

ORIGINAL ARTICLE

Iron deficiency anaemia in general practice: clinical outcomes over three years and factors influencing diagnostic investigations

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Background: Iron deficiency anaemia (IDA) may be a sign of significant gastrointestinal disease, and delayed diagnosis may result in chronic morbidity. Studies in patients referred to hospital for investigation of their anaemia have shown that 5%–15% have a gastrointestinal cancer but there are few studies of patients presenting to primary care. Factors influencing further investigation in these patients have not previously been identified.

Patients and methods: A cohort of patients presenting to their general practitioners (GPs) with IDA was identified and clinical outcomes recorded. Logistic regression was used to determine which factors influenced GPs to investigate the anaemia.

Results: 43% of patients had investigations within three months and serious pathology was found in 30% of these; 13% of patients were considered unfit for further investigation and 8% refused to have any. Independent predictors of non-investigation were a mild anaemia (odds ratio (OR) 0.38, confidence interval (CI) 0.23 to 0.61, $p < 0.001$), female gender (OR 0.49, CI 0.3 to 0.8, $p = 0.004$), a previous history of anaemia (OR 0.39, CI 0.24 to 0.64, $p < 0.001$), and age < 65 years (OR 0.44, CI 0.26 to 0.74, $p = 0.002$). During the entire study period gastrointestinal cancer was diagnosed in 48 patients (11%); 17% of men had colorectal cancer. Of 263 patients alive at 12 months without a confirmed diagnosis, 113 (43%) had recurrent or persistent anaemia during the study period.

Conclusion: Although the overall prevalence of gastrointestinal cancer in patients presenting to primary care is similar to that seen in secondary care, the diagnosis may be delayed due to lack of appropriate investigations resulting in significant morbidity.

Iron deficiency anaemia (IDA) resulting from gastrointestinal bleeding is a common feature of many gastrointestinal conditions, several of which may be asymptomatic, including tumours of the upper and lower bowel.¹ In addition, IDA is now one of the most common presenting features of coeliac disease.² It has thus become standard practice to recommend investigation of IDA to establish a cause, although nearly a fifth of patients may not have an underlying cause found in spite of intensive investigation.³ Investigations are often unpleasant and demanding on patients who therefore need to be persuaded of the reason for the tests.

The majority of studies of the outcome of episodes of IDA have been performed in patients who have been referred to hospital for further investigation.^{4–9} Our community based study has shown that fewer than half the patients presenting to their general practitioner (GP) with IDA will be investigated and a fifth will either be unfit or unwilling for further tests.¹⁰

We have therefore investigated the factors that influenced the management of these patients. We also followed up this cohort of patients to establish what diagnosis was made over a four year period with particular reference to gastrointestinal cancers and to the presence of persistent anaemia.

PATIENTS AND METHODS

Identification of patients

We identified patients with probable IDA from full blood counts that had been requested by GPs and processed by either of two district general hospitals, between June 1997 and May 1998. All general practices in the two districts which

used the two laboratories were included. The extended follow up period was to May 2001.

Inclusion criteria were:

- Age over 20 years (men) or over 50 years (women).
- A haemoglobin concentration of 120 g/l or less (men) or 110 g/l or less (women).
- A mean cell volume of less than 82 fl in district 1 or 78 fl in district 2 (the blood autoanalysers used by the two hospitals had different normal ranges).
- Red cell count not exceeding $5.5 \times 10^{12}/l$.

Exclusion criteria were:

- A history of anaemia within the previous 12 months.
- Known haematological abnormalities such as haemoglobinopathy.

The North Nottinghamshire and North Derbyshire Local Research Ethics Committees and the Local Medical Committees approved the study.

Data collection

After identification of the patients, we contacted their GPs at least one year afterwards and extracted detailed anonymised data from the medical records for the period of 12 months after the date of the anaemia (the index date).

Abbreviations: BSG, British Society of Gastroenterology; CI, confidence interval; GP, general practitioner; IDA, iron deficiency anaemia; OR, odds ratio

The data collected included:

- The reason for the initial full blood count request.
- Signs and symptoms documented at the time.
- Dates and results of laboratory and radiological investigations that were initiated within three months of the index date.
- Dates and results of all hospital based investigations, whether requested directly by the GP, done via outpatient referrals, or done after inpatient admissions.
- Previous medical history that might affect management, including previous anaemia, gastrointestinal complaints, and chronic comorbidity
- For patients who did not have a definitive diagnosis (defined as cancer, bleeding peptic ulcer, coeliac disease, any causative diagnosis after adequate upper and lower gastrointestinal investigations, or any other firm diagnosis not related to the gastrointestinal tract) a longer follow up was carried out by consulting hospital records and databases and health authority death notifications, but not the GP records.

Statistical methods

Data were collected in an Access database and analysed with SPSS (v10). We assessed factors that influenced management by random effects logistic regression (Stata 7), to take account of the clustering of patients within practices. Our main outcome variable was whether investigations had been offered to those patients apparently fit and willing for them. Logistic regression was used to calculate odds ratios with 95% confidence intervals, assessing significance at $p = 0.05$ (two tailed). Explanatory variables included age, sex, presenting haemoglobin, previous anaemia, and presenting symptoms.

RESULTS

Factors influencing the initial management of patients

Patient characteristics and initial management
Six hundred and three patients from 89 practices were identified as fitting our inclusion criteria. One hundred and seventy two patients were subsequently excluded, mainly due to the finding of an anaemic episode within 12 months or because the patients' notes were unavailable (see Logan *et al* for full details¹⁰). Table 1 describes our cohort of 431 patients from 79 practices, 64% (277/431) being female (95% confidence interval (CI) 59.6 to 68.6). The 154 males included 20 aged under 50. Table 2 describes their initial management. There were 58 patients (13%, 95% CI 10.6 to 17.0) who were considered unfit for investigation, 33 (8%, 95% CI 5.5 to 10.6) who refused, and 140 (32%, 95% CI 28.2 to 37.0) who appeared fit but had no investigation.

Factors affecting likelihood of gastrointestinal investigation

Table 3 compares the characteristics of the 140 fit but non-investigated patients with the 217 who were offered gastrointestinal investigation (184 who were investigated plus 33 with documented refusal). Random effects logistic regression of single explanatory variables showed that female sex, age under 65, mild presenting anaemia (haemoglobin 90 g/l or more) and a history of anaemia more than 12 months previously were significantly associated with a reduced likelihood of being offered investigation (odds ratio (OR) 0.49, CI 0.30 to 0.80, $p = 0.004$; OR 0.44, CI 0.26 to 0.74, $p = 0.002$; OR 0.38, CI 0.23 to 0.61, $p < 0.001$; OR 0.39, CI 0.24 to 0.64, $p < 0.001$, respectively). Current use of aspirin or non-steroidal anti-inflammatory drugs had no effect. In those patients (294/431, 68%) with symptoms recorded at presentation, documen-

Table 1 Characteristics of the patient sample at presentation; values are number (%) unless otherwise stated

	Men (n = 154)	Women (n = 277)	Total (n = 431)
Median age at index date (years)	72	76	75
IQR	63–79	66–82	65–81
Median haemoglobin at index date (g/l)	94	89	92
IQR	76–109	77–101	76–103
History of anaemia*	39 (25)	87 (31)	126 (29)
History of any gastrointestinal complaint	89 (58)	128 (46)	217 (50)
Symptomatic presentation	130 (84)	228 (82)	358 (83)
Symptomatic patients with documented symptoms of anaemia	68 (52)	140 (61)	208 (58)
Symptomatic patients with documented upper gastrointestinal symptoms	31 (24)	20 (9)	51 (14)
Symptomatic patients with documented lower gastrointestinal symptoms	25 (19)	30 (13)	55 (15)

*History of IDA within five years of the index date but not within the immediate 12 months before that date. IQR, interquartile range.

tation of gastrointestinal symptoms was a significant predictor of investigation but symptoms of clinical anaemia were not.

Multivariate analysis using the explanatory variables of sex, age, haemoglobin concentration, and previous history of anaemia showed that these remained statistically significant predictors of the likelihood of investigation, also shown in table 3. Presenting symptoms were excluded from this analysis since we did not have this information for all patients.

Clinical diagnoses up to four years from the index date

Gastrointestinal investigations initiated within three months

Table 4 illustrates the gastrointestinal investigations initiated within three months of the index date. Of the 339 procedures

Table 2 Management in the first three months after the index date; values are number (%)

	Men (n = 154)	Women (n = 277)	Total (n = 431)
Site of management*			
GP	58 (38)	167 (60)	225 (52)
Shared	78 (51)	97 (35)	175 (41)
Hospital	18 (12)	13 (5)	31 (7)
Immediate management			
(1) Patients investigated			
Gastrointestinal			
Upper only	15 (10)	21 (8)	36 (8)
Lower only	33 (21)	30 (11)	63 (15)
Upper and lower	38 (25)	47 (17)	85 (20)
Total of all having gastrointestinal investigations	86 (56)	98 (35)	184 (43)
Other investigations (for example, renal, gynaecological)	4 (3)	12 (4)	16 (4)
(2) Patients not investigated			
Not suitable or died within days	16 (11)	42 (16)	58 (13)
Patient refused	8 (5)	25 (9)	33 (8)
No documented reason for non-investigation	40 (26)	100 (36)	140 (32)

*Site of management—GP: all treatment and investigations organised by GP; shared: non-urgent referral to secondary care; hospital: emergency, or urgent admission.

Table 3 Comparison of patients who were offered gastrointestinal investigation with those who were not

	No (%) of patients offered investigation	No (%) of patients not offered investigation	Adjusted odds ratio*	95% CI	p Value
Factor	(n=217)	(n=140)			
Female sex	123 (57)	100 (71)	0.49	0.30 to 0.80	0.004
Aged <65	41 (19)	47 (34)	0.44	0.26 to 0.74	0.002
Haemoglobin ≥90 g/l	97 (45)	92 (66)	0.38	0.23 to 0.61	<0.001
History of gastrointestinal complaints	102 (47)	78 (56)	0.68	0.43 to 1.08	0.10
History of anaemia	46 (21)	56 (40)	0.39	0.24 to 0.64	<0.001
Use of aspirin or NSAID in previous 3 months	74 (34)	41 (29)	1.33	0.82 to 2.17	0.25
Clinical symptoms of anaemia noted	(n=186) 112 (52)	(n=108) 61 (44)	1.17	0.70 to 1.95	0.55
Gastrointestinal symptoms noted	61 (28)	14 (10)	3.51	1.78 to 6.94	<0.001
Multivariate analysis					
Female sex	-	-	0.40	0.23 to 0.69	0.001
Age <65 years	-	-	0.48	0.27 to 0.85	0.01
Haemoglobin ≥90 g/l	-	-	0.37	0.22 to 0.62	<0.001
Previous anaemia	-	-	0.43	0.25 to 0.73	0.002

*Random effects logistic regression, adjusted for patients within practices. NSAID, non-steroidal anti-inflammatory drug.

carried out (excluding duodenal biopsies and non-invasive tests such as ultrasound), 206 (61%) demonstrated some abnormality. Fewer than half the upper gastrointestinal endoscopies included duodenal biopsy. GPs had requested 22/120 (18%) of the upper endoscopies and 56/131 (43%) of the barium enemas via open access.

Table 5 describes the major pathology found from these investigations. Almost one third of investigated patients (55/184, 30%, 95% CI 23.7 to 36.9) had a major diagnosis and only 30 (16%, 95% CI 11.7 to 22.3) had no diagnosis at all. In those who had upper and lower tract examinations, dual pathology was found in 26, five of these showing an initial minor diagnosis of gastritis followed by that of colorectal carcinoma or polyps. Those listed as having minor pathology had no major abnormalities.

Additional major diagnoses in the first 12 months

Two patients who died within days of the index date were found to have gastrointestinal cancer at postmortem examination (one gastric, one rectal), and one man with investigations planned was admitted for an emergency

laparotomy which showed a colonic tumour. One patient with an active duodenal ulcer was later found to have a caecal carcinoma. Four patients who had not been offered gastrointestinal investigation, and one who had refused, had colorectal tumours.

Seven patients who had the iron deficient parameters, and who had other investigations within three months, had non-gastrointestinal cancer (three lung, including one secondary to previous breast cancer, one ovarian, one bladder, one Hodgkin's and one non-Hodgkin's lymphoma). An additional five non-gastrointestinal cancers were found within the first 12 months; two patients with negative gastrointestinal tests were subsequently found to have endometrial sarcoma and lymphoma respectively; and three non-investigated patients were found to have endometrial, lung, and bladder cancer.

Overall, only 128/431 (30%, 95% CI 25.6 to 34.2) patients had a definitive diagnosis made within 12 months, 102 (24%, 95% CI 19.9 to 27.9) had a provisional or assumed diagnosis on the basis of partial investigations or medical history, and the remaining 201 (46%, 95% CI 42.0 to 51.4) had no diagnosis associated with the anaemia.

Table 4 Number and origin of gastrointestinal investigations

Investigation	Done by direct GP access		Done as outpatient		Done as inpatient		Total	
	No	No with pathology	No	No with pathology	No	No with pathology	No	No (%) with pathology
Upper endoscopy*	22	15	63	42	35	22	120	79 (66)
Duodenal biopsy	8	0	35	6	11	2	54	8(15)
Barium meal*	4	3	4	2	3	3	11	8(73)
Barium enema*	56	37	61	44	14	11	131	92(70)
Rigid sigmoidoscopy	3	0	30	1	4	1	37	2(5)
Flexible sigmoidoscopy	0	0	12	6	5	4	17	10(59)
Colonoscopy	0	0	13	10	2	1	15	11(73)
Small bowel investigation	0	0	5	2	3	2	8	4(50)
Abdominal ultrasound*	6	2	18	8	13	7	37	17(46)

*Denotes investigations which GPs could request directly. Some individual GPs carry out rigid sigmoidoscopy in surgery.

Table 5 Gastrointestinal abnormalities found by investigations initiated within three months; values are number (%)

Pathology	Upper tract investigation only (n = 36)	Lower tract investigation only (n = 63)	Upper and lower tract investigation (n = 85)	Total (n = 184)
Significant pathology				
Cancer upper tract	6	–	1	7
Active peptic ulcer	9	–	1	10
Telangiectasia	–	–	2	2
Coeliac disease	2	–	3	5
Cancer lower tract	–	11	9	20
Colon polyps	–	2	3	5
Angiodysplasia	–	1	2	3
Inflammatory bowel disease	–	1	2	3
Total significant pathology	17 (47)	15 (24)	23 (27)	55 (30)
Minor pathology*	14 (39)	31 (49)	54 (63)	99 (54)
No abnormalities detected	5 (14)	17 (27)	8 (9)	30 (16)

*Number of patients with any other abnormalities of upper and lower tract, whether or not considered causative of the anaemia.

Extended follow up

At 12 months, 365 patients were still alive and 263 of these had no confirmed diagnosis so were followed up. Table 6 shows that two thirds of these patients had had no investigations, and although 176 (67%) had had a normal haemoglobin recorded during the first year, recurrent or chronic anaemia was present in at least 40% at follow up.

Forty three patients had new gastrointestinal investigations initiated and 24 of these had a new diagnosis for their anaemia, including seven gastrointestinal cancers. These constituted two gastric tumours (one patient had refused earlier tests, one had not been offered any); four colorectal tumours (one had previously refused, one not offered, and two had negative barium enemas); and one small bowel leiomyosarcoma was found in a patient after prolonged investigations. Six of these patients had presented with mild anaemia. Other significant gastrointestinal pathology included a further case of coeliac disease, in a man aged 69, and two of perforated peptic ulcer, one patient dying as a result and the other requiring emergency laparotomy. One woman was found to have a rectal tumour but refused further tests to confirm its nature.

Table 6 Characteristics of the cohort with extended follow up

	Men (n = 83)	Women (n = 180)	All (n = 263)
Maximum follow up, months from index date*	45	46	46
Median (approximately)	38	38	38
IQR (approximately)	35–41	35–41	35–41
Haemoglobin at index date (g/l)			
Median	100	93	95
IQR	83–111	79–102	81–104
Age at index date			
Median	71	75	74
IQR	61–78	64–82	63–80
Gastrointestinal investigation in first year (%)	34 (41)	47 (26)	81 (31)
Normal haemoglobin in first year	41 (49)	135 (75)	176 (67)
Full blood count in follow up period	69 (83)	132 (73)	201 (76)
Haemoglobin below normal in follow up period	46 (55)	67 (37)	113 (43)
New gastrointestinal investigation	17 (20)	26 (14)	43 (16)
New cancer diagnosed			
In gastrointestinal tract	5	2	7
Not in gastrointestinal tract	5	2	7
Metastatic with unknown primary	3	–	3

*For the 210 patients alive at the end of the period. IQR, interquartile range.

Seven patients were found to have non-gastrointestinal cancers and three more had metastatic disease with unknown primaries. Of these, two had refused in year 1, three had not been offered tests, two had severe comorbidity, and three had had negative barium enemas with no further investigations.

Overall, 17/24 (71%) patients with a new diagnosis had had no investigation in year 1.

Colorectal tumours

Table 7 summarises all patients diagnosed with colorectal tumours, representing 28/154 (18%) of men and 9/277 (3%) of women. Right sided tumours were more common and presented with more severe anaemia; 14/20 (70%) patients with the disease in the right bowel had a presenting haemoglobin of under 90 g/l compared with 4/12 (33%) of patients with rectosigmoid disease (data not shown). At least 20/35 (57%) new tumours were Dukes's stage C or metastatic at diagnosis.

Final diagnoses

Forty eight patients (11%) had gastrointestinal cancer (11 upper, two small bowel, and 35 lower, including recurrent tumours) and 150 (35%) had other gastrointestinal disease. Twenty three (5%) had non-gastrointestinal cancer, 43 (10%) had other non-gastrointestinal disease, and the remaining 167 (39%) had no diagnosis.

Deaths

At least 119 patients died during the entire study period, 28% of the cohort, of which 66 (15%) were in the first year (data not obtained for all patients). Including the three patients

Table 7 Characteristics of patients diagnosed with colorectal cancers; values are number (%) unless otherwise stated

Characteristic	Men (n = 28)	Women (n = 9)	All (n = 37)
Age range (years)	26–86	50–87	26–87
Presenting haemoglobin <90 g/l	13 (46)	7 (78)	20 (54)
Tumour site			
Small bowel	1	0	1
Right/transverse colon	15	5	20
Rectosigmoid (including two recurrent)	11	3	14
Primary site unknown	1*	1	2

*Metastatic small bowel carcinoid.

with recurrent disease at the index date, at least 23 of the 50 patients with gastrointestinal cancer died (46%), as did 13/23 (56%) of those with non-gastrointestinal cancer. Most of these deaths were a direct result of the malignant disease. The 53 deaths in the follow up period included 41 patients who had had no investigation at first, and eight of these died from advanced cancer.

Comparison of the number of deaths with age/sex standardised mortality rates showed that the cohort had an increased risk of death.¹¹ In the first 12 months this was approximately three times greater than in the normal population (standardised mortality rate for males 322, 95% CI 214 to 466 and for females 262, 95% CI 185 to 359).

DISCUSSION

We describe the initial management and clinical outcome of a cohort of patients who presented to their GPs over a 10 month period with a new episode of IDA. A substantial number were not fit for investigation. However, a third of patients who appeared to be suitable for investigation had none. Although the prevalence of gastrointestinal cancer was similar to that in hospital based studies, diagnosis was delayed for three months or more in 14/46 (30%).

A strength of our study is that we identified patients consecutively from the pathology laboratories of two district general hospitals, each serving populations of about 275 000 people, drawn from small towns and more rural areas, and unselected apart from the broad criteria set. We would therefore consider our results to be generalisable to demographically similar areas, though not necessarily to practices in large urban areas or with ethnic minority populations. A potential weakness is that GP records are of varying quality and completeness.

The majority of studies that have documented the investigation of IDA have used selected populations such as those already referred to hospital.⁴⁻⁹ The recent British Society of Gastroenterology (BSG) guidelines for investigation of such patients are based on studies using such groups.¹ Our cohort was relatively unselected and demonstrates that a substantial number of patients presenting in general practice are unlikely to be investigated along the lines recommended by the BSG. These patients include the very frail elderly and those with disabling comorbidity, although our study showed that older age by itself was not considered a contraindication to further tests.

We found less frequent investigation of patients under 65 years. It is possible that the GPs felt that this age group was less likely to have an underlying malignancy, although a significant number of younger patients were eventually diagnosed as having a malignant or premalignant condition. The BSG guidelines note that few data are available for the yield of gastrointestinal investigations in younger men and women, but that such tests may be necessary. The recent government guidelines for urgent referral of suspected colon cancer suggest a minimum age of 60 years for fast tracking, but also comment that "Local cancer networks may elect to set a lower age threshold (for example, 55 or 50 years)".¹² The importance of considering colorectal cancer as a potential diagnosis in younger patients is shown by the inclusion in our study of four cases in men under 55, including one aged 26 years. The prompt diagnosis of malignant disease in the young leads to a proportionately greater effect on life expectancy.

Women were significantly less likely to be investigated than men. IDA is more prevalent in females of all ages,¹³ so it is possible that GPs are so used to seeing younger women with IDA that they are less alert to the possibility of underlying pathology in older women. The less frequent investigation of patients with a previous history of anaemia

may also reflect a GP's knowledge of the patient's past history which was not obvious on record review.

Colorectal cancer is only slightly more prevalent in men than in women.^{14 15} We found only seven new cases in women during the first year, but 23 in men. As fewer women were investigated, we expected more to present later, but they did not. We must conclude that women with cancer may present differently, and our sample of anaemic patients excluded those who presented with other symptoms. Women are known to consult with their GPs more frequently than men¹³ and may therefore be more likely to be investigated for gastrointestinal symptoms or referred before anaemia becomes a presenting feature.

We also found an excess of right sided cancers, known to be associated with greater levels of anaemia,¹⁵ and therefore likely to predominate in a cohort of anaemic patients. However, there was no correlation between the anaemia and the histological stage of the cancer at diagnosis. Our results agree with established evidence that the degree of anaemia in patients presenting with iron deficiency is not by itself a guide to the seriousness of the underlying disorder. There may be an educational need to ensure that all doctors are aware of the potential significance of even a mild degree of unexplained IDA.

We are not able to define which of the less serious pathologies were definitely causative of the anaemia. In many cases, the hospital clinicians who reported the results of tests failed to provide GPs with clear guidance in this respect, and there may be conflict between hospital led guidelines and community based practice. Current guidelines produced by the BSG state that oesophagitis is an uncommon cause of occult blood loss, and do not mention hiatus hernia or diverticular disease at all.¹ However, many GPs may consider these conditions to be causative, and a previous history of such complaints may have been responsible for the lack of new investigations in some of the patients, even if not documented as such in the notes. A recent study did include hiatus hernia with linear erosions as a cause of bleeding.¹⁶ In this respect it is important to note that many of our patients who were sent for non-urgent tests may have had a course of acid-reducing medication, stoppage of non-steroidal inflammatory drugs or aspirin, and perhaps dietary and lifestyle advice, before upper endoscopy was performed. They may well have had inflammatory lesions at first that had had time to heal. Hiatus hernia may be a risk factor in readmission rates for IDA.¹⁷

Our study revealed six cases of coeliac disease. It is well established that this condition may be under-diagnosed, particularly in patients with no symptoms other than anaemia; a study of anaemic blood donors suggested that 7% might have coeliac disease.¹⁸ Blood tests for coeliac disease were not readily available to GPs at the time of our study, and fewer than half of the patients who had an upper endoscopy had a duodenal biopsy, as found elsewhere,¹⁹ so further cases may well have been missed.

We accept that the 23 patients with non-gastrointestinal cancer may not have been truly iron deficient. Our study did not require an assessment of iron stores before treatment and investigations were initiated. A normal ferritin in patients presenting with iron deficient indices might occur as a result of an inflammatory or reactive process and should not preclude investigation and treatment with follow up of the response to iron therapy.

The extent of recurrent anaemia in our follow up period is disturbing. During the first year, about 60% were known to have had a return to a normal haemoglobin within the year, but many had no evidence of a full therapeutic course of oral iron.¹⁰ In the follow up study, a higher proportion of women than men had a normal blood count, perhaps reflecting a

Learning points

What is known about this topic:

- Fewer than 50% of patients presenting to their GP with iron deficiency anaemia (IDA) will be adequately investigated to find a cause.
- In patients referred to hospital for investigation of IDA, gastrointestinal cancer is found in about 10%. No cause for the anaemia will be found in about 20%.

What this paper adds:

- The prevalence of gastrointestinal cancer in patients presenting to their GP with IDA is similar to that in hospital based series but diagnosis is delayed in a third.
- Nearly one fifth of men presenting with IDA will have colorectal cancer.
- Women aged under 65 are less likely to be offered investigation.
- Recurrent or persistent anaemia is common in patients without a diagnosis by 12 months.

greater compliance with medication. The combination of inadequate treatment and monitoring of the anaemia means that there is continuing unnecessary morbidity from anaemia even in patients who were unfit for investigation but who could have received adequate iron replacement.^{20 21}

CONCLUSIONS

We have shown that a considerable number of patients who present in general practice with an episode of IDA may be unsuitable for invasive investigations, and that clinical guidelines should reflect this. However, others may be denied appropriate investigations, suggesting that there are educational issues which require addressing in order to ensure a uniformly high standard of patient care for those who present to their GPs with IDA.

Gastrointestinal cancer remains a significant cause of IDA in a cohort of patients presenting to their GP. Women presenting with IDA to their GP are less likely to have gastrointestinal cancer than men but we suggest that a high index of suspicion should be maintained when treating anaemic patients, even when the anaemia is mild. All should be encouraged to take a full course of iron therapy and to return for follow up blood tests, to avoid missed diagnoses and recurrent anaemia.

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REFERENCES

- 1 **Goddard A**, McIntyre A, Scott B. Guidelines for the management of iron deficiency anaemia. *Gut* 2000;**46**(suppl IV):iv1-5.
- 2 **Hin H**, Bird G, Fisher P, et al. Coeliac disease in primary care: case finding study. *BMJ* 1999;**318**:164-7.
- 3 **Sahay R**, Scott B. Iron deficiency anaemia—how far to investigate? *Gut* 1993;**34**:1427-8.
- 4 **Cook I**, Pavli P, Riley J, et al. Gastrointestinal investigation of iron deficiency anaemia. *BMJ* 1986;**292**:1380-2.
- 5 **Rockey D**, Cello J. Evaluation of the gastrointestinal tract in patients with iron-deficiency anaemia. *N Engl J Med* 1993;**329**:1691-5.
- 6 **McIntyre A**, Long R. Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut* 1993;**34**:1102-7.
- 7 **Wilcox C**, Alexander L, Clarke W. Prospective evaluation of the gastrointestinal tract in patients with iron deficiency and no systemic or gastrointestinal symptoms or signs. *Am J Med* 1997;**103**:405-9.
- 8 **Joosten E**, Ghesquiere B, Linhoudt H, et al. Upper and lower gastrointestinal evaluation of elderly inpatients who are iron deficient. *Am J Med* 1999;**107**:24-9.
- 9 **Willoughby J**, Laitner S. Audit of the investigation of iron deficiency anaemia in a district general hospital, with sample guidelines for future practice. *Postgrad Med J* 2000;**76**:218-22.
- 10 **Logan E**, Yates J, Stewart R, et al. Investigation and management of iron deficiency anaemia in general practice: a cluster randomised trial of a simple management prompt. *Postgrad Med J* 2002;**78**:533-7.
- 11 **Office for National Statistics**. *Mortality statistics, general, 1999*. London: HMSO, 2001.
- 12 **Department of Health**. *Referral guidelines for suspected cancer*. London: Department of Health, 2000.
- 13 **Office of Population Censuses and Surveys**. *Morbidity statistics from general practice. Fourth national study 1991-1992*. London: OPCS, 1995.
- 14 **Department of Health**. *National Cancer Survey 2000-2001*. London: Department of Health, 2002:14-15.
- 15 **Majumdar S**, Fletcher R, Evans A. How does colorectal cancer present? Symptoms, duration and clues to location. *Am J Gastroenterol* 1999;**94**:3039-45.
- 16 **Annibale B**, Capurso G, Chistolini A, et al. Gastrointestinal causes of refractory iron deficiency anemia in patients without gastrointestinal symptoms. *Am J Med* 2001;**111**:439-45.
- 17 **Ruhl C**, Everhart J. Relationship of iron deficiency anaemia with esophagitis and hiatal hernia: hospital findings from a prospective, population-based study. *Am J Gastroenterol* 2000;**96**:322-6.
- 18 **Harvey R**, Lock R, Unsworth D. Anaemia in blood donors is not being properly investigated (letter). *BMJ* 1999;**318**:1214.
- 19 **Patterson R**, Johnston S. Iron deficiency anaemia: are the British Society of Gastroenterology guidelines being adhered to? *Postgrad Med J* 2003;**79**:226-8.
- 20 **Waller D**, Smith A. Attitudes to prescribing iron supplements in general practice. *BMJ* 1987;**294**:94-6.
- 21 **Beardon P**, McGilchrist M, McKendrick A, et al. Primary non-compliance with prescribed medication in primary care. *BMJ* 1993;**307**:846-8.