldt zo nodig het nummer van de vraag):

Appendix IV. Doctor's form, study B

BLOEDVERLIES PER ANUM/BUIKPIJN

Naam patiënt: ☐ m ☐ v
Geboortedatum:
Adres:
Woonplaats:
Naam huisarts:
Naam onderzoekend huisarts:

Datum onderzoek:
☐ consult ☐ visite

onb	nee	ja	ANAMNESE
☐	☐	☐	Buikpijn (bij nee -> andere symptomen)
			
☐			Begin pijn: ☐ acuut ☐ geleidelijk
☐			Duur pijn: dagen uren
☐	☐	☐	Pijn ondraaglijk
☐			Aard pijn: ☐ koliek ☐ continu
			☐ anders:
☐	☐	☐	Pijn erger geworden
☐	☐	☐	Verergerende factoren:
☐	☐	☐	Verlichtende factoren:
☐	☐	☐	Nachtelijke pijn
☐	☐	☐	Hongerpijn
☐	☐	☐	Uitstraling
			ANDERE SYMPTOMEN
☐			Gewicht: ☐ afgenomen ☐ constant
			☐ toegenomen
☐	☐	☐	Recent verminderde eetlust
☐	☐	☐	Misselijk
☐	☐	☐	Braken Aspect:
☐	☐	☐	Pyrosis
☐	☐	☐	Ructus
☐	☐	☐	Periode van geel zien
☐	☐	☐	ANALE PIJN
☐	☐	☐	VERANDERD DEFAECATIEPATROON:
☐	☐	☐	Abn. ontlasting: ☐diarree ☐obstipatie
			☐slijm ☐zwart/bloed: weken dagen
			☐ anders:
			ALLEEN VOOR VROUWEN
☐	☐	☐	Abn. menstruatie:
☐	☐	☐	Dyspareunie: ☐ oppervlakkig ☐ diep
☐	☐	☐	Afscheiding:
			VOORGESCHIEDENIS/FAMILIE
☐	☐	☐	Vroegere buikaandoeningen:
☐	☐	☐	Vroegere buikoperaties:
☐	☐	☐	Buikaandoeningen in de familie:
☐	☐	☐	Eerder bloedverlies per anum:
☐	☐	☐	Medicamenten:
☐	☐	☐	Alcohol: per dag
☐	☐	☐	Psychosociale problematiek:
			STATUS PRAESENS
☐	☐	☐	Abn. kleur:
☐	☐	☐	Abn. psych. gesteldheid:
☐	☐	☐	Ziek indruk:

onb	nee	ja	BUIKONDERZOEK
			INSPECTIE
☐	☐	☐	Opgezette buik
☐	☐	☐	Andere afwijkingen:
			AUSCULTATIE
☐	☐	☐	Abn. peristaltiek:
☐	☐	☐	Andere afwijkingen:
			PERCUSSIE
☐	☐	☐	Percussiepijn:
☐	☐	☐	Abn. demping:
☐	☐	☐	Andere afwijkingen:
			PALPATIE
☐	☐	☐	Drukpijn
☐	☐	☐	Loslaatpijn:
☐	☐	☐	Actief spierverzet:
☐	☐	☐	Défense:
			INSPECTIE PERIANAAL GEBIED
☐	☐	☐	Hemorroiden: getromboseerd: ☐ja ☐nee
☐	☐	☐	Overige afwijkingen: ☐fissuur ☐fistel
			☐ eczeem ☐ andere:
			RECTAAL ONDERZOEK
☐	☐	☐	Pijnlijke anaalring
☐	☐	☐	Tumoren:
☐	☐	☐	Afwijkingen prostaat:
☐	☐	☐	Bloed aan handschoen:
☐	☐	☐	Overige afwijkingen: ☐ lage ampulla
			☐ harde ontlasting ☐ andere:
☐	☐	☐	Abn. bevindingen bij proctoscopie:
			VAGINAAL ONDERZOEK
☐	☐	☐	Abn. uterus: ☐ drukpijn
			☐ vergroot:
☐	☐	☐	Drukpijn adnexgebied: ☐links ☐rechts
☐	☐	☐	Andere afwijkingen:
			VOORLOPIGE DIAGNOSE:
			BELEID (meerdere antwoorden mogelijk)
		☐	Geruststelling
		☐	Heronderzoek als klacht niet overgaat
			of toeneemt
		☐	Heronderzoek na dagen, uren
		☐	Aanvullend onderzoek:
		☐	Medicamenten:
		☐	Verwijzing naar:
		☐	Ander:

Table 2. Doctors' forms: history variables in relation to the diagnostic outcome.with rectal. Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Change in bowel habit y/n missings 6								
1. diarrhoea**	22	4	9	0	5	9	5	68
2. variously	16	6	0	0	6	6	6	76
3. more frequently***	40	13	2	5	7	10	10	53
constipation	26	0	0	4	12	0	15	69
other	5	0	0	20	0	0	60	20
together 1+2+3***	78	9	4	3	6	9	8	62
no change***	154	1	2	5	3	1	29	59
Abdominal pain** missings 8								
yes	135	4	2	5	6	2	31	50
no	126	1	3	4	4	4	14	70
Pain at night** missings 53	50	0	2	2	4	10	14	68
Appetite decreased** missings 3	42	2	2	0	5	12	2	77
Nausea** missings 3	68	2	0	3	4	7	10	74

Tabel 2 continued

Vomiting missings 6	17	0	0	0	0	6	17	77
Anal pain missings 9	101	5	3	5	4	2	28	53
Weight loss[***] missings 6	42	10	2	7	0	5	7	69
Mucous discharge[****] missings 4	87	5	4	8	10	7	13	53
Tenesmus[*] missings 4	59	2	0	8	8	7	17	58
Previous history missings 18 anal, colorectal disorder	8	0	0	0	0	0	25	75
History of abdominal surgery missings 30	39	3	3	3	5	0	20	66
Family history of abdominal disorders missings 45	83	0	4	4	4	2	32	54
Previous period of rectal bleeding[**] missings 4	96	0	3	4	3	2	31	57
Problems related to work missings 27	38	0	8	3	5	3	21	60
Relational problems missings 25	20	0	5	5	0	5	10	75

Tabel 2 continued

Medication use								
missings 17								
no	102	5	2	4	1	3	24	61
treatment for haemorrhoids, colitis, diarrhoea or obstipation	9	0	0	0	11	0	44	45
other drugs	141	3	3	6	6	3	18	61
Smoking > 1/day	86	2	2	4	1	1	19	71
missings 23								
Alcohol > 2 glasses/day	0							
missings 25								

Table 3. Doctors' forms: physical examination variables in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Sclerae pale	6	17	17	0	0	0	17	49
missings 10								
Mood**								
missings 12								
anxious/depressive	34	3	6	12	3	9	12	55
normal	223	3	1	4	5	2	24	61
Abdominal inspection								
missings 5								
not done	27	0	4	11	0	0	30	55
abnormality	47	4	2	6	2	2	21	63
no abnormality	190	4	2	3	6	4	21	60
Abdominal auscultation**								
missings 5								
not done	55	5	2	4	9	2	29	49
abnormality	28	0	4	14	4	14	11	53
no abnormality	181	3	2	3	3	2	22	65
Abdominal percussion								
missings 5								
not done	53	4	4	4	9	2	26	51
abnormality	7	0	0	0	0	0	29	71
no abnormality	204	3	2	5	3	3	21	63

Table 3 continued

Abdominal palpation								
missings 5								
not done	36	3	3	8	6	0	31	49
abnormality	103	0	3	3	4	3	15	72
no abnormality	125	6	2	5	5	4	25	53
Perianal inspection y/n								
missings 6								
not done*	34	3	6	0	3	3	6	79
haemorrhoid	71	3	1	6	1	1	28	59
fissure***	29	0	0	3	7	0	55	35
fistula	1	0	0	0	0	0	0	100
eczema*	17	18	0	6	6	0	18	52
no abnormality	118	2	2	6	7	5	17	61
Rectal palpation y/n								
missings 5								
not done	56	2	5	2	4	4	14	69
haemorrhoid	20	10	0	0	0	0	25	65
tumour***	1	100	0	0	0	0	0	0
pain*	42	2	0	5	7	0	38	48
prostate abnormality**	2	50	0	0	0	0	50	0
others	19	0	0	5	0	11	16	68
normal	122	3	2	5	5	3	22	60
Proctoscopy y/n								
missings 9								
not done***	215	3	2	4	3	2	19	67
haemorrhoid	13	0	0	8	8	8	46	30
proctitis***	11	0	0	27	46	0	18	9
tumour***	2	0	50	50	0	0	0	0
other	6	0	0	0	0	0	50	50
fissura	0							
normal***	15	13	0	0	0	20	33	34

Table 4. Doctors' forms: management (at the end of the first consultation) in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Preliminary diagnosis** (12 df) missings 48								
fissura ani	27	0	0	0	4	0	59	37
malignant disease	7	29	14	14	0	0	0	43
others or?	187	3	3	5	5	3	20	61
Further diagnostic workup** missings 14	108	6	3	6	6	6	14	59
blood (other than protocol)	24	4	0	0	4	12	12	68
röntgen colon*	26	8	0	15	4	4	8	61
endoscopy****	35	9	6	9	6	0	14	56
faecal culture****	13	0	0	8	15	31	0	46
Reassurance** missings 14	76	0	0	3	1	3	29	64
Controle appointment* missings 14	86	5	2	4	8	7	16	58
Medication* missings 14	96	1	0	3	5	2	28	61
Referral* (18 df) missings 14								
none	232	3	2	4	4	3	22	62
to internist	14	14	7	14	7	0	7	51
to surgeon	8	12	12	12	13	0	38	13
to others	1	0	0	0	0	0	100	0

Table 5. Patients' forms: answers on questions regarding bleeding (variables) related to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Reason for encounter**								
missings 24								
rectal bleeding	145	3	1	8	6	3	28	51
others (e.g. pain)	100	1	3	2	3	2	12	77
Length of history of bleeding								
missings 53								
<2 weeks	59	2	5	3	3	3	22	62
≥2 weeks <month	47	6	0	9	4	2	30	49
≥1 month ≤1 year	66	2	1	9	9	1	23	55
>1 year	24	4	0	4	4	4	33	51
unknown	20	0	0	0	0	0	5	95
First episode**								
missings 27								
yes	118	4	2	9	5	3	16	61
no	74	1	3	3	4	3	31	55
unknown	50	0	0	0	6	0	24	70
Previous episode >1 year ago	56	2	4	4	4	2	29	55
missings 29								
Anxiety because of bleeding	149	3	3	6	4	2	27	55
missings 27								

Table 5 continued

Worries because								
missings 37								
severe complaint(s)	10	0	0	10	10	0	50	30
others (e.g. fear for serious disease)	121	3	3	6	4	3	26	55
Considered cause cancer	54	0	6	7	6	0	28	53
missings 28								
Frequency of bleeding**								
missings 30								
once or seldom	100	1	2	1	2	4	21	69
more than once	139	4	2	9	7	1	23	55
Bleeding without stool	49	4	2	10	10	2	27	45
missings 26								
Where noticed** (24 df)								
missings 27								
unknown	27	0	0	4	4	0	15	77
on the stool only	40	5	2	5	2	0	18	68
mixed with stool	14	14	14	7	0	0	0	65
on the paper only	39	0	3	5	0	5	31	56
others/combinations	122	1	0	6	8	3	25	57
When noticed y/n								
missings 25								
unknown*	35	0	3	6	9	9	11	62
before defaecation****	45	7	4	4	2	0	38	45
during defaecation	121	2	2	7	6	1	23	59
end of defaecation	51	0	0	4	6	2	27	61
after defaecation**	60	2	2	3	2	3	38	50
without	22	5	0	9	9	0	41	36

Table 5 continued

Amount of blood seen								
missings 29								
unknown	20	0	0	0	0	0	5	95
streak	41	0	2	0	7	5	15	71
drops	87	5	2	6	5	1	29	52
thimble	82	2	0	10	6	4	21	57
a cup	10	0	0	0	0	0	40	60
more than a cup	0							
Color** (18 df)								
missings 30								
unknown	20	0	0	0	0	0	5	95
bright red	141	4	1	4	4	3	26	58
dark red	35	3	3	6	3	3	11	71
variously	43	0	2	12	14	2	26	44

Table 6. Patients' forms: answers on questions regarding other complaints (variables) related to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Rumbles** (30 df)								
missings 27								
unknown	20	0	0	0	0	0	5	95
continiously	21	5	5	19	5	0	14	52
every day	63	5	2	5	6	6	17	59
often	26	0	0	0	0	4	11	85
sometimes	68	3	3	4	4	2	27	57
never	44	0	0	7	9	0	41	43
Abdominal distension** (30 df)								
missings 27	20	0	0	0	0	0	5	95
unknown	27	0	4	4	11	0	11	70
continiously	29	7	0	17	10	0	17	49
every day	22	0	0	5	0	9	18	68
often	58	2	3	0	2	2	29	62
sometimes	86	3	1	7	6	3	28	52
never								
Abdominal pain**	152	1	2	4	3	3	16	71
Duration abdominal pain >2 week	109	1	2	6	4	4	17	67
missings 13								

Table 6 continued

Frequency of bowel movements								
missings 38								
<2/week	1	0	0	0	0	0	0	100
3-10/week	127	2	3	5	4	1	24	61
11-21/week	67	3	0	5	8	4	28	52
>21/week	36	0	3	11	6	6	6	68
Change in bowel frequency								
missings 48								
more frequent	70	3	1	10	7	6	21	52
less frequent	28	0	4	4	7	0	14	71
not changed	123	2	2	4	4	2	24	62
Stool consistency y/n								
missings 31								
normal**	58	7	5	5	4	0	28	51
hard	25	0	0	0	8	0	36	56
soft	54	2	2	7	6	2	24	57
watery	21	5	5	0	0	5	14	71
variously	98	0	1	6	5	4	16	68
Other complaints y/n								
missings 40								
mucous with stool*	86	4	2	9	9	4	17	55
mucous discharge*	34	3	0	12	12	6	23	44
undigested food in stool	46	2	0	4	4	2	20	68
painful motion	73	3	3	4	1	3	25	61
rumbles*	116	2	2	6	5	3	12	70
flatulence	112	2	3	6	8	3	18	60
incomplete evacuation	111	3	3	4	2	4	21	63
diarrhoe at night**	9	0	0	11	0	22	11	56
tenesmus	93	2	1	7	5	2	19	64
Black stool	23	2	2	5	5	2	21	63
missings 26								

Table 6 continued

Appetite decreased[***] missings 26	59	2	0	3	5	5	9	76
Nausea[***] missings 28	105	1	1	5	4	5	13	71
Vomiting missings 26	25	0	0	4	4	4	20	68
Abdominal distension missings 25								
often	66	4	1	5	8	3	11	68
sometimes	87	0	2	5	2	2	24	65
no	91	3	2	7	5	2	28	53
Anal symptoms y/n missings 24								
anal pain*	87	0	5	7	2	1	25	60
pruritis ani	91	1	1	9	5	1	20	63
feeling of anal protrusion	53	4	2	6	4	0	23	61
no anal symptoms	90	3	1	2	7	4	19	64
Feeling ill[***] missings 27	66	0	3	4	3	6	8	76
no	176	3	2	6	6	1	27	55
Change in eating habit missings 26	86	5	1	5	4	3	16	66
>3 kg weight loss*	27	11	0	7	0	0	7	75
Fever missings 27	15	0	0	7	7	13	20	53

Table 7. Patients' forms; answers on questions regarding intoxications, risk factors and psychological factors (variables) related to the diagnostic outcome.
Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Medication intake y/n missings 29								
for gastrointestinal disorder	42	0	5	5	9	5	12	64
laxantives	17	0	0	0	6	0	35	59
anticoagulantia	8	0	0	0	12	0	25	63
others	75	1	0	5	5	3	27	59
Smoking >1/day sigarets, sigares or pipe missings 22	101	4	2	5	2	3	16	68
Alcohol >2 glasses/day missings 25	28	0	4	4	0	7	29	56
Busy times missings 25	69	1	3	10	4	1	17	62
Stressful times missings 23	88	1	3	8	2	1	22	63

Table 7 continued

History of abdominal surgery (including haemorrhoid operation) missings 26	81	1	2	7	3	3	19	65
Family history of abdominal cancer or polyps	19	0	0	0	5	0	26	69
Visits abroad (tropical/ mediterranean countries) missings 25	56	2	4	2	5	2	30	55
General health state[***] (psychobiological stress) missings 39								
VOEG score ≤3	69	4	1	12	9	1	29	44
VOEG score >3	161	1	1	3	4	3	19	69
Self-esteem NPV SI missings 32								
low ≤21	150	3	3	5	3	3	20	63
normal	87	0	0	6	7	2	25	60
Social inadequacy NPV ZW missings 29								
normal	206	2	2	6	4	2	22	62
high >17	34	3	6	3	6	3	15	64
Signs of depression missings 46								
ZUNG ≤40	163	2	2	6	5	2	25	58
ZUNG >40	60	0	2	5	3	3	8	79
ZUNG >50	14	0	0	0	7	7	0	86

Table 8. Laboratory tests according to the study protocol (variables) in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=269	3	2	5	5	3	22	60
Haemoglobin mmol/l**								
missings 41								
normal	214	2	1	5	5	3	22	62
low ♀<7.5, ♂<8.5	14	14	7	0	0	0	14	65
ESR mm/h								
missings 44								
normal	202	1	1	5	5	1	23	64
high ♀>28, ♂>12****	23	9	4	9	4	13	17	44
high ≥30****	12	17	8	8	8	0	17	42
White blood cells count**								
missings 50								
normal	194	1	1	5	5	3	23	62
high $>10^9$/l	25	12	0	4	8	4	12	60
Haemoccult** (18 df)								
missings 46								
3 x negative	182	1	2	3	4	2	23	65
one positive	24	4	4	0	13	4	33	42
two positive	5	0	0	0	0	20	0	80
three positive	12	8	0	25	8	0	17	42

Appendix V, Study C.

Table 9. Patients' age, gender and insurance variables in relation to the diagnostic outcome.
Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Age (in 1988)* (30 df)								
18-39 year	54	2	2	20	11	4	15	46
40-44 year	15	0	0	20	7	0	27	46
45-49 year	4	0	0	50	0	0	25	25
50-54 year	11	0	9	0	0	18	36	37
55-59 year	4	0	25	0	0	50	25	0
≥ 60 year	16	12	0	19	6	12	12	39
<40 year	54	2	2	20	11	4	15	46
≥40 year	50	4	4	16	4	12	24	36
<50 year**	73	1	1	22	10	3	18	45
≥50 year	31	6	6	10	3	19	23	33
<60 year	88	1	3	18	8	7	21	42
≥60 year	16	12	0	19	6	12	12	39
Gender								
female	54	4	2	18	9	11	15	41
male	50	2	4	18	6	4	24	42
Insurance**								
missings 22								
sick fund	69	1	1	16	6	9	25	42
privat	13	15	8	31	15	0	8	23

Table 10. Doctors' forms: history variables in relation to the diagnostic outcome.
Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Change in bowel habit y/n missings 2								
1. diarrhoea***	14	0	0	42	0	29	0	29
2. variously	15	0	7	7	20	7	20	39
3. more frequently*	12	8	8	34	8	0	17	25
constipation	11	0	9	0	18	0	18	55
other	3	0	0	67	0	0	0	33
together 1+2+3**	43	7	5	25	9	12	12	30
no change	48	0	2	13	4	6	27	48
Abdominal pain* missings 1								
yes	78	1	4	19	8	10	14	44
no	25	8	4	16	8	0	36	32
Pain at night missings 14	27	4	0	15	4	18	11	48
Appetite decreased missings 1	14	0	0	43	7	14	14	22
Nausea missings 1	23	0	0	13	4	13	26	44
Vomiting*** missings 1	8	0	0	0	0	38	50	12

Table 10 continued

Anal pain missings 1	22	0	5	9	9	0	36	41
Weight loss missings 1	28	4	0	25	4	14	18	35
Mucous discharge missings 0	41	2	2	29	10	2	20	35
Tenesmus missings 0	35	6	6	20	14	6	20	31
Previous history missings 12								
no	72	3	4	18	7	6	19	43
anal, colorectal disorder	1	0	0	0	0	0	0	100
other	19	5	0	5	16	11	26	37
Family history of abdominal disorders missings 15	32	0	3	22	9	9	22	35
Previous period of rectal bleeding missings 3	27	0	0	22	11	7	22	37
Medication use missings 3								
no	49	2	6	16	6	4	18	48
treatment for haemorrhoids, colitis, diarrhoea or obstipation	7	14	0	44	14	0	14	14
other drugs	45	2	0	18	9	13	22	36
Smoking > 1/day missing 1	42	5	5	10	2	7	26	45
Alcohol > 2 glasses/day missing 1	0							

Table 11. Doctors' forms: physical examination variables in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Sclerae								
missings 1								
pale	4	0	0	25	25	0	50	0
not pale	99	3	3	19	7	8	18	42
Mood								
missings 5								
anxious/depressive	13	0	0	15	0	8	23	54
normal	86	3	3	20	9	8	19	38
Abdominal inspection*								
missings 1								
abnormality	26	0	8	8	0	19	23	42
no abnormality	77	4	1	22	10	4	18	41
Abdominal auscultation								
missings 1								
abnormality	14	3	3	19	8	7	20	40
no abnormality	89	0	0	11	7	11	11	50
Abdominal percussion								
missings 1								
abnormality	1	0	0	0	0	0	100	0
no abnormality	102	3	3	17	8	8	19	42

Table 11 continued

Abdominal palpation								
missings 1								
abnormality	50	0	2	12	6	12	18	50
no abnormality	53	6	4	24	9	4	21	32
Perianal Inspection y/n								
missings 2								
not done	1	0	0	0	0	0	0	100
haemorrhoid	12	0	0	17	0	0	25	58
fissure	2	0	0	0	0	0	50	50
fistula	1	0	0	0	0	0	0	100
eczema	0							
no abnormality	85	3	3	19	9	9	18	39
Rectal palpation y/n								
missings 1								
not done	6	0	0	17	0	0	0	83
haemorrhoid	5	0	0	0	0	0	40	60
tumour***	1	100	0	0	0	0	0	0
pain	5	0	0	0	20	0	60	20
prostate abnormality	0							
others	9	11	0	22	11	11	11	34
normal	73	0	4	20	7	10	19	40
Proctoscopy y/n								
missings 6	88	3	2	21	7	9	19	39
not done	1	0	0	0	0	0	0	100
haemorrhoid	1	0	0	0	100	0	0	0
proctitis***	0							
tumour	0							
polyp(s)	3	0	0	33	0	0	33	34
other	0							
fissura	5	0	0	0	0	0	20	80
normal								

Table 12. Doctors' forms; management (at the end of the first consultation) variables in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Preliminary diagnosis** (12 df)								
missings 8	3	0	0	0	0	0	67	33
fissura ani	3	67	0	0	0	0	0	33
malignant disease	90	0	2	20	9	8	19	42
others or ?								
Further diagnostic workup								
missings 2								
blood (other than protocol)	18	11	0	17	0	6	17	49
röntgen colon	11	18	0	9	0	18	9	46
endoscopy	72	4	4	22	8	7	21	34
faecal culture	8	0	0	12	12	12	12	52
Reassurance	41	0	5	7	7	7	20	54
missings 2								
Controle appointment	50	4	4	22	8	10	20	32
missings 2								
Medication	22	0	0	36	14	5	9	36
missings 2								
Referral** (12df)								
missings 2								
none	100	2	3	19	8	8	20	40
to surgeon	1	100						
to gynaecologist	1							100

Table 13. Patients' forms: answers on questions regarding bleeding (variables) related to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

Variables		Diagnoses ranked in order of severity						
		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Reason for encounter**								
missings 4								
rectal bleeding	64	5	5	22	12	5	22	29
others (e.g. pain)	36	0	0	11	0	14	17	58
Length of history of bleeding								
missings 23								
<2 weeks	4	0	0	25	0	50	25	0
≥2 weeks <month	8	12	0	12	12	12	12	40
≥1 month ≤1 year	52	4	4	23	8	2	25	35
>1 year	16	0	6	19	19	6	12	38
unknown	1	0	0	0	0	0	0	100
First episode* (12 df)								
missings 10								
yes	41	5	7	17	5	12	22	32
no	36	3	0	30	17	3	22	25
unknown	17	0	0	0	0	6	18	76
Previous episode of bleeding** (12 df)								
missings 10								
1st >1 year ago	29	0	0	37	17	3	24	17
1st ≤ 1 year	7	14	0	0	14	0	14	58
not applicable (first time)	58	3	5	12	3	10	21	46

Table 13 continued

Anxiety because of bleeding								
missings 10								
yes	62	3	3	23	11	5	18	37
no	32	3	3	12	3	12	28	39
Worries because								
missings 18								
severe complaint(s)	14	7	0	7	21	7	21	37
others (e.g. fear for serious disease)	34	3	6	29	6	3	21	32
Considered cause cancer	19	5	5	21	16	10	16	27
missings 11								
Frequency of bleeding**								
missings 9								
once or seldom	31	0	7	0	3	13	32	45
more than once	64	5	2	28	11	5	16	33
Bleeding without stool								
missings 9								
yes	34	6	3	18	18	9	18	28
no	61	2	3	20	3	7	23	42
Where noticed y/n								
missings 9								
unknown	4	0	0	25	0	25	0	50
on the stool only	9	0	0	22	0	22	11	45
mixed with stool only	4	0	0	50	0	25	0	25
on the paper only	11	9	0	0	9	0	55	27
others/combinations	67	3	5	19	10	5	19	39
When noticed y/n								
missings 11								
unknown	5	0	0	40	0	20	20	20
before defaecation	25	4	4	16	12	8	24	32
during defaecation	56	4	0	20	9	7	20	40
end of defaecation*	30	0	7	23	17	7	13	33
after defaecation	23	0	0	22	13	0	30	35
without	15	0	0	17	38	14	20	11

Table 13 continued

Amount of blood seen								
missings 12								
unknown	1	0	0	0	0	0	0	100
streak	17	0	6	18	0	0	23	53
drops	37	3	5	24	5	8	24	31
thimble	33	6	0	15	18	12	15	34
a cup	3	0	0	0	0	0	33	67
more than a cup	1	0	0	0	0	0	0	100
Color								
missings 11								
bright red	58	3	5	12	9	9	19	43
dark red	14	0	0	29	7	7	36	21
variously	21	5	0	33	9	5	19	29

Table 14. Patients' forms: answers on questions regarding other complaints (variables) related to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Rumbles								
missings 11								
continiously	12	0	0	17	0	17	25	41
every day	28	0	0	25	7	11	18	39
often	20	10	5	10	10	0	15	50
sometimes	23	0	4	22	13	8	31	22
never	10	10	10	20	10	0	20	30
Abdominal distension								
missings 11								
continiously	11	9	9	28	0	18	18	18
every day	12	0	0	17	8	0	17	58
often	18	6	6	11	17	0	6	54
sometimes	27	4	4	18	7	7	26	34
never	25	0	0	24	8	12	28	28
Abdominal pain								
missings 1								
yes	75	1	3	17	7	9	16	47
no	28	7	4	21	11	0	28	29
Duration abdominal pain**								
missings 8								
≤2 week	29	7	3	28	10	0	28	24
>2 week	67	2	3	13	8	12	13	49

Table 14 continued

Frequency of bowel movements (18 df)								
period with complaints								
≤2/week	3	0	0	0	0	0	33	67
3-10/week	46	0	0	9	11	11	24	45
11-21/week	25	8	8	12	8	4	20	40
>21/week	27	4	4	40	4	7	11	30
period without complaints*								
missings 6								
≤2/week	1	0	0	0	0	0	0	100
3-10/week	70	3	4	14	10	9	17	43
11-21/week	25	0	0	32	0	8	28	32
>21/week	2	50	0	0	0	0	0	50
Change in bowel frequency** (12 df)								
missings 6								
more frequent	49	6	6	31	6	4	10	37
less frequent	13	0	0	0	8	8	15	69
not changed	36	0	0	8	8	14	33	37
Stool consistency y/n								
missings 4								
normal	12	0	0	0	17	8	25	50
hard	7	0	0	0	0	0	29	71
soft	30	3	3	23	10	0	30	31
watery*	12	8	8	42	0	0	8	34
variously	47	2	2	15	6	15	13	47
Other complaints y/n								
missings 8								
mucous with stool*	49	0	2	29	12	8	16	33
anal mucous discharge	23	0	4	22	13	4	22	35
undigested food in stool	23	0	0	26	4	9	17	44
painful motion	32	3	3	19	6	9	9	51
rumbles	66	3	1	17	8	9	20	42
flatulence	57	3	3	16	11	11	19	37
incomplete evacuation	52	6	4	17	11	6	19	37
diarrhoe at night	8	12	0	25	0	25	12	26
tenesmus	49	4	4	18	12	6	20	36

Table 14 continued

Black stool missings 5	9	0	0	0	11	0	22	67
Appetite decreased missings 3	25	4	0	16	4	8	20	48
Nausea missings 3	56	2	0	9	9	9	18	53
Vomiting missings 5	12	0	0	0	8	25	17	50
Abdominal distension missings 4 often sometimes no	 31 45 24	 3 4 0	 3 4 0	 10 20 25	 7 9 8	 3 9 13	 13 20 25	 61 34 29
Anal symptoms y/n missings 3 anal pain pruritus ani feeling of anal protrusion no anal symptoms	 26 35 17 41	 0 0 0 7	 0 3 0 5	 15 20 6 19	 8 6 18 5	 4 9 18 10	 19 26 12 17	 54 36 46 37
Feeling ill missings 5	29	3	0	21	7	14	7	48
Change in eating habit missings 4	38	3	3	8	10	8	18	50
>3 kg weight loss missings 1	18	6	0	17	6	22	17	33
Fever missings 4	9	0	0	11	0	33	22	34

Table 15. Patients' forms: answers on questions regarding intoxications, risk factors and psychological factors (variables) related to the diagnostic outcome.
Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Medication intake y/n missings 4								
for gastrointestinal disorder	26	8	4	27	11	8	11	31
laxantives	8	0	12	12	0	0	12	64
anticoagulantia	4	0	0	0	25	25	0	50
others	40	5	0	10	10	15	22	38
Smoking > 1/day sigarets, sigares or pipe missings 3	42	5	5	9	2	5	26	48
Alcohol > 2 glasses/day missings 3	9	0	0	11	11	11	33	34
Busy times missings 3	20	5	0	15	5	5	30	40
Stressful times missings 5	28	4	0	14	21	7	18	36
History of abdominal surgery (including haemorrhoid operation) missings 4	31	6	6	13	3	16	20	36

Table 15 continued

Family history of abdominal cancer or polyps missings 24	16	6	6	25	6	6	25	26
Visits abroad (tropical/ mediterranean countries) missings 5	25	0	4	16	12	4	20	44
General health state (psychobiological stress) missings 7								
VOEG score >3	77	4	4	13	6	9	21	43
Self-esteem low missings 9								
NPV SI ≤21	57	2	3	19	7	7	25	37
Social inadequacy missings 10								
NPV ZW >17	14	7	7	14	0	14	7	51
Signs of depression missings 16								
ZUNG ≤40	69	1	3	20	12	3	26	35
ZUNG >40**	19	0	5	5	0	21	11	58
ZUNG >50*	7	0	14	0	0	29	0	57

Table 16. Laboratory tests according to the study protocol (variables) in relation to the diagnostic outcome. Row percentages of several diagnoses related to rectal bleeding per variable.

		Diagnoses ranked in order of severity						
Variables		[1]cancer	[2]polyp	[3]colitis	[4]proctitis	[5]infection/ diverticulosis	[6]anal cause	[7]unknown cause
	number	%	%	%	%	%	%	%
Total	N=104	3	3	18	8	8	19	41
Haemoglobin mmol/l								
missings 5								
normal	86	3	3	19	7	7	20	41
low ♀<7.5, ♂<8.5	13	0	0	23	15	15	15	32
ESR mm/h								
missings 5								
normal	83	2	4	13	10	6	20	45
high ♀>28, ♂>12***	16	6	0	50	0	19	12	13
high ≥30***	9	11	0	45	0	22	11	11
White blood cells count								
missings 7								
normal	88	3	3	16	9	7	19	43
high $>10^9$/l	9	0	0	45	0	11	22	22
Haemoccult** (18 df)								
missings 16								
3 x negative	59	2	2	3	5	5	24	59
one positive	7	0	0	71	29	0	0	0
two positive	11	0	18	46	9	9	9	9
three positive	11	9	0	37	9	18	18	9