Department of Veterans Affairs
Health Services Research & Development Service | Evidence-based Synthesis Program

QUERI

Patients with Positive Screening Fecal Occult Blood Tests: Evidence Brief on the Relationship Between Time Delay to Colonoscopy and Colorectal Cancer Outcomes

SUPPLEMENTARY MATERIALS

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SEARCH STRATEGY

MEDLINE (PubMed) searched December 28, 2012

((“Colonoscopy”[Mesh])) AND (((((((((delay OR timing OR time OR delayed OR lagtime OR lagtimes[Title/Abstract])) OR (wait OR duration OR lagtimes OR duration OR lag OR longer[Title/Abstract])) OR (waiting OR shortened OR shorter OR time OR dwell[Title/Abstract])) OR (Schedule OR interval OR postponement OR early OR late OR later OR longer[Title/Abstract])))) OR (“Time Factors”[Mesh])) OR (“Early Diagnosis”[Mesh])) OR (“Early Detection of Cancer”[Mesh]))

EXCLUDED STUDIES

Reasons for exclusions:

1 = Wrong delay period (e.g., delay from symptom onset to diagnosis; delay to referral for colonoscopy; delay from diagnosis to treatment, etc.)
2 = Wrong outcome (e.g., reasons for delays, colonoscopy rates, etc.)
3 = Wrong publication type (e.g., editorial, non-systematic review)
4 = Wrong population (e.g., patients admitted for urgent colonoscopies due to massive lower-GI hemorrhage)

Citations	Reason for exclusion
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TABLE 1. DATA ABSTRACTION

Author Year Setting Sample Size	Demographics Comorbidities	Delay Definition	Delay Durations	Key Question 1 Results	Key Question 2 Results
Fisher 2010[1] 15 VAMCs N=447	Mean age 67 years (SD 10.9) 98% Men 66% White Comorbidity (ACE-27): None: 15% Mild: 38% Moderate: 24% Severe: 23%	Abnormal screening test result date (FOBT, barium enema, flexible sigmoidoscopy or colonoscopy) OR first medical visit detecting symptoms to diagnosis	Median: 91 days (range, 0 to 726)	Odds ratio (95% CI) for late stage (III/IV) at diagnosis (reference=0-30 days): 31-90 days: 0.90 (0.53 to 1.53) 91-180 days: 0.63 (0.34 to 1.16) >180 days: 0.93 (0.54 to 1.61) Mortality NR	NR
Gellad 2009[2] Durham VAMC N=231	Mean age 66 years (SD 9.6) 97% Men 59% White 32% Black 1% Hispanic 8% Missing/Unknown race Comorbidities NR	Positive FOBT to colonoscopy	Mean: 236 days (SD, 112)	Odds ratio (95% CI) for the effect of additional 30-day wait: Advanced neoplasia: 1.07 (0.98 to 1.18) Neoplasia: 1.10 (1.02 to 1.19) Mortality NR	NR
Gomez-Dominguez 2006[3] Endoscopy Unit of 3rd-level hospital in Madrid N=96	Mean age 64 years (SD 18) 54% Men Race NR Comorbidities NR	Physician Delay: Physician recommendation of colonoscopy for hematochezia, fecal occult blood, ferropenic anemia in the absence of other hemorrhagic lesions, palpable abdominal mass, or change in bowel habit to colonoscopy performance	Mean: 38 days (SD, 78)	Dukes' stage by length of administrative delay (mean days): Stage A: 15 (SD 15) Stage B: 28 (SD 26) Stage C: 36 (SD 55) Stage D: 20 (SD 20) NS (*P*-value NR) Mortality NR	NR
Iversen 2009[4] 3 Danish counties N=740	Mean age 69 years (95% CI 68 to 70) 54% Men Race NR Charlson co-morbidity score: 0 (None): 66% 1-2 (Moderate): 27% 3 or higher (Severe): 7%	First physician contact for symptoms (types not described) to initiation of treatment	Median days (IQR): Colon: 52 (25-123) Rectal: 49 (28-103)	Hazard ratio for survival (95% CI): (Model controlled for age, sex, comorbidity, and urgency of surgery) Provider delay 60 days or more: Colon: 0.85 (0.64 to 1.13), Rectal: 1.16 (0.82 to 1.65) Hospital delay of at least 30 days: Colon: 0.84 (0.62 to 1.13); Rectal: 0.84 (0.60 to 1.20) Hospital delay of at least 60 days: Colon: 0.82 (0.57 to 1.18); Rectal: 1.07 (0.69 to 1.67)	Neither provider delay (time from first physician contact to initiation of treatment) of 60 days or more nor hospital delay (interval from referral to a hospital until initiation of treatment) of at least 30 days or at least 60 days was associated with survival. Model controlled for age, sex, co-morbidity score, and urgency of surgery.

Author Year Setting Sample Size	Demographics Comorbidities	Delay Definition	Delay Durations	Key Question 1 Results	Key Question 2 Results
Majumdar 1999[5] North Carolina Memorial Hospital N=194	Mean age 66 years (range 15-95) 53% Men 70% White Comorbidities NR	Time from first MD presentation for any of 15 symptoms and signs, including positive FOBT, to tissue diagnosis	Weeks: Median=3, Mean=11, IQR=1 to 9	No association (*P*=0.94) between overall duration of symptoms and stage of cancer. No association between physician delay (*P*=0.92) in diagnosis and stage of cancer.	No evidence of confounding of the duration-stage relationship by any particular symptom, including FOBT. Clinical presentation (stage or location) did not vary according to age or gender.
Neal 2007[6] 1 UK NHS Trust N=239	Demographics NR Comorbidities NR	GP referral to date of first hospital appointment	Referral delay; median days (IQR): Urgent guideline referrals: 12 (9 to 13); 86% seen within 2 weeks Diagnosed through other routes: 8 (0 to 22); 49% seen within 2 weeks	Urgent guideline referrals vs those diagnosed through other routes Survival: 73% vs 67% (*P*=0.74) Mean survival days (SE): 609.5 (46.0) vs 720.3 (36.2); NS Duke's stage at diagnosis: A: 12% vs 18%; B: 42% vs 37%; C: 46% vs 43%; D: 0% vs 2% (*P*=0.68) TNM stage at diagnosis: No difference (*P*=0.77) All urgent referrals (guideline and letter) vs other routes Survival: No difference (*P*=0.18) Dukes' stage at diagnosis: More advanced stages found among urgent referrals (*P*=0.03) TNM stage at diagnosis: No difference (*P*=0.45)	NR
Rupassara 2006[7] Association of Coloproctology of Great Britain and Ireland Colorectal Database N=154	Mean age 69 years (SD 10) 47% female Race NR Comorbidities NR	Receipt of referral letter (80% had high risk symptoms, but not described) to diagnosis	Median (range) Late group: 108 (50-1092) Early group: 15 (range NR)	Late (50 days or more from referral letter to diagnosis) vs Early (referral to diagnosis time less than 50 days): 5-year cancer specific survival was higher in the Late group (82.7% vs 51.6%; *P*=0.007) No difference in time to death (28.3 vs 29.2 months) Significantly higher proportion of Stage A cancers in the Late group (38.6% vs 15.2%; *P*=0.006) Other Dukes stages: No differences (data NR)'	No difference in age, sex, comorbidity index, date of diagnosis, number of lymph nodes in the operative specimen or histological grading between the early and late groups. No difference in 5-year cancer specific survival between low and high risk symptoms (2/27 deaths in low risk vs 16/112 in high risk group; *P*=0.27)

Author Year Setting Sample Size	Demographics Comorbidities	Delay Definition	Delay Durations	Key Question 1 Results	Key Question 2 Results
Terhaar sive Droste 2010[8] Northern Holland N=272	Mean age 70 years (SD 11) 49% Men Comorbidities NR	Hospital referral date for symptoms (rectal bleeding, weight loss, change in bowel habits, anemia, abdominal pain, tenesmus or bloatedness) to diagnosis	Weeks: Mean=5.7, Median=3, SD=7.9, SE=0.5	Hospital diagnostic delay (time from referral date and diagnosis): Early stage CRC (Dukes' A and B): Mean 6.1 weeks (SD 7.5); median 3 weeks Late stage CRC (Dukes' C and D): Mean 5.2 weeks (SD 8.2); median 2 weeks *P*=0.09 In early stage CRC, no difference in survival associated with longer delay. In late stage CRC, patients with a shorter delay had shorter survival.	Correction for potential confounders (age, gender, tumor-site, history of CRC or polyps, number and type of symptoms) did not modify findings.
Valentin-Lopez 2011[9] Madrid healthcare district N=272	Mean age 69 years (SD 14) 51% Men Race NR Comorbidities: None: 51% <3: 33% 3 or more: 16%	Referral to and completion of colonoscopy: Rapid pathway for high-risk patients vs standard	Rapid referral: Mean 18.5 (SD 19.1); median 15 (0-138) Standard referral: NR for whole group. *Patients with CRC:* Rapid referral: 13.8 days (SD 8.8 days) Standard referral: 33.8 days (SD 38.7)	Rapid pathway vs standard pathway Stage A: 26.0% vs 11.6% (*P*=0.063) Stage B: 36% vs 41.1% Stage C: 24.0% vs 32.4% Stage D: 14.0% vs 14.9%	NR
Viiala 2007[10] Fremantle Hospital, Western Australia N=1632	Mean age 59 years 49% Men Race NR Comorbidities NR	Referral for colonoscopy for any sign or symptom to date of outpatient colonoscopy	NR	Early (Stage A and B) vs Late (Stage C and D) Cancer stage Median (range) waiting time: 43 (15-463) days vs 51 (12-313) days Colonoscopies performed within 90 days: 54% vs 70% No significant differences between early vs late stages	No demographic variable or procedural indication predicted diagnosis of early stage compared with late stage CRC

Author Year Setting Sample Size	Demographics Comorbidities	Delay Definition	Delay Durations	Key Question 1 Results	Key Question 2 Results
Wattacheril 2008[11] Michael E. DeBakey VAMC Overall N=289 Subgroup N=100	Overall (NR for Subgroup of abnormal screening patients): Mean age 68.2 years 99% Men 68.5% White 29.8% Black 23.9% Coronary artery disease 6.6% Congestive heart failure 57.4% Hypertension 25.6% Diabetes 14.5% Chronic obstructive airway disease 12.1% Psychiatric disorders	Referral for colonoscopy to diagnosis; Evaluated Delay overall and in subgroup who was referred for colonoscopy due to abnormal screening (positive FOBT OR polyps seen in flexible sigmoidoscopy)	Overall: Median=41 days (range, 1-2063) Abnormal screening subgroup: Median=60.0 days (range NR)	Association between delay and stage: Overall: A=62.0, B=41.0, C=31.0, D=18.0, *P*=0.0001 Median lagtime in days for Dukes' stage A=60.0, B=62.0, C=12.0, or D=80.0; *P*=0.39 Mortality for ≥ median vs < median: Overall: HR 0.75 (95% CI, 0.47 to 1.21) Abnormal screening subgroup: No association (data NR)	NR

Abbreviations: ACE-27=Adult Comorbidity Evaluation-27 Scale; CI=confidence interval; CRC=colorectal cancer; FOBT=Fecal Occult Blood Test; GP=general practitioner; HR=hazards ratio; IQR=interquarile range; MD=medical doctor; NR=not reported; NS=not significant; SD=standard deviation; SE=standard error; TNM=Tumour, Node, Metastasis Staging System; VAMC=Veterans Affairs Medical Center; vs=versus

TABLE 2. QUALITY RATINGS – COHORT STUDIES

Author, year	Did the study attempt to enroll all (or a random sample of) patients meeting inclusion criteria, or a random sample (inception cohort)?	Were the groups comparable at baseline on key prognostic factors (e.g., by restriction or matching)?	Did the study use accurate methods for ascertaining exposures and potential confounders?	Were outcome assessors and/or data analysts blinded to the exposure being studied?	Did the article maintain comparable groups (report attrition, contamination, adherence, and cross-over)?	Did the study perform appropriate statistical analyses on potential confounders?	Was there acceptable differential loss to follow-up and or overall high loss to follow-up?	Were outcomes pre-specified and defined, and ascertained using accurate methods?	Quality rating
Fisher 2010[1]	Unclear; Patients were from those enrolled in an observational study, but selection methods are not described in detail, not clear if 468 enrolled represented all eligible.	NA; Single group	Yes; Data from survey and medical record abstraction using experienced abstractors	Unclear; Not reported	NA; Single group	Yes; Adjusted for relevant confounders	Yes; 4% of those presenting emergently were excluded from analysis; imputation used for missing survey items (25% missing education data, 26% missing income data), but not included in final model	Yes	Fair
Gellad 2009[2]	Unclear; Excluded people who got colonoscopy after 18 months and those who were followed-up outside the VA system	NA; Single group	Unclear; Abstracted from medical records using trained personnel and standardized data abstraction form; but unclear; whether colonoscopies were ordered as a direct result of positive FOBT's or for development of symptoms	Unclear; Not reported	Unclear; Missing data not reported	Unclear; Only adjusted for age, race, gender, but no information about comparability of patients on comorbidities and/or development of symptoms after positive FOBT	Unclear; Missing data not reported	Yes	Fair
Gomez-Dominguez 2006[3]	Unclear; Consecutive patients, but other inclusion criteria and recruitment time frame not reported	NA; Single group	No; Patient self-report, no validation: Data collected during interviews during endoscopic procedures. Also, lack of clarity about accuracy of process for grading tumor extension based on specimens. No information about assessor characteristics.	Unclear; Data collected prospectively, but interviews conducted during examinations	NA; Single group	Unclear; Study states that multivariate analysis was performed, but no details about methods or results. Only results of chi-square test reported.	Unclear; No information on missing data	Yes	Poor

Author, year	Did the study attempt to enroll all (or a random sample of) patients meeting inclusion criteria, or a random sample (inception cohort)?	Were the groups comparable at baseline on key prognostic factors (e.g., by restriction or matching)?	Did the study use accurate methods for ascertaining exposures and potential confounders?	Were outcome assessors and/or data analysts blinded to the exposure being studied?	Did the article maintain comparable groups (report attrition, contamination, adherence, and cross-over)?	Did the study perform appropriate statistical analyses on potential confounders?	Was there acceptable differential loss to follow-up and or overall high loss to follow-up?	Were outcomes pre-specified and defined, and ascertained using accurate methods?	Quality rating
Iverson 2009[4]	Yes	NA; Single group	Unclear; Delay determined by self-report and verification methods NR	Unclear	NA	Yes	Yes	Yes	Fair
Majumdar 1999[5]	Yes; Consecutive patients meeting inclusion criteria	NA; Single group	Yes; Medical record abstraction with standardized instrument; reliability of abstractors checked	No; Unmasked abstractors	NA; Single group	No; For the duration analysis, adjusted only for age and gender. Also, they appeared to only be looking at the confounding effects of each symptom individually and not the potential interactions between different symptoms and other variables.	Yes; Only those with complete data included in analyses (92% for symptom variables, 87% for duration variables	Yes	Poor
Neal 2007[6]	Yes; All patients meeting inclusion criteria within a defined period	No; Comparison groups were urgent referral vs standard referral	Unclear; Medical records, but no information on abstractors	Unclear; Not reported	NA	No	No; Data reported only on those whose medical records were available (60%)	Yes	Poor
Rupassara 2006[7]	Yes.; All patients with CRC admitted to a single unit during a defined period	NA; Single group	Yes.; ACP database or notes	Unclear	NA	Yes	Yes; Data on 402/411 patients (97.8%)	Yes	Fair
Terhaar sive Droste 2010[8]	Yes; Consecutive patients diagnosed with symptomatic CRC were registered	NA; Single group	Unclear; Some diagnostic delay information based on self-report with no validation and used different methods across patients as necessary	Unclear for data abstraction; no for patient interviews	NA	Yes	No; 104/376 (28%) excluded; 81/338 (22%) excluded due to lack of participation of general practitioner and lack of data on patient delay, healthcare delay, or tumor stage	Yes	Fair

Author, year	Did the study attempt to enroll all (or a random sample of) patients meeting inclusion criteria, or a random sample (inception cohort)?	Were the groups comparable at baseline on key prognostic factors (e.g., by restriction or matching)?	Did the study use accurate methods for ascertaining exposures and potential confounders?	Were outcome assessors and/or data analysts blinded to the exposure being studied?	Did the article maintain comparable groups (report attrition, contamination, adherence, and cross-over)?	Did the study perform appropriate statistical analyses on potential confounders?	Was there acceptable differential loss to follow-up and or overall high loss to follow-up?	Were outcomes pre-specified and defined, and ascertained using accurate methods?	Quality rating
Valentin-Lopez 2011[9]	Yes; All patients entering referral pathway during specified time period	No; Although patients in referral vs standard pathway were similar in demographics and comorbidities, they differed in symptom presentations. By definition, patients routed via the rapid referral pathway met prespecified high-risk signs/symptoms criteria.	Unclear; Database, but no information on data collectors	Unclear; Data collected prospectively but no information on blinding of data collectors	Unclear; Missing data not reported	No; No control for baseline differences	No; 20 patients in the rapid referral pathway did not receive colonoscopy (13 missed appointment, 5 because of comorbidities, 2 rejected the procedure). "Large number of missing data for the standard pathway" but number not specified.	Yes	Poor
Viiala 2007[10]	Unclear; Does not specify consecutive or a random sample of patients, but gives number screened and number meeting inclusion criteria	NA; Single group	Yes	Unclear	NA	Yes	Yes; Reports data on all patients included	Unclear; CRC stage not prespecified and methods are not described	Fair
Wattacheril 2008[11]	Yes; All patients with a new diagnosis within a stated time period; independent review of records by 2 investigators to determine eligibility	NA; Single group	Unclear; Medical records and documented reports from healthcare providers, but no information on process and who collected the data	Unclear; not reported	Unclear; Missing data not reported	Yes for overall sample (adjusted for earliest treatment, earliest initiator, anatomic location, and Dukes' stage); evaluated determinants (demographics and clinical features); linear regression analysis used to evaluate these variables. No for subgroup of 100 patients with abnormal screening test.	Unclear; Missing data not reported	Yes	Fair for overall sample; Poor for subgroup of 100 patients with abnormal screening test

Abbreviations: ACP= Association of Coloproctology; CRC=colorectal cancer; FOBT=Fecal Occult Blood Test; NA=not applicable; VA=Veterans Administration; vs=versus

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