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Postoperative Ileus, A Surgical Perspective

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Magnitude of the Problem

- Approximately 400,000 patients undergo small and large bowel resection each year[a]
  - 90% open surgery, 10% laparoscopic[b]
  - ALL of these patients experience POI of some degree
  - At least 10% to 15% require intervention or a change in hospital management due to unresolving POI
  - Prolonged POI CANNOT be reliably predicted before bowel resection surgery

[a] Premier Inc. Procedural Data, 2006 Projections.
[b] Hinojosa MW. *J Gastrointest Surg*. 2007;11:423-429.

Definition and Clinical Signs

- Transient cessation of coordinated bowel motility after surgery preventing effective transit of intestinal contents and/or tolerance of oral intake[a]
- No physiological benefit of POI
- Clinical signs
  - Nausea/vomiting
  - Absence of passage of flatus/stool
  - Bloating, abdominal pain, discomfort

[a] Delaney C, et al. In: Bosker G, ed. *Clinical Consensus Update in General Surgery*. Roswell, Ga: Pharmatecture, LLC; 2006. http://www.clinicalwebcasts.com/updates/index.htm.

Etiology

- Surgical stress response
  - Neurogenic[a]
  - Hormones and neuropeptides[b]
  - Inflammatory mediators[c,d]
- Surgical anesthesia
  - Many impair GI motility[e,f,g]
  - Primary effect on colon[f]

[a] Holzer P, et al. *Neuroscience*. 1992;48:715-722; [b] Zittel TT, et al. *Surgery*. 1998;123:518-527;
[c] Moojen TM, et al. *Neurogastroenterol Motil*. 1999;11:403-408; [d] Kalff JC, et al. *Gastroenterology*. 2000;118:316-327;
[e] Ogilvy AJ, et al. *Eur J Anaesthesiol*. 1995;10 Suppl:35-42; [f] Condon RE, et al. *Surgery*. 1987;101:81-85;
[g] Freye E, et al. *Acta Anaesthesiol Scand*. 1998;42:664-669.

Etiology—
Opioid Analgesic Agents

- Bind to μ-opioid receptors within the enteric nervous system[a]
- Block excitatory neurons innervating intestinal smooth muscle[b]
- Inhibit GI motility[a,b,c]

[a] Austrup ML, et al. *Surg Clin North Am*. 1999;79:253-273.
[b] Bauer AJ, et al. *Gastroenterology*. 1991;101:970-976.
[c] Kaufman PN, et al. *Gastroenterology*. 1988;94:1351-1356.

Patient-Controlled Analgesia (PCA)

- Opioid-based PCA standard care for pain management following bowel resection[a,b]
  - More effective analgesia
  - Shorter hospital stay
  - Improved patient satisfaction
- Associated with higher incidence of "coded" POI[c]

[a] Ballantyne JC, et al. *J Clin Anesth*. 1993;5:182-193.
[b] Petros JG, et al. *Am J Surg*. 1995;170:371-374.
[c] Goettsch WG, et al. *Pharmacoepidemiol Drug Saf*. 2007;16:668-674.

Gastrointestinal Recovery—How Long Is Too Long?

- GI recovery after 5 days increases risk of
  - Prolonged hospital length of stay (LOS)[a,b]
  - Morbidity, including nosocomial infections[c]
  - Medical or surgical intervention

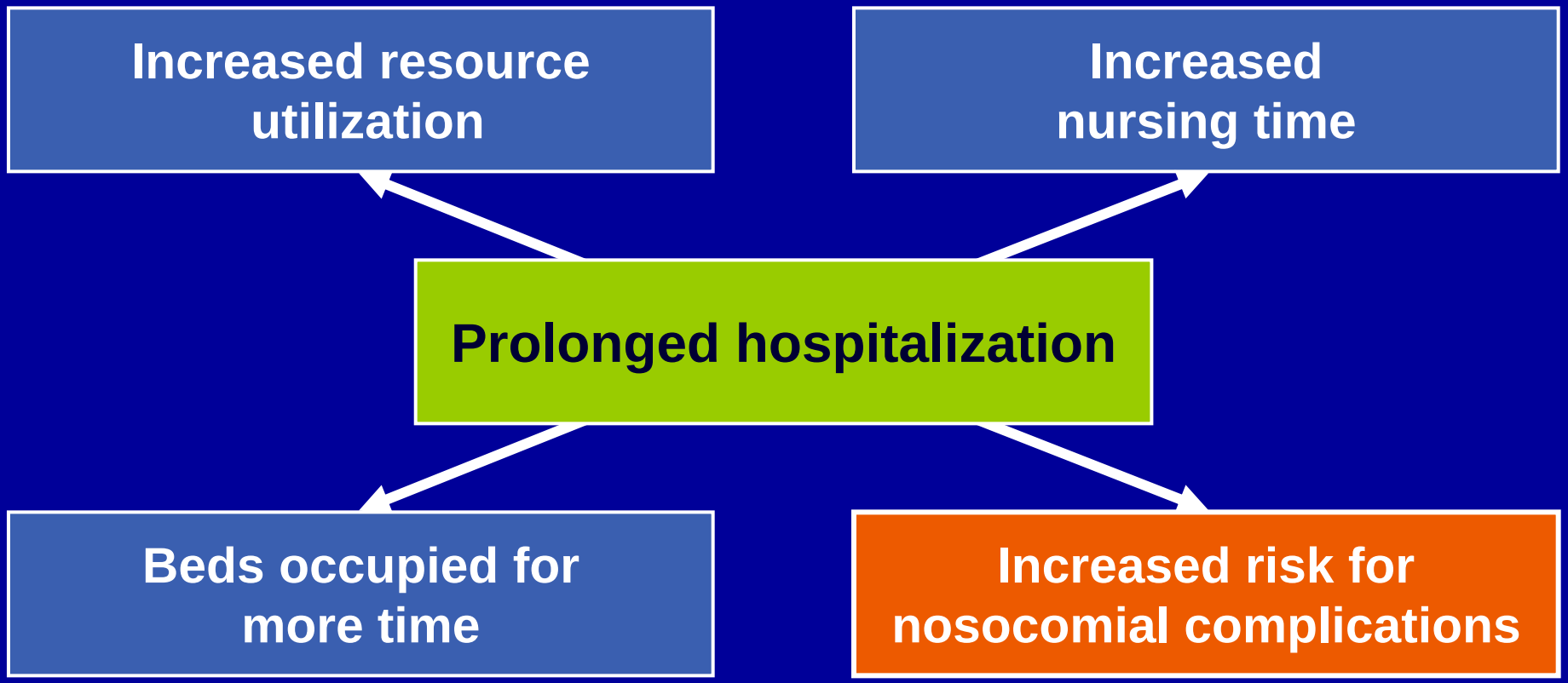
[a] Person B, et al. *Curr Prob Surg.* 2006;43:6-65; [b]Delaney CP, et al. *Br J Surg.* 2001;88:1533-1538; [c]Buchner AM, et al. *Dig Dis Sci.* 2002;47:201-207.

Gastrointestinal Recovery—How Long Is Too Long?

- For this reason, the primary clinical objective following BR is avoidance of POI
- Most studies in the area of perioperative care protocols are powered based on a 1-day reduction in length of stay, by accelerating recovery of bowel function

Patient Characterization

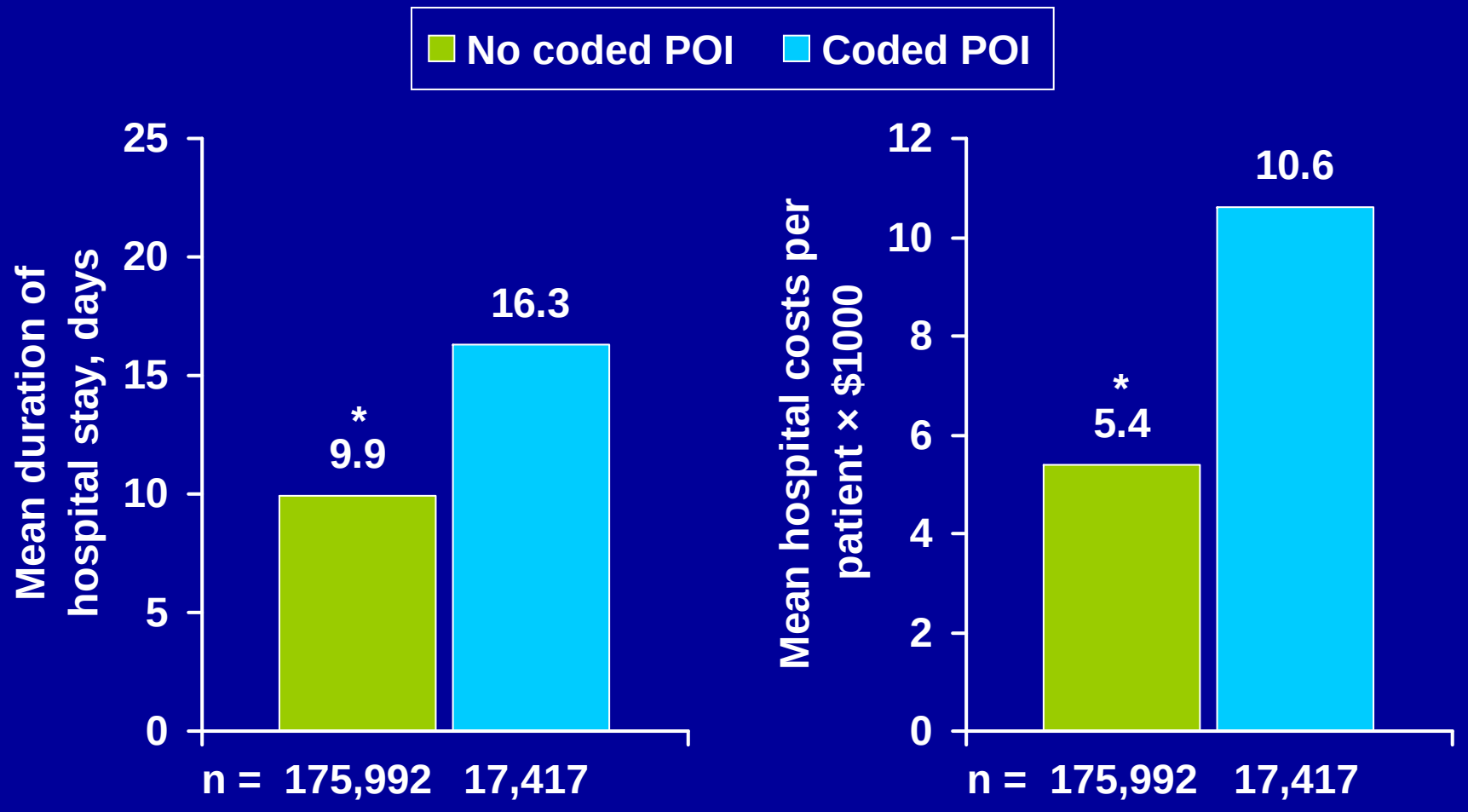
Overall Healthcare Burden Associated With POI[a,b,c,d]



[a] Schuster TG, Montie JE. *Urology*. 2002;59:465. [b] Holte K, Kehlet H. *Br J Surg*. 2000;87:1480.
[c] Chang SS, et al. *J Urol*. 2002;67:208; [d] Sarawate CA, et al. *Gastroenterology*. 2003;124:A-828.

Length of Hospital Stay and Associated Costs Increase With Coded POI

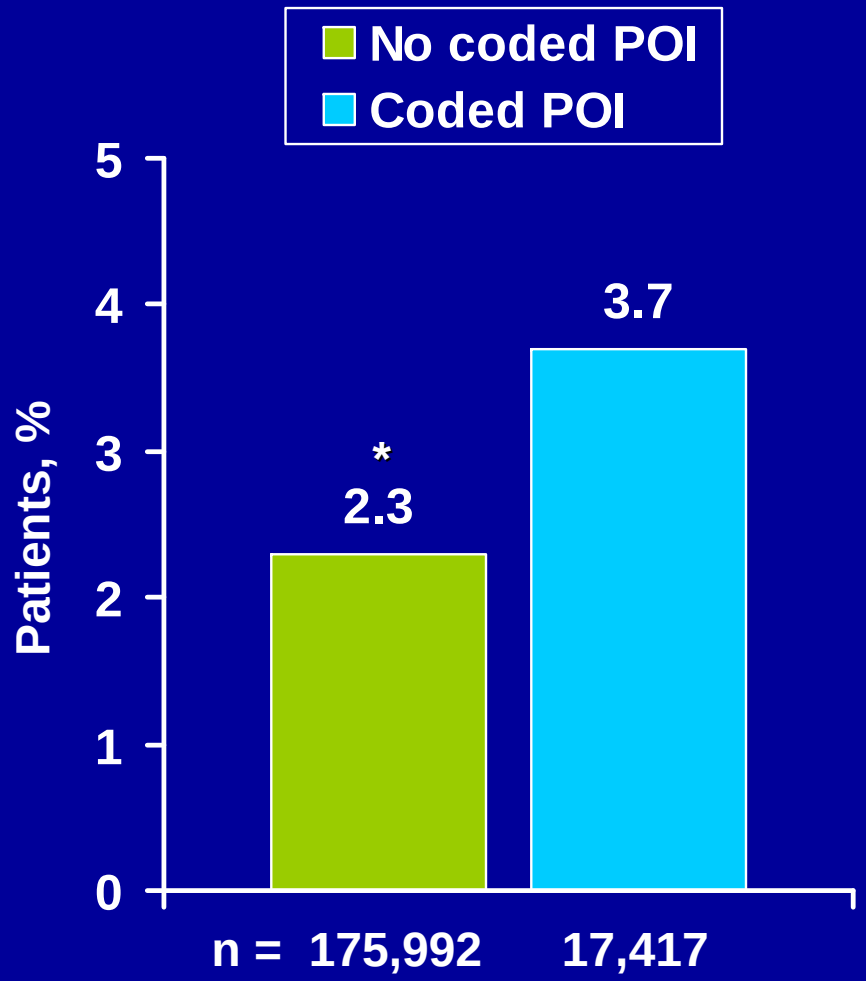
Premier's Perspective Database



****p* < 0.01 for coded POI vs no coded POI.**

Senagore A, et al. Presented at ASHP, June 2006.

In-Hospital Mortality Associated With POI
Premier's Perspective Database



*$p < 0.01$ for coded POI vs no coded POI.
Senagore A, et al. Presented at ASHP, June 2006.

POI—Current Treatment Options

- Multimodal accelerated care pathways
  - Intensive nursing and physician input
  - Early NG tube removal, diet advancement, ambulation
  - Opioid-sparing analgesia
  - Prokinetics—none approved for POI
  - Minimally invasive surgery

Delaney CP, et al. *Dis Colon Rect*. 2003; Delaney CP, et al. *Ann Surg*. 2003; Basse L. *Ann Surg*. 2000; Smith AJ, et al. *Dis Colon Rect*. 2000; Bungard TJ. *Pharmacotherapy*. 1999; Marret E, et al. *Br J Surg*. 2007.

Prophylaxis of POI Versus DVT/Surgical Site Infection

	NNT
DVT/surgical site infection[a]	4 - 17
POI (discharge order written before Day 7)	5 - 9

[a] Song F. *Health Technol Assess*. 1998;2:1-111.
Anderson DR, et al. *Ann Intern Med*. 1993;119:1105-1112.
Wells PS, et al. *Arch Intern Med*. 1994;154:67-72.

POI—Current Unmet Need

- No approved drugs for management of POI
- Current management options limited and not consistently effective
- No reliable criteria to predict who will develop prolonged or severe POI
- POI should be managed proactively in patients undergoing bowel resection