Report 2 / Rapport 2
Due Date / Date Limite: October 14 Octobre 2005

Request for Applications (RFA): Toward Canadian Benchmarks for Health Services Wait Times – Evidence, Application and Research Priorities

Appel de demandes: Établir des points de repères canadiens concernant les temps d'attente dans les services de santé - Preuves, application et priorités de recherche

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TITLE OF YOUR RESEARCH GRANT / TITRE DE VOTRE SUBVENTION DE RECHERCHE:
An evidence based assessment of appropriate waiting times for gastrointestinal cancers.

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A) SUMMARY OF RESEARCH RESULTS:
Provide, in one page or less, a bulleted list of the report's main messages, for objectives #1 and #2 of the RFA, followed by a two to three page executive summary of your report.

Note: The bulleted list and executive summary should summarize the detailed answers provided for questions B) and C) below.

- The presence of any alarm symptoms are poor predictors of upper gastrointestinal malignancy
- Weight loss, dysphagia, and anemia are poor predictors of upper gastrointestinal malignancy
- Rectal bleeding, diarrhea, constipation and abdominal pain are poor predictors of colorectal cancer
- There is a paucity of studies on pancreatic, biliary and liver cancer symptoms
- Obvious jaundice has a 34% positive predictive value for pancreatic, biliary or liver cancer.
- Few Western countries have official waiting time guidelines
- The most comprehensive waiting time guidelines for suspected cancer are from UK and Denmark
- No guidelines bases wait times for suspected cancer on a systematic review of the literature
- We conducted a systematic review of the literature for GI cancers and identified 17 papers evaluating 4491 patients. This suggested delay in diagnosis is not associated with an adverse outcome either of tumor stage or survival.

B) RESEARCH RESULTS - OBJECTIVE 1:
Describe in detail the extent to which the first objective of the RFA has been achieved. Specifically, the following point must be addressed:

1) Synthesis of research evidence regarding relationships between patient characteristics (e.g. age, clinical severity or stage of illness, co-morbidities, etc.), health services wait times and mortality, health status or quality of life.

Upper GI cancer
Overall we identified 18 papers that evaluated patient symptom presentation and the risk of upper gastrointestinal cancer. A total of 57,363 dyspeptic patients were evaluated in the eligible papers of whom 458 (0.8%) had upper gastrointestinal cancer. Data in this review included unpublished results from the US CORI database and the UK two week audit kindly provided by Drs Fennerty and Kapoor respectively.

Overall accuracy of alarm features
We identified 7 studies evaluating 46161 patients with 150 (0.3%) having upper GI cancer. Overall 8669 (19%) patients had one or more alarm features (e.g. dysphagia, weight loss, and anemia). The sensitivity of alarm features varied between 0% and 83% with a pooled sensitivity of 67% (95% CI = 54% to 83%). The specificity of alarm features varied between 40% and 98% with a pooled specificity of 66% (95% CI = 55% to 79%). The positive likelihood ratio values varied between 0 and 13.7 with a pooled LR+ of 1.35 (95% CI 1.19 to 1.52).

Weight loss
There were 8 studies evaluating weight loss as a symptom of gastro-esophageal malignancy in 48,499 patients with 340 (0.7%) upper GI cancers. A total of 3219 (6.6%) patients reported weight loss. The sensitivity of weight loss varied between 13% and 78% with a pooled sensitivity of 49% (95% CI = 37% to 65%). The specificity of weight loss varied between 70% and 99% with a pooled specificity of 84% (95% CI = 81% to 87%). The positive likelihood ratio values varied between 1.77 and 21.23 with a pooled LR+ of 4.15 (95% CI 2.44 to 7.07).

Dysphagia
There were 5 studies evaluating dysphagia as a symptom of gastro-esophageal malignancy in 9646 patients with 192 (2.0%) upper GI cancers. A total of 1217 (13%) patients reported dysphagia. The sensitivity of dysphagia varied between 4% and 62% with a pooled sensitivity of 39% (95% CI = 23% to 66%). The specificity of dysphagia varied between 67% and 99% with a pooled specificity of 85% (95% CI = 78% to 92%). The positive likelihood ratio values varied between 1.77 and 4.04 with a pooled LR+ of 2.60 (95% CI 1.81 to 3.75).

Dysphagia is thought to be an important alarm feature for esophageal cancer. The accuracy of this symptom in diagnosing esophageal cancer was assessed. There were only two studies evaluating 5492 patients that provided data that subdivided by cancer site. Ninety three (1.7%) had esophageal cancer and 203 (4%) had dysphagia. These studies reported sensitivities of 33% and 60% and specificities of 99% and 94% respectively.

Anemia
There were 4 studies evaluating anemia as a feature of gastro-esophageal malignancy in 42327 patients with 190 (0.4%) upper GI cancers. A total of 1518 (3.6%) patients had anemia. The sensitivity of anemia varied between 0% and 13.5% with a pooled sensitivity of 13% (95% CI = 8% to 20%). The specificity of anemia varied between 90% and 97% with a pooled specificity of 95% (95% CI = 92% to 97%). The positive likelihood ratio values varied between 0 and 4.05 with a pooled LR+ of 2.14 (95% CI 0.88 to 5.25).

Lower GI cancer

Overall we identified 31 papers that evaluated patient symptom presentation and risk of colorectal cancer. A total of 54,126 patients were evaluated with 1,817 (3.4%) diagnosed with colorectal cancer. There were no data on the overall accuracy of alarm features in detecting colorectal cancer and insufficient data on iron deficiency anemia and weight loss.

Rectal bleeding

We identified 19 papers evaluating 36,842 patients with 927 (2.5%) having colorectal cancer. 6445 (17.5%) patients had rectal bleeding. The sensitivity of rectal bleeding for detecting colorectal cancer varied between 0 and 86% with a pooled sensitivity of 41% (95% CI = 32% to 53%). The specificity of rectal bleeding varied between 31% and 91% with a pooled specificity of 73% (95% CI = 70% to 77%) and the positive likelihood values ranged between 0 and 3.69 with a pooled LR+ of 1.80 (95% CI = 1.49 to 2.18).

Diarrhea

We identified 7 papers evaluating 11,487 patients with 563 (4.9%) having colorectal cancer. 1323 (11.5%) patients had diarrhea. The sensitivity of diarrhea for detecting colorectal cancer varied between 0 and 70% with a pooled sensitivity of 24% (95% CI = 10% to 57%). The specificity of diarrhea varied between 61% and 92% with a pooled specificity of 75% (95% CI = 61% to 92%) and the positive likelihood values ranged between 0 and1.78 with a pooled LR+ of 0.93 (95% CI = 0.53 to 1.63).

Constipation

We identified 4 papers evaluating 3,866 patients with 201 (5.2%) having colorectal cancer. 513 (13.3%) patients had constipation. The sensitivity of constipation for detecting colorectal cancer varied between 0 and 51% with a pooled sensitivity of 9% (95% CI = 1% to 82%). The specificity of constipation varied between 53% and 94% with a pooled specificity of 79% (95% CI = 71% to 88%) and the positive likelihood values ranged between 0 and 1.08 with a pooled LR+ of 0.56 (95% CI = 0.2 to 1.51).

Abdominal pain

We identified 9 papers evaluating 8,646 patients with 412 (4.8%) having colorectal cancer. 3,492 (40.4%) patients had abdominal pain. The sensitivity of abdominal pain for detecting colorectal cancer varied between 0 and 73% with a pooled sensitivity of 32% (95% CI = 20% to 50%). The specificity of abdominal pain varied between 19% and 91% with a pooled specificity of 54% (95% CI = 43% to 68%) and the positive likelihood values ranged between 0 and 1.10 with a pooled LR+ of 0.69 (95% CI = 0.52 to 0.91).

Pancreatic, liver and bile duct cancer

There is a paucity of data on the diagnostic utility of symptoms in pancreatic cancer, cholangiocarcinoma and hepatocellular carcinoma. We identified only one study that fulfilled our eligibility criteria. This study enrolled 1020 patients and reported the sensitivity and specificity of 62% and 65% respectively for a raised bilirubin in detecting pancreatic cancer (LR+ = 1.75). Weight loss had a sensitivity of 66% and a specificity of 71% (LR+ = 2.28), anemia had a sensitivity of 29% and specificity of 73% (LR+ = 0.97), and abdominal pain had a sensitivity of 51% and a specificity of 38% (LR+ = 0.83).

There were some papers that reported on the diagnosis in a consecutive series of jaundice patients. There were three studies evaluating 847 patients with any raise in serum bilirubin. There were 173 malignancies (pancreatic cancer, cholangiocarcinoma and hepatic metastases) and the positive predictive value (PPV) varied between 20% and 21% with a pooled PPV of 20% (95% CI = 18% to 23%). There were two studies evaluating 283 patients with severe clinically evident jaundice. There were 73 malignancies (pancreatic cancer, cholangiocarcinoma and hepatic metastases) and the PPVs were 35% and 34% with a pooled PPV of 34% (95% CI = 29% to 40%).

C) RESEARCH RESULTS – OBJECTIVE 2:

1) Summary of wait time wait time benchmarks that are currently used nationally or internationally.

This was outlined in the previous report and has been updated. A summary table is presented here (for more details see previous report)

Country	Official policy	Wait to see specialist	Wait for treatment	Explicit definition for suspected cancer
Australia	No	Waiting a problem	Not defined	Not applicable
Spain	No	Waiting a problem	Not defined	Not applicable
Greece	No	Waiting a problem	Not defined	Not applicable
New Zealand	No	Waiting a problem	Not defined	Not applicable
Portugal	No	Waiting a problem	Not defined	Not applicable
France	No	Seen within 2 weeks	Not defined	Not applicable
Belgium	No	Seen within 2 weeks	Not defined	Not applicable
Holland	No	Seen within 2 weeks	Not defined	Not applicable
Switzerland	No	Seen immediately	Not defined	Not applicable
US (insured)	No	Seen immediately	Not defined	Not applicable
US (local VA)	Yes	30 days	Not defined	Case scenarios
Denmark	Yes	2 weeks	Not defined	No
Finland	Yes	3 days	14 days	No
UK	Yes	2 weeks	30 days	Yes

In cases where there is an official policy this is not based on any systematic review and there appears to be no clear rationale for the maximum allowable time chosen.

2) Synthesis of research evidence (if any) that has been used to support these benchmarks.

We have conducted a systematic review of the literature that relates diagnostic delay to the stage or survival from gastrointestinal cancer. This work is still ongoing and we are awaiting three interlibrary loan papers. Currently we have identified 17 papers evaluating 4491 patients. The papers present the disparate outcomes and define diagnosis delay in different ways so it was not possible to synthesize the data quantitatively. The summary of these studies is given in the appendix. Overall 10 papers reported no association between diagnostic delay and GI cancer stage or survival. Three reported that delayed diagnosis was associated with a more advanced tumor stage whilst four papers reported that a delayed diagnosis was associated with an earlier tumor stage. There are problems interpreting all of these studies as any result could be due to bias or confounding but there is no clear impact of waiting time on GI cancer stage.

D) ADDITIONAL COMMENTS (e.g. challenges you have faced and how you have/are addressed/ing them, deviation(s) from your original research proposal…)

Work on synthesizing the evidence for patient preference on waiting times is currently ongoing.

SIGNATURE OF PRINCIPAL INVESTIGATOR: DATE: 14th October 2005