

Iron deficiency and symptoms in women age 20-49 and relation to upper gastrointestinal and colon cancers: On-line supplement

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eTable 1. Symptom categories and ICD-9-CM diagnosis codes

Category	Symptom	ICD-9-CM
Upper gastrointestinal symptoms		
	upper abdominal pain	789.01, 789.02
	epigastric pain	789.06
	dyspepsia	536.8
	gastritis	535
	gastrointestinal reflux	530.81
Dysphagia	dysphagia	438.82, 787.2
Lower gastrointestinal symptoms		
	change in bowel habits	787.99
	constipation	564
	diarrhea	787.91
	left lower quadrant pain	789.04
	right lower quadrant pain	789.03
	irritable bowel	564.1
Rectal bleed	rectal bleed	569.3
Weight loss	weight loss	783.21

eTable 2. Adjusted odds ratios for cancers in women age 20-49 with anemia who were tested for iron deficiency

Risk Factors	Age 20-49	
	Gastric Cancer ^a aOR (95% CI)	Colon Cancer ^a aOR (95% CI)
Iron deficiency	1.08 (0.32-3.65)	1.11 (0.52-2.37)
Any UGI symptoms	4.03 (0.98-16.66)	2.49 (1.15-5.39)
Any dysphagia symptoms	6.41 (1.69-24.27)	0.32 (0.03-4.25)
Any LGI symptoms	0.92 (0.26-3.28)	3.02 (1.44-6.36)
Any rectal bleed	1.12 (0.12-10.66)	7.15 (3.44-14.85)
Any weight loss	24.38 (7.05-84.31)	1.64 (0.35-7.68)
Age group ^b , years		
20-29	0.99 (0.08-12.88)	0.90 (0.19-4.22)
30-39	2.84 (0.87-9.31)	1.10 (0.50-2.43)
40-49 (reference group)	1	1
Race/Ethnicity		
White (reference group)	1	1
Asian	0.75 (0.13-4.45)	1.02 (0.42-2.48)
Black	0.73 (0.13-4.18)	0.42 (0.14-1.27)
Hispanic	1.31 (0.30-5.80)	0.42 (0.15-1.19)
Other ^c	0.87 (0.07-10.38)	0.42 (0.09-2.08)
Charlson comorbidity index score ≥1	1.04 (0.31-3.47)	2.00 (0.97-4.09)

Multivariable logistic regression analyses were used to assess the risk of being iron deficient and having cancer in women age 20-49 and 50-55, controlling for symptom groups, patient race/ethnicity, and Charlson score.

In bold are risk factors that are statistically significant at two-sided $P < 0.05$.

ID = iron deficiency; aOR = adjusted odds ratio; UGI = upper gastrointestinal; LGI = lower gastrointestinal; -- = not applicable.

^a Within five years of the iron deficiency test date.

^b Not included in the multivariable logistic regression modeling for colon cancer in women aged 50-55.

^c Including American Indians, Alaskan Natives, more than one racial groups, and unknown.

eTable 3. Adjusted odd ratios of receiving endoscopy^a in women age 20-49 who were tested for iron deficiency.

Risk Factors	Age 20-49	
	Anemic	Non-Anemic
	aOR (95% CI)	aOR (95% CI)
Iron Deficient	2.08 (1.69-2.55)	1.66 (1.45-1.91)
Any UGI symptom	2.82 (2.37-3.35)	2.79 (2.40-3.24)
Any dysphagia	1.77 (1.25-2.50)	2.02 (1.56-2.61)
Any LGI symptom	1.43 (1.20-1.70)	2.18 (1.89-2.51)
Any rectal bleed	1.97 (1.52-2.55)	2.97 (2.49-3.55)
Any weight loss	1.61 (1.06-2.46)	2.61 (1.99-3.43)
Age group ^b , years		
20-29	0.33 (0.19-0.55)	0.50 (0.39-0.63)
30-39	0.61 (0.49-0.75)	0.57 (0.49-0.68)
40-49 (reference group)	1	1
Race/Ethnicity		
White (reference group)	1	1
Asian	0.70 (0.55-0.89)	0.78 (0.63-0.96)
Black	0.60 (0.46-0.77)	0.65 (0.49-0.85)
Hispanic	0.79 (0.64-0.98)	0.82 (0.69-0.97)
Other ^c	0.79 (0.57-1.08)	0.90 (0.70-1.17)
Charlson comorbidity index score ≥1	1.22 (1.03-1.44)	1.24 (1.08-1.42)

Multivariable logistic regression analyses were used to assess the risk of having endoscopy within one year of testing for iron deficiency in women age 20-49 and 50-55, controlling for symptom groups, patient race/ethnicity, and Charlson score.

In bold are risk factors that are statistically significant.

ID = iron deficiency; aOR = adjusted odds ratio; UGI = upper gastrointestinal; LGI = lower gastrointestinal; -- = not applicable.

^a Defined as undergoing endoscopy within one year of the iron deficiency test date.

^b Not included in the multivariable logistic regression modeling for receiving endoscopy in women aged 50-55.

^c Including American Indians, Alaskan Natives, more than one racial groups, and unknown.

eTable 4. Symptoms among women age 20-49 who underwent endoscopy within one year of testing for iron-deficiency

Symptom	Iron Deficient n= 527)		Non-Iron Deficient n= 126		P value
Anemic					
Any	398	75.5%	108	85.7%	.01
UGI symptoms	336	63.8%	88	69.8%	.20
Dysphagia	35	6.6%	9	7.1%	.84
UGI and/or dysphagia	342	64.9%	91	72.2%	.12
LGI symptoms	184	34.9%	67	53.2%	<.001
Rectal bleed	67	12.7%	15	11.9%	.81
LGI and/or rectal bleed	307220	41.8%	75	59.5%	<.001
Non-anemic					
Any	342	88.1%	495	89.8%	.41
UGI symptoms	273	70.5%	386	70.1%	.92
Dysphagia	31	8.0%	52	9.4%	.44
UGI and/or dysphagia	277	71.4%	393	71.3%	.98
LGI symptoms	208	53.6%	320	58.1%	.17
Rectal bleed	72	18.6%	123	22.3%	.16
LGI and/or rectal bleed	235	60.6%	376	68.2%	.02

Comparisons were made using Fisher's exact tests.

eTable 5. Sample number needed to detect a cancer in women with anemia age 20-49 with selected symptoms-by age subgroups.

Sample size/n of cancers^a = number needed to detect one cancer	20-29	30-39	40-49
Gastric cancer			
Random	648/0 =	2591/3 = 864	6544/3 = 2182
Iron deficiency			
Yes	379/0 =	1656/3 = 552	4592/1 = 4592
No	269/0 =	935/0 =	1952/2 = 976
Any symptom			
Yes	319/0 =	1313/3 = 438	3446/3 = 1149
No	329/0 =	1278/0 =	3098/0 =
Weight loss			
Yes	23/0 =	53/1 = 53	144/2 = 72
No	625/0 =	2538/2 = 1269	6400/1 = 6400
Any gastric symptoms: UGI and/or dysphagia			
<i>All women</i>			
Yes	214/0 =	959/3 = 320	2620/2 = 1310
No	434/0 =	1632/0 =	3924/1 = 3924
<i>Iron deficient (+) women (n = 7919)</i>			
Yes	125/0 =	615/3 = 205	1823/1 = 1823
No	254/0 =	1041/0 =	2769/0 =
<i>Iron deficient (-) women (n = 4165)</i>			
Yes	89/0 =	344/0 =	797/1 = 797
No	180/0 =	591/0 =	1155/1 = 1155
Colon cancer			
Random	648/1 = 648	2591/7 = 371	6544/18 = 364
Iron deficiency			
Yes	379/1 = 379	1656/5 = 332	4592/12 = 383
No	269/0 =	935/2 = 468	1952/6 = 326
Any symptoms			
Yes	319/1 = 319	1313/7 = 188	3446/13 = 266
No	329/0 =	1278/0 =	3098/5 = 620
Weight loss			
Yes	23/0 =	53/0 =	144/1 = 144
No	625/1 = 625	2538/7 = 363	6400/17 = 377
Any colon symptoms: LGI and/or rectal bleed			
<i>All women</i>			

Sample size/n of cancers^a = number needed to detect one cancer	20-29	30-39	40-49
Yes	202/1 = 202	750/7 = 108	1841/11 = 168
No	446/0 =	1841/0 =	4703/7 = 672
<i>Iron deficient (+) women (n = 7919)</i>			
Yes	120/1 = 120	485/5 = 97	1244/8 = 156
No	259/0 =	1171/0 =	3348/4 = 837
<i>Iron deficient (-) women (n = 4165)</i>			
Yes	82/0 =	265/2 = 133	597/3 = 199
No	187/0 =	670/0 =	1355/3 = 452

IDA = iron deficiency anemia, UGI = upper gastrointestinal, LGI = lower gastrointestinal

^a Within five years of the iron deficiency test date.

eTable 6. Unadjusted incidence of esophagitis, ulcers and IBD in women who underwent endoscopy procedure within one year of testing for iron deficiency

	Iron Deficient			Non-Iron Deficient			<i>P</i> Value
	Sample Size (N)	Pathology ^a (n)	Incidence/1000 Patients (95% CI)	Sample Size (N)	Pathology ^a (n)	Incidence/1000 Patients (95% CI)	
Anemic women (N = 6536)							
Esophagitis							
Age 20-49, years	527	39	74.00 (54.61-99.57)	126	12	95.24 (55.32-159.10)	.42
20-29	11	2	181.80 (51.37-477.00)	4	0	--	>.99
30-39	82	10	122.00 (67.61-210.10)	36	7	194.40 (97.53-350.30)	.30
40-49	434	27	62.21 (43.10-89.00)	86	5	58.14 (25.09-129.00)	.89
Ulcer							
Age 20-49, years	527	20	37.95 (24.70-57.89)	126	10	79.37 (43.68-139.90)	.046
20-29	11	0	--	4	0	--	--
30-39	82	6	73.17 (33.96-150.60)	36	2	55.56 (15.37-181.50)	>.99
40-49	434	14	32.26 (19.31-53.41)	86	8	93.02 (47.89-173.00)	.02
IBD							
Age 20-49, years	527	4	7.59 (2.96-19.35)	126	3	23.81 (8.13-67.67)	.14
20-29	11	0	--	4	0	--	
30-39	82	0	--	36	1	27.78 (4.92-141.70)	.31
40-49	434	4	9.22 (3.59-23.46)	86	2	23.26 (6.40-80.88)	.26
Non-Anemic women							

	Iron Deficient			Non-Iron Deficient			P Value
	Sample Size (N)	Pathology ^a (n)	Incidence/1000 Patients (95% CI)	Sample Size (N)	Pathology ^a (n)	Incidence/1000 Patients (95% CI)	
(N = 939)							
Esophagitis							
Age 20-49, years	388	19	48.97 (31.57-75.21)	551	43	78.04 (58.45-103.50)	.08
20-29	33	1	30.30 (5.37-153.20)	47	4	85.11 (33.59-199.30)	.40
30-39	75	4	53.33 (20.93-129.30)	132	7	53.03 (25.92-105.40)	>.99
40-49	280	14	50.00 (30.01-82.17)	372	32	86.02 (61.59-118.90)	.08
Ulcer							
Age 20-49, years	388	19	48.97 (31.57-75.21)	551	24	43.56 (29.44-63.99)	.70
20-29	33	1	30.30 (5.37-153.20)	47	2	42.55 (11.75-142.50)	>.99
30-39	75	4	53.33 (20.93-129.30)	132	6	45.45 (21.00-95.62)	>.99
40-49	280	14	50.00 (30.01-82.17)	372	16	43.01 (26.65-68.72)	.67
IBD							
Age 20-49, years	388	9	23.20 (12.25-43.49)	551	13	23.59 (13.84-39.94)	.97
20-29	33	0	--	47	2	42.55 (11.75-142.50)	.51
30-39	75	2	13.33 (2.36-71.73)	132	2	15.15 (4.16-53.56)	>.99
40-49	280	8	28.57 (14.55-55.36)	372	9	24.19 (12.78-45.33)	.73

IBD= inflammatory bowel disease

- Not applicable

^a Within five years of the iron deficiency test date.

eTable 7. Demographic and clinical characteristics in women age 20-49 without anemia who were tested for iron deficiency.

Characteristics	Iron Deficiency		Had Endoscopy ^a	
	Yes	No	Yes	No
Women age 20-49 (N = 22,657 [100])	n = 6979	n = 15,678	n = 939	n = 21,718
Iron deficiency	--	--	388 (41.3)	6591 (30.4)
Had endoscopy ^a	388 (5.6)	551 (3.5)	--	--
Age groups (year)				
20-29	1010 (14.5)	2122 (13.5)	80 (8.5)	3052 (14.1)
30-39	2068 (29.6)	5076 (32.4)	202 (22.0)	6937 (31.9)
40-49	3901 (55.9)	8480 (54.1)	652 (69.4)	11,729 (54.0)
Age (year), mean \pm SD	38.9 \pm 7.9	39.0 \pm 7.7	41.4 \pm 7.2	38.8 \pm 7.8
Charlson comorbidity index score				
Mean \pm SD	0.4 \pm 0.8	0.5 \pm 1.0	0.8 \pm 1.2	0.5 \pm 0.9
≥ 1	2372 (34.0)	5641 (36.0)	441 (47.0)	7572 (34.9)
Race/Ethnicity				
White	3075 (44.1)	7324 (46.7)	481 (51.2)	9918 (45.7)
Black	520 (7.5)	1382 (8.8)	60 (6.4)	1842 (8.5)
Hispanic	1672 (24.0)	2987 (19.1)	199 (21.2)	4460 (20.5)
Asian	1192 (17.1)	2771 (17.5)	125 (13.3)	3838 (17.7)
Other ^b	520 (7.5)	1214 (7.7)	74 (7.9)	1660 (7.6)
Any comorbidity	1454 (20.8)	2816 (18.0)	211 (22.5)	4059 (18.7)
Diabetes mellitus	558 (8.0)	1370 (8.7)	97 (10.3)	1831 (8.4)
Kidney disease	41 (0.6)	206 (1.3)	17 (1.8)	230 (1.1)
Cardiovascular disease	58 (0.8)	136 (0.9)	10 (1.1)	184 (0.9)
Pulmonary disease	75 (1.1)	388 (2.5)	17 (1.8)	446 (2.1)
Menorrhagia	854 (12.2)	1046 (6.7)	97 (10.3)	1803 (8.3)
Cirrhosis	8 (0.1)	39 (0.3)	9 (1.0)	38 (0.2)
Any symptoms	3810 (54.6)	8504 (54.3)	837 (89.1)	11,477 (52.9)

Characteristics	Iron Deficiency		Had Endoscopy ^a	
	Yes	No	Yes	No
UGI symptoms	2769 (39.7)	6052 (38.6)	659 (70.2)	8162 (37.6)
Dysphagia	187 (2.7)	433 (2.8)	83 (8.8)	537 (2.5)
LGI symptoms	2016 (28.9)	4628 (29.5)	528 (56.2)	6116 (28.2)
Rectal bleed	463 (6.6)	1023 (6.5)	195 (20.8)	1291 (5.9)
Weight loss	160 (2.3)	374 (2.4)	74 (7.9)	460 (2.1)
Any gastric symptoms: UGI and/or dysphagia	2870 (41.1)	6304 (40.2)	684 (72.8)	8490 (39.1)
Any colon symptoms: LGI and/or rectal bleed	2314 (33.2)	5303 (33.8)	630 (67.1)	6987 (32.2)
Endoscopy within 5 years of study entry	1028 (14.7)	1766 (11.3)	939 (100)	1855 (8.5)

Data are column % unless otherwise stated.

-- = Not applicable; SD = standard deviation; UGI = upper gastrointestinal; LGI = lower gastrointestinal.

^a Defined as undergoing endoscopy within one year of the iron deficiency test date.

^b Including American Indians, Alaskan Natives, more than one racial groups, and unknown.

eTable 8. Unadjusted incidence of gastric and colon cancers stratified by iron deficiency and symptoms in 22,657 non-anemic women age 20-49.

	Sample Size (N)	Cancer ^a (n)	NND One Cancer (95% CI)	Incidence/1000 Patients (95% CI)	P Value
Gastric cancer					
Random	22,657	3	7553 (2569-22,207)	0.13 (0.05-0.39)	--
Iron deficiency					
Yes	6979	0	--	--	.56
No	15,678	3	5226 (1778-15,367)	0.19 (0.07-0.56)	
Any symptoms					
Yes	12,314	3	4105 (1397-12,069)	0.24 (0.08-0.72)	.26
No	10,343	3	--	--	
UGI symptoms					
Yes	8821	3	2941 (1001-8646)	0.34 (0.12-1.00)	.06
No	13,836	0	--	--	
Dysphagia					
Yes	620	1	620 (111-3512)	1.61 (0.28-9.08)	.08
No	22,037	2	11,019 (3023-40,179)	0.09 (0.02-0.33)	
LGI symptoms					
Yes	6644	1	6644 (1174-37,638)	--	>.99
No	16,013	2	8007 (2197-29,196)	0.12 (0.03-0.46)	
Rectal bleed					
Yes	1486	1	1486 (264-8418)	0.67 (0.12-3.80)	.18
No	21,171	2	10,586 (2904-38,600)	0.09 (0.03-0.34)	
Weight loss					
Yes	534	1	534 (95-3025)	1.87 (0.33-10.5)	.07
No	22,123	2	11,062 (3035-40,336)	0.09 (0.02-0.33)	
Any gastric symptoms: UGI and/or dysphagia					
All women					
Yes	8968	3	2990 (1018-8790)	0.33 (0.11-0.98)	.06
No	13,689	0	--	--	
Iron deficient (+) women (n = 6979)					
Yes	2801	0	--	--	
No	4178	0	--	--	
Iron deficient (-) women (n = 15,678)					
Yes	6167	3	2056 (700-6044)	0.49 (0.17-1.43)	.06
No	9511	0	--	--	
Colon cancer					
Random	22,657	28	810 (561-1170)	1.24 (0.86-1.79)	--
Iron deficiency					
(+)	6979	16	437 (269-709)	2.29 (1.41-3.72)	<.01
(-)	15,678	12	1307 (748-2284)	0.77 (0.44-1.34)	

	Sample Size (N)	Cancer ^a (n)	NND One Cancer (95% CI)	Incidence/1000 Patients (95% CI)	P Value
Any symptoms					
Yes	12,314	25	493 (334-727)	2.03 (1.38-3.00)	<.01
No	10,343	3	3448 (1174-10,138)	0.29 (0.10-0.85)	
UGI symptoms					
Yes	8821	9	981 (516-1863)	1.02 (0.54-1.94)	.46
No	13,836	19	729 (467-1138)	1.37 (0.88-2.14)	
Dysphagia					
Yes	620	1	620 (111-3512)	1.61 (0.28-9.08)	.54
No	22,037	27	817 (562-1188)	1.23 (0.84-1.78)	
LGI symptoms					
Yes	6644	15	443 (269-731)	2.26 (1.37-3.72)	<.01
No	16,013	13	1232 (721-2108)	0.81 (0.47-1.39)	
Rectal bleed					
Yes	1486	16	93 (58-151)	10.8 (6.64-17.4)	<.01
No	21,171	12	1765 (1010-3084)	0.57 (0.32-0.99)	
Weight loss					
Yes	534	7	77 (38-158)	12.1 (6.36-26.8)	<.01
No	22,123	21	1054 (690-1611)	0.95 (0.62-1.45)	
Any colon symptoms: LGI and/or rectal bleed					
All women					
Yes	7364	19	388 (249-606)	2.58 (1.65-4.03)	<.01
No	15,293	9	1700 (895-3230)	0.59 (0.31-1.12)	
Iron deficient (+) women (n = 6979)					
Yes	2232	10	224 (122-411)	4.48 (2.44-8.23)	.01
No	4747	6	792 (363-1726)	1.26 (0.58-2.76)	
Iron deficient (-) women (n = 15,678)					
Yes	5132	9	571 (301-1084)	1.75 (0.92-3.33)	<.01
No	10,546	3	3516 (1197-10,336)	0.28 (0.10-0.84)	

Comparisons were made using Fisher's exact tests.

NND = number needed to detect; -- = not applicable; (+) = positive; (-) = negative; - = not applicable; UGI = upper gastrointestinal; LGI = lower gastrointestinal.

^a Within five years of the iron deficiency test date.