Risk assessment tools for the symptomatic population

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Overview

- The target population
- Symptoms
- Current strategies and endpoints
- The ideal tool or test
- Current data

The Target Population

- Individuals with lower abdominal symptoms:
  abdominal pain
  altered bowel habit
  rectal bleeding
  unexplained weight loss…
- Presenting to primary care physician
- Increasing prevalence
- Make up majority of patients referred for colonoscopy in Australia[1] – over 90% including those on surveillance (as compared to those in a national screening programme)

[1]Department of Health AG. Public Release of Linkable 10% Sample of Medicare Benefits Scheme (Medicare) and Pharmaceutical Benefits Scheme (PBS) Data 2016
[2]National Bowel Cancer Screening Program: Monitoring Report [press release], 2016

Symptoms

- Poor indicator of underlying significant bowel pathology
- Lack of either sensitivity and/or specificity where colorectal cancer detection is primary endpoint[1]:

  Iron deficiency – 0.13 (sensitivity) and 0.92 (specificity)
  rectal bleeding – 0.44 (sensitivity) and 0.66 (specificity)
- Does not add much to demographics – age, gender and other items in medical history[2]

[1]Jellema P, et al. Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis. BMJ (Clinical research ed). 2010;340:c1269

[2]Adelstein BA, Irwig L, Macaskill P, Turner RM, Chan SF, Katelaris PH. Who needs colonoscopy to identify colorectal cancer? Bowel symptoms do not add substantially to age and other medical history. Aliment Pharmacol Ther. 2010;32(2):270-81

PPV of referral symptoms for CRC

Symptom or sign at referral	Positive predictive value (%)
Palpable mass	50.0
Weight loss	14.3
Anaemia	9.0
Rectal bleeding	4.3
Abdominal pain	3.6
Diarrhoea	2.4
Altered bowel habit	2.2

Taken from Mowat, A et al. 755 referred cases who had undergone both FIT test and a colonoscopy.

Current strategies

- Refinement and update of guidelines
- GP education
- But pick up rate of significant bowel pathology (SBP) (CRC, high risk adenoma, inflammatory bowel disease) in symptomatic patients remains low

- Simplicity of approach (FIT ± additional data)

[1]Mowat C, Digby J, Strachan JA, Wilson R, Carey FA, Fraser CG, et al. Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms. Gut. 2016;65(9):1463-9

[2]Cubiella J, Vega P, Salve M, Diaz-Ondina M, Alves MT, Quintero E, et al. Development and external validation of a faecal immunochemical test-based prediction model for colorectal cancer detection in symptomatic patients. BMC Med. 2016;14(1):128

The ideal diagnostic test

- Results are different between those with and without condition(s) of interest
- Patients with specific test results are more likely to have the condition(s)
- Results distinguish patients between those with and without condition(s)
- Patients undergoing the diagnostic test fare better than a similar group not undergoing test

Sackett D, Haynes RB. BMJ 2002;324:539-41

Recent studies

Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms

Craig Mowat,[1] Jayne Digby,[2] Judith A Strachan,[3] Robyn Wilson,[3] Francis A Carey,[4] Callum G Fraser,[2] Robert J C Steele[2]

- Embedded within a primary care setting
- FIT performance ± Faecal calprotectin (FC)
- CRC ± “significant bowel pathology (SBP)”
- 1043 subjects returned samples
- 755 of these went on to have a colonoscopy

- CRC in 28 (3.8%), HRA 41 (5.4%), SBP 103 (13.6%)
- Normal 241 (32%), diverticular disease 190 (25%)

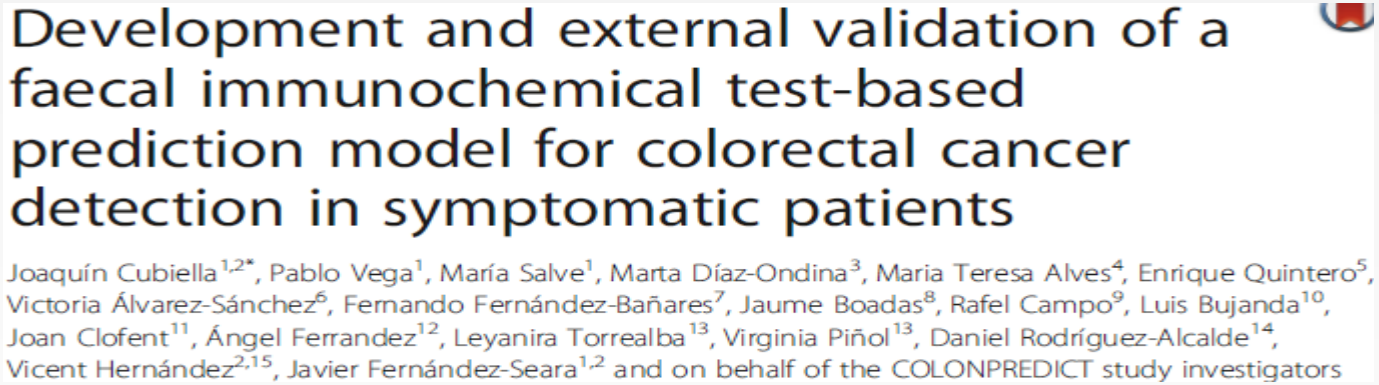
- For any detectable faecal Hb, NPVs were:
  CRC – 100%
  High Risk Adenoma – 97.8%
  Inflammatory Bowel Disease – 98.4%

- Adding faecal calprotectin (cut off ≥ 200) detected further 3 lesions (2 IBD, 1 HRA, no CRC)

	FHb ≥10	FC ≥50	FHb detectable
Positivity rate	23.5%	62.0%	58.3%
CRC (n=28)			
Number of cases	28	28	28
True positives	25	23	28
False negatives	3	5	0
False positives	151	427	409
True negatives	571	271	313
PPV	14.2%	5.1%	6.4%
NPV	99.5%	98.2%	100%
Sensitivity	89.3%	82.1%	100%
Specificity	79.1%	38.8%	43.4%

- Simplicity and availability of test
- More scopes using any detectable FHb
- “Rule out” principal for symptomatic patients
- Requires further user acceptability testing

Further studies



Development and external validation of a faecal immunochemical test-based prediction model for colorectal cancer detection in symptomatic patients

Joaquín Cubiella[1,2*], Pablo Vega[1], María Salve[1], Marta Díaz-Ondina[3], Maria Teresa Alves[4], Enrique Quintero[5], Victoria Álvarez-Sánchez[6], Fernando Fernández-Bañares[7], Jaume Boadas[8], Rafel Campo[9], Luis Bujanda[10], Joan Clofent[11], Ángel Ferrandez[12], Leyanira Torrealba[13], Virginia Piñol[13], Daniel Rodríguez-Alcalde[14], Vicent Hernández[2,15], Javier Fernández-Seara[1,2] and on behalf of the COLONPREDICT study investigators

- Embedded in a secondary care setting
- Derivation and validation cohorts
- Faecal, blood tests and clinical variables
- Risk stratification of target population
- Primary endpoint CRC

- 1572 subjects in derivation cohort:
  214 CRC (13.6%) [3.8%*]
  251 HRA (16%) [5.4%]
  36 “colitis” (2.3%) [4.5%]
  501 with SBP (31.8%) [13.6%]

- Study nurses administered questionnaire
- Stool and blood samples collected per protocol
- Prediction score identified 11 variables (from 32)

*As compared to Mowat A, et al.

	NICE referral criteria	COLONPREDICT score ≥5.6	COLONPREDICT score ≥3.5
Number positives	52.2 %	30.9 %	60.5 %
Sensitivity[a]	68.2 % (61.5–74.3)	90.1 % (85.1–93.6)	99.5 % (97.0–100.0)
Significance[b]		<0.001	<0.001
Specificity[a]	50.3 % (47.6–53.0)	78.7 % (76.4–80.9)	45.8 % (43.1–48.2)
Significance[c]		<0.001	<0.001
Positive predictive value[a]	17.8 % (15.3–20.6)	40.7 % (36.2–45.3)	22.9 % (20.3–25.8)
Negative predictive value[a]	91.0 % (89–93)	98.0 % (96.9–98.7)	99.8 % (98.9–100.0)
Positive likelihood ratio[d]	1.4 (1.2–1.5)	4.2 (3.8–4.7)	1.8 (1.7–1.9)
Negative likelihood ratio[d]	0.6 (0.5–0.8)	0.1 (0.08–0.2)	0.01 (0.0–0.07)
Diagnostic odds ratio[d]	2.2 (1.6–2.9)	33.8 (21.1–54.0)	179 (25–1280)

- Above table provides two score thresholds
- Greater number of variables
- 23% of subjects from primary care
- Can be used as a rule out test
- Cut-offs in score – cut-offs in FIT

Summary

- Active field of investigation
- A number of issues that require further study:
  single or multiple variables (simplicity)
  cut-offs, definitions (HRA, SBP)
  implementation – “real-life” – studies
  primary care and/or secondary care settings
  cost-effectiveness
  dealing with the “fear factor”

Thank you

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		Low risk[a]	Intermediate risk[b]	High risk[c]
Number of patients (%)		39.5	29.6	30.9
Colorectal cancer	PPV (%)[d]	0.2 (0.0– 1.1)	4.4 (2.8–6.8)	40.7 (36.7–45.9)
	NNE (95 % CI)	603 (91–10,000)	22.6 (14.7– 35.7)	2.5 (2.2– 2.7)
	OR (95 % CI)	1.0	27.8 (3.7–208)	413 (57.5–2961)
Advanced neoplasia[e]	PPV (%)[d]	7.1 (5.3– 9.6)	20.8 (17.2– 24.8)	58.1 (53.4– 62.5)
	NNE (95 % CI)	14.1 (10.4– 18.9)	4.8 (4.0– 5.8)	1.7 (1.6– 1.9)
	OR (95 % CI)	1.0	3.4 (2.3–5.0)	18.0 (12.6–25.8)
Significant colonic lesion[f]	PPV (%)[d]	8.5 (6.4– 10.0)	24.5 (20.7–28.8)	61.4 (56.9–65.8)
	NNE (95 % CI)	11.8 (10.0–15.6)	4.1 (3.5– 4.8)	1.6 (1.5– 1.7)
	OR (95 % CI)	1.0	3.5 (2.5–5)	17.2 (12.3–24.3)

- Low risk has predict score of < 3.5
- High risk predict score of ≥ 5.6
- Number needed to colonoscope increases

Name of presenter