

At A Glance

March 2010

Monthly highlights of ICES research findings for stakeholders

Popular antidepressants block life-saving benefits of tamoxifen in breast cancer patients

Kelly C, Juurlink D, Gomes T, Duong-Hua M, Pritchard K, Austin P, Paszat L. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study. *BMJ*. 2010; 340:c693.

Issue	Based on how these drugs are metabolized in the body, it is predicted that a class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs) could reduce the effectiveness of tamoxifen, an important drug in the treatment of breast cancer. The clinical importance of this drug interaction is unknown.
Study	Examined 2,430 women aged 66 or older with breast cancer living in Ontario who were treated with tamoxifen and a single SSRI between 1993 and 2005. Patients were followed from completion of tamoxifen treatment to death or the end of the study period (on average, 2.4 years).
Key Findings	About 30% of women were prescribed an SSRI during tamoxifen therapy, and paroxetine was the most commonly used SSRI (taken by 25.9% of the women). After adjusting for age, duration of tamoxifen treatment and other confounders, absolute increases of 25%, 50% and 75% in the proportion of time on tamoxifen with overlapping use of paroxetine were associated with 24%, 54% and 91% increases, respectively, in the risk of death from breast cancer. No such risk was seen with other SSRIs. Treatment with paroxetine for 41% of the total time on tamoxifen (the median in this study) would result in one additional breast cancer death at five years for every 20 women so treated.
Implications	When co-prescription of tamoxifen with an anti-depressant is necessary, preference should be given to anti-depressants that do not interfere with tamoxifen's effectiveness.

Major complications after ICD implantation linked to increased mortality risk

Lee D, Krahn A, Healey J, Birnie D, Crystal E, Dorian P, Simpson C, Khaykin Y, Cameron D, Janmohamed A, Yee R, Austin P, Chen Z, Hardy J, Tu J. Evaluation of early complications related to de novo cardioverter defibrillator implantation insights from the Ontario ICD Database. *J Am Coll Cardiol*. 2010; 55(8):774–82.

Issue	Implantable cardioverter-defibrillators (ICDs) are used to restore a normal heartbeat to patients with arrhythmia. Little is known about the rates and predictors of complications associated with the devices.
Study	Examined 45-day complications and all-cause mortality in 3,340 patients aged 16 or older who received their first ICD at one of 18 Ontario centres between February 2007 and May 2009.
Key Findings	Complications occurred in 7.5% of patients within 45 days of implantation. Major complications (mechanical problems with the devices, heart failure, fluid in the lungs or serious surgical infections) occurred in 4.1% of patients within 45 days; these patients had more than three times the risk of dying within the next six months. Women and those with enlarged left ventricles were approximately 50% more likely to develop major complications. The most complex defibrillators (those involving leads to pace the left and right sides of the heart) were associated with double the risk of major complications compared to simpler devices.
Implications	These findings highlight the importance of patient selection. Implanting physicians should ensure that the risk involved in using more complex devices is justified by the expected benefit.

Urological infections a concern for men undergoing TRUS-guided prostate biopsy

Nam R, Saskin R, Lee Y, Liu Y, Law C, Klotz L, Loblaw A, Trachtenberg J, Stanimirovic A, Simor A, Seth A, Urbach D, Narod S. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. *J Urology*. 2010; 183(3):963–9.

Issue	Transrectal ultrasound (TRUS) guided prostate biopsy is widely used to diagnose prostate cancer. No previous study has used a large population-based sample to determine rates of hospital admission and mortality associated with the procedure.
Study	Identified all men over age 18 who underwent a TRUS biopsy in Ontario between January 1996 and December 2005, and calculated hospital admission rates for urological complications (infection, bleeding or obstruction) and all-cause hospital mortality rates at 30 days post-biopsy.
Key Findings	Of the 75,190 men who underwent a TRUS biopsy, 44.6% were diagnosed with prostate cancer. The 30-day hospital admission rate was 0.8% for men with cancer and 1.9% for those without cancer. Among men without cancer, the 30-day hospital admission rate increased from 1% in 1996 to 4% in 2005. Urological infection was the most responsible diagnosis in 72% of admissions. During the 10-year study period, there was no significant change in 30-day hospital mortality rates among all patients.
Implications	These findings support the need for the development of TRUS biopsy prophylaxis protocols with the overall goal of decreasing post-biopsy complications from infection.

Simple tool identifies patients who may need closer monitoring after leaving hospital

van Walraven C, Dhalla I, Bell C, Etchells E, Stiell I, Zarnke K, Austin P, Forster A. Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. *CMAJ*. 2010 Mar 8 [Epub ahead of print].

Issue	Readmissions to hospital are common, costly and often preventable. An easy-to-use index to quantify the risk of readmission or death after discharge from hospital would help clinicians identify patients who might benefit from more intensive post-discharge care.
Study	Identified 48 patient- and admission-level variables for 4,812 patients who were discharged to the community from 11 Ontario hospitals between October 2002 and July 2006, and determined their outcome status at 30 days. Data from half of the patients was used to formulate the index and data from the other half was used to test index validity. External validation of the index was performed using one million randomly selected patients discharged from hospital between 2004 and 2008.
Key Findings	Only four variables were independently associated with death or readmission within 30 days of discharge: hospital length of stay (“L”), acute admission (“A”), presence of comorbidities (“C”) and emergency department visits during the previous six months (“E”). After modeling the four variables into a risk index with points assigned to each variable according to severity (the “LACE” score), it was determined that each one-point increase in the LACE score increased the likelihood of unplanned readmission within 30 days by 18% and the odds of early death by 29%.
Implications	Further research is needed to identify other factors that may improve the accuracy and discriminatory ability of the LACE index. Until the index has been further validated using primary data, its use should be reserved for outcomes research and quality assurance purposes rather than for clinical decision-making.

Off-label use of Avastin to treat macular degeneration mushrooming in Ontario

Campbell R, Bronskill S, Bell C, Paterson M, Whitehead M, Gill S. Rapid expansion of intravitreal drug injection procedures, 2000 to 2008: a population-based analysis. *Arch Ophthalmol*. 2010; 128(3):359-62.

Issue	In September 2005, bevacizumab (Avastin) was approved for use in Canada as a colorectal cancer drug. In June 2007, ranibizumab (Lucentis) was approved for treating age-related macular degeneration (AMD)—the abnormal growth of blood vessels in the retina of the eye—through intravitreal injection. Both drugs inhibit vascular endothelial tissue growth. However, because of Avastin’s earlier availability and significantly lower cost (\$30 per injection vs. \$1,950 for Lucentis), it became an off-label treatment of choice for AMD. What patterns of care for AMD have emerged with the introduction of Avastin?
Study	Analyzed monthly fee claims for intravitreal injections submitted to the Ontario Health Insurance Plan between January 2000 and March 2008 and linked procedures to the physicians who performed them.
Key Findings	<ul style="list-style-type: none"> • Following approval of Avastin for colorectal cancer, the rate of intravitreal injections grew eight-fold between September 2005 and November 2007—from 3.5 to 25.9 per 100,000 residents per month. The fact that the increase occurred before Lucentis was available indicates that Avastin accounted for the vast majority of such injections during the 27-month period. • Based on peak projections in Ontario, the estimated annual cost of treating AMD exclusively with Lucentis in Canada would be \$180 million; were it shown to be safe and effective, using Avastin would reduce the cost to \$2.8 million. • In 2007, more than half of intravitreal injections in Ontario were performed by 3% of ophthalmologists, and the monthly number of injections performed by this group grew from 162 to 1,436 between September 2005 and November 2007.
Implications	Although the off-label use of Avastin to treat AMD provides great cost savings, its efficacy and safety will have to await the outcomes of ongoing clinical trials. The number of injection procedures required together with the limited supply of ophthalmologists has the potential to limit equitable access to intravitreal injections in some regions, and may negatively affect access to services for other vision-threatening eye conditions.