

At A Glance

May 2012

Monthly highlights of ICES research findings for stakeholders

Postpartum maternal prescribing of codeine not a major risk to newborns

Juurlink DN, Gomes T, Guttman A, Hellings C, Sivilotti ML, Harvey MA, Mamdani MM. Postpartum maternal codeine therapy and the risk of adverse neonatal outcomes: a retrospective cohort study. *Clin Toxicol (Phila)*. 2012; 50(5):390–5.

Issue	Does the use of codeine by nursing mothers pose a threat to their newborn children?
Study	Identified 7,804 infants whose mothers were prescribed codeine through a publicly funded drug plan within seven days of delivery in Ontario hospitals between April 1998 and March 2008 and compared them to an equal number of infants whose mothers did not receive codeine. Infant readmission to hospital for any reason within 30 days was determined for both groups.
Key Findings	Overall, 3.8% of infants born to mothers who filled a prescription for codeine, and 4.0% of infants whose mothers did not, were hospitalized within 30 days.
Implications	These findings suggest that serious neonatal harm is unlikely when codeine is prescribed to breastfeeding women postpartum. This is not an endorsement of codeine use by women during pregnancy and labour. Study limitations include a lack of information on breastfeeding patterns or the genetic makeup of the study subjects, as well as the possibility that some women were given codeine without a prescription.

Common cholesterol medication may impair renal function in elderly patients

Zhao YY, Weir MA, Manno M, Cordy P, Gomes T, Hackam DG, Juurlink DN, Mamdani M, Moist L, Parikh CR, Paterson JM, Wald R, Yao Z, Garg AX. New fibrate use and acute renal outcomes in elderly adults: a population-based study. *Ann Intern Med*. 2012; 156(8):560–9.

Issue	In controlled clinical trials, fibrates, a class of drugs used to treat high cholesterol, were observed to cause a rise in the serum creatinine level, a sign of kidney damage. What is the association between fibrate use and renal outcomes among community-dwelling older adults in Ontario?
Study	Identified 80,903 patients aged 66 or older with a new outpatient prescription for a fibrate or ezetimibe (a comparator drug) between January 2004 and December 2008, and determined the following outcomes at 90 days: hospitalization for an increase in serum creatinine level, consultation with a nephrologist, receipt of dialysis for severe kidney injury, all-cause mortality, and increase in serum creatinine level.
Key Findings	Compared with ezetimibe users (n=61,831), fibrate users (n=19,072) were more likely to be hospitalized for an increase in serum creatinine level and to consult with a nephrologist. There were no differences between the two groups in the risk for all-cause mortality or receiving dialysis; 9.1% of fibrate users and 0.3% of ezetimibe users had an increase in serum creatinine level of 50% or more.
Implications	Until the underlying mechanism by which fibrates increase serum creatinine levels is better understood, physicians prescribing fibrates to older patients should start the prescription at a low dose and arrange for close monitoring of renal function. This is especially true for patients with existing chronic kidney disease.

Less than half of Ontario patients newly diagnosed with asthma receive lung function test

Gershon AS, Victor JC, Guan J, Aaron SD, To T. Pulmonary function testing in the diagnosis of asthma: a population study. *Chest*. 2012; 141(5):1190–6.

Issue	Canadian guidelines specify that asthma diagnoses should be based both on symptoms and on pulmonary function testing, which provides objective evidence of airflow obstruction and airway hyper-responsiveness. What proportion of Ontarians receive this test around the time of asthma diagnosis?
Study	Examined the health data of 465,866 individuals aged 7 years and older with newly physician-diagnosed asthma living in Ontario between 1996 and 2007. Receipt of pulmonary function testing between one year before and 2.5 years after diagnosis was determined and examined across patient sociodemographic and clinical factors.
Key Findings	Forty-three percent of patients newly diagnosed with asthma received pulmonary function testing around the time of diagnosis. Individuals 7–9 years old, those 70 years and older, and those of lower socioeconomic status were less likely to receive testing. Individuals seeing a medical specialist were more likely to receive testing than those seeing only a general practitioner.
Implications	Clinicians should be encouraged to use pulmonary function testing to both facilitate more accurate asthma diagnosis and improve its management. Further study is needed to determine why more of this testing is not being used to diagnose asthma and how barriers to its appropriate use can be overcome.

More than two-thirds of Ontarians with diabetes live in major urban centres

Booth GL, Polsky JY, Gozdyra G, Cauch-Dudek K, Kiran T, Shah BR, Lipscombe LL, Glazier RH. *Regional Measures of Diabetes Burden in Ontario*. Toronto: ICES; 2012.

Issue	Currently, more than one million Ontarians are living with diabetes, a number that is expected to climb significantly over the next decade. A better understanding of the characteristics of this population will enable local policymakers and health planners to examine the performance of key measures relevant to diabetes care in a given region or community and set priorities for program planning and development.
Study	Linked administrative health claims and census data to create maps showing indicators of diabetes burden and access to diabetes services in Ontario and at regional and community levels between 2006/07 and 2010/11.
Key Findings	<ul style="list-style-type: none"> • Over two-thirds of all Ontarians with diabetes lived in major urban centres, with approximately one-half in the Greater Toronto Area. • Diabetes prevalence was highest in the Greater Toronto Area (up to 13% in some areas) and in Ontario's First Nations communities (as high as 32%). The provincial average was 9.6%. • Chronic complication rates were highest in northern Ontario and in rural areas in southern Ontario. In some communities, as many as two of every 10 adults with diabetes had at least one chronic complication (e.g., hospitalization for cardiovascular disease, lower limb amputation or end-stage kidney disease). • Mental health problems were common among Ontarians living with diabetes, with more than a third making one or more visits to a physician for this reason. • Access to diabetes programs and services was greatest in urban centres, although education programs were fairly extensively distributed across the province. Numbers of endocrinologists and ophthalmologists were fairly sparse outside of major centres.
Implications	These findings will aid in the evaluation of diabetes service programs and care delivery models currently underway or in development in Ontario.

Antidepressant–beta blocker pairing does not pose increased risk for bradycardia in seniors

Kurdyak PA, Manno M, Gomes T, Mamdani MM, Juurlink DN. Antidepressants, metoprolol and the risk of bradycardia. *Ther Adv Psychopharmacol*. 2012; 2(2):43–9.

Issue	Case reports suggest that some antidepressants can interfere with the liver metabolism of metoprolol, a medication frequently used to treat hypertension, by inhibiting the enzyme CYP2D6, thereby potentially increasing the risk of bradycardia (an abnormally low heart rate). What are the clinical consequences of this drug interaction at the population level?
Study	Identified Ontario residents aged 65 and older with a first metoprolol prescription following their 66 th birthday between April 1997 and March 2009 and tracked them until a hospital visit for bradycardia, death, discontinuation of metoprolol, addition of another beta blocker or the end of the study period. Cases hospitalized for bradycardia were compared with matched controls and their exposure to one of the CYP2D6-inhibiting antidepressants, fluoxetine and paroxetine, or the non-CYP2D6-inhibiting antidepressants, fluvoxamine, citalopram, venlafaxine and sertraline, in the 30 days before hospitalization was determined.
Key Findings	Of 332,254 elderly people receiving metoprolol, 3.9% also were prescribed the CYP2D6-inhibiting antidepressants and 10.2% the non-CYP2D6-inhibiting antidepressants. Overall, 8,232 patients (2.5%) were hospitalized for bradycardia. Within this group, 99 were newly treated with a study antidepressant in the 30 days preceding hospitalization: 23.2% received the CYP2D6-inhibiting antidepressants; and 76.8% received the non-CYP2D6-inhibiting antidepressants. The adjusted odds of exposure to the CYP2D6-inhibiting antidepressants (relative to the non-inhibiting antidepressants) was not significantly elevated (odds ratio: 0.76; 95% confidence interval, 0.42-1.37).
Implications	The results suggest that CYP2D6-inhibiting antidepressants do not increase the risk of hospitalized bradycardia among people taking metoprolol. This does not mean that an interaction did not exist; simply that, if present, it did not lead to hospitalization. Patients who have multiple copies of CYP2D6 or who are ultra-rapid metabolizers (and therefore receive high doses of metoprolol) may still be at risk of bradycardia if antidepressants that inhibit CYP2D6 are added to existing drug regimens that include metoprolol.