FOR THE RECORD

Alcohol-related deaths high in Ireland

As many as 170 people in Ireland suffer alcohol-related poisoning deaths each year, according to new statistics released by the Health Research Board, the country's lead agency in supporting and funding health research. For the years 2004–2008, a total of 672 people died from poisoning related to alcohol, most of them men under the age of 50, according to the report, released July 12 (www.hrb.ie/uploads/tx_hrbpublications/HRB_Trend_Series_10.pdf).

The report states that the per-capita consumption of alcohol in Ireland, though lower than its peak in 2000, is still high. In 2009, the average Irish adult consumed 11.3 litres of pure alcohol. "This is more than twice the average in 1960," the report states. "Irish adults had the third highest per capita consumption in Europe in 2008. A national survey in 2007 found that half of the drinkers surveyed had a harmful drinking pattern, which equates to nearly one and a half million Irish adults drinking in a harmful manner."

The statistics indicate that non-poisoning deaths related to alcohol for 2004–2008 totalled 3336, increasing annually over that period from 508 to 799. The most common medical causes of death were liver disease (24%), cardiac conditions (17%) and respiratory infections (11%). About 11% of deaths were the result of trauma. Of these, 40% were attributed to falls and 19% to hanging.

"The figures show very clearly that many of those who died were still in their prime, aged between 40 and 59," the paper states. "The detrimental effect of alcohol is further illustrated by the high proportion of those aged 44 or under who died as a result of alcoholic liver disease. This paper cannot estimate the considerable social cost of premature mortality of these individuals, its detrimental effect on the family, and burden to society."

The paper lists several alcohol policies that the World Health Organization suggests could reduce alcohol-related harm, including raising taxes on alcohol, restricting retailers' hours of sale, lowering the legal blood alcohol concentration for drivers and creating accessible treatment programs. — Roger Collier, *CMAJ*

Food safety summit advocates research on drug resistance

The world food standard body is urging governments to further investigate the health impact of using antibiotics in livestock production with the release of new guidelines aimed at curbing the spread of antimicrobial resistance.

The new guidelines on the use of antimicrobials in livestock production adopted at the 34th session of the Codex Alimentarius Commission in Geneva, Switzerland, advocate for member states to assess the human and animal health risks posed by the use of antibiotics in food and animal feed production.

Specifically, the guidelines urge governments to:

- analyze the level of risk caused by the use of antibiotics in the production of food and animal feed;
- assess the risk of antimicrobial resistance associated with its presence in food and animal feed, and its impact on human health;
- assess the risk of transmission of antimicrobial resistance to humans and provide measures to reduce it.

Antimicrobial resistance has emerged as a growing health concern in recent years, largely as a consequence of the widespread use of antibiotics by the livestock industry for veterinary purposes or as growth promoters, the commission says.

Moreover, the global nature of the industry represents an obstacle in stemming the emergence and spread of resistant micro-organisms, as food traded worldwide can be a major vector for the spread of resistance between humans and animals.

The commission also adopted new guidance on genetically modified foods at the meeting. Governments are free to decide whether and how to label foods derived from modern biotechnology, including foods containing genetically modified organisms, according to the new guidelines. Labeling, however, should conform to text approved by the commission to avoid potential trade barriers. — Lauren Vogel, *CMAJ*

CIHR to develop therapeutic clinical trial of liberation therapy for multiple sclerosis

The Canadian Institutes of Health Research (CIHR) will issue a call for proposals before the end of the year for a Phase I/II interventional trial on whether balloon venoplasty is a valid therapy for multiple sclerosis (MS).

Less than a year after concluding that Italian physician Dr. Paolo Zamboni's controversial liberation therapy lacked scientific validity and posed risks to patients (www.cmaj.ca/lookup/doi/10.1503/cmaj.109-3665), CIHR's Scientific Expert Working Group on Chronic Cerebrospinal Venous Insufficiency and Multiple Sclerosis (CCSVI) has lined-up squarely behind the federal government's decision to fund CCSVI trials.

Minister of Health Leona Aglukkaq said in late June that the federal government had decided to support phase 1 and phase 2 trials after hearing "moving" anecdotal evidence from MS patients and their families. Aglukkaq indicated that the CIHR working group

was unanimously in favour of a trial (www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2011/2011_87-eng.php). "I have asked CIHR to establish the terms of reference for this clinical trial. We are committed to launching an open and transparent call for applications as quickly as possible," she said, adding that "it has been a moving experience to meet with and hear from so many MS patients and their families who have shown tremendous courage in the face of such a difficult illness. I wholeheartedly applaud those affected and their families who have to go through such difficult moments."

Zamboni hypothesizes that multiple sclerosis is a vascular disorder caused by narrowing or blocking of internal jugular veins or the azygos vein, leading to accumulation of iron within the brain, and triggering the condition he calls CCSVI, which he treats by using angioplasty to eliminate the blockages.

CIHR indicated that the timing of the trial "is not determined at this time" (www.cihr-irsc.gc.ca/e/43953.html). "CIHR will be working over the fall with its Scientific Expert Working Group to develop the terms of reference for the trial and will then select, through a competitive and rigorous peer-review process, a research team to conduct the clinical trial."

The Phase I/II interventional trail "will be designed to: (i) ensure standardized and accurate identification of MS patients meeting defined criteria for CCSVI; (ii) evaluate key measures that are sensitive to patient-reported outcomes of venoplasty; (iii) conduct the necessary safety evaluations of venoplasty for CCSVI including health risks such as blood clots; and (iv) evaluate whether the results of venoplasty are sustained over several months post-procedure," CIHR said in a release (www.cihr-irsc.gc.ca/e/43952.html).

CIHR also indicated that it will convene a "consensus workshop" for ultrasound imaging in hopes of developing a process to improve the comparability of seven North American studies of CCSVI now being funded by the MS Society of Canada and National MS Society (US). The workshop "will be held to share information and determine the best way of standardizing imaging of veins in the neck and brain. The standardized ultrasound methods optimized in this workshop will help ensure standardization of the seven ongoing studies and will contribute to the design of a Phase I/II interventional trial." — Wayne Kondro, *CMAJ*

Commercial serological tests for tuberculosis endanger patients' lives

The World Health Organization (WHO) has called for a global ban on the use of antibody detection-based diagnostic tests for pulmonary and extrapulmonary tuberculosis (TB) after a systematic review of the tests' efficacy revealed they provide dangerously inconsistent and imprecise results.

More than a million of these inaccurate commercial serological tests are carried out annually, and often result in misdiagnosis, mistreatment and harm to public health, the WHO warned in a statement on Commercial Serodiagnostic Tests for Diagnosis of Tuberculosis (http://whqlibdoc.who.int/publications/2011/9789241502054_eng.pdf).

The policy urges countries to rely instead on more accurate microbiological and molecular tests.

The recommendation comes after a 12-month analysis by WHO experts revealed "low sensitivity" in commercial serological tests, which leads to an unacceptably high number of patients being given false-negative results when they have active TB. This can result in patients dying from untreated TB, or transmitting the disease to others.

The systematic review also revealed "low specificity" in the commercial serodiagnostic tests, which leads to an unacceptably high number of patients being wrongly diagnosed with TB. Those patients may then undergo unnecessary treatment, while the real cause of their illness remains undiagnosed.

The systematic review indicated that "for pulmonary tuberculosis, 67 unique studies were identified, including 32 studies from low- and middle-income countries. None of these studies evaluated the tests in children. The results demonstrated that (1) for all commercial tests, sensitivity (0% to 100%) and specificity (31% to 100%) from individual studies were highly variable; (2) using bivariate meta-analysis for Anda-TB IgG (the most commonly evaluated test), the pooled sensitivity was 76% (95% CI 63% to 87%) in studies of smear-positive and 59% (95% CI 10% to 96%) in studies of smear-negative patients, respectively; the pooled specificity in these studies was similar: 92% (95% CI 74% to 98%) and 91% (95% CI 79% to 96%), respectively; (3) for Anda-TB IgG, sensitivity values in smear-positive (54% to 85%) and smear-negative (35% to 73%) patients from individual studies were highly variable; (4) for Anda-TB IgG, specificity values from individual studies were variable (68% to 100%); (5) a TDR evaluation of 19 rapid commercial tests, in comparison with culture plus clinical follow-up, showed similar variability with sensitivity values of 1% to 60% and specificity of 53% to 99%; (6) compared with ELISAs [60% (95% CI 6% to 65%], immuno-chromatographic assays had lower sensitivity [53%, 95% CI 42% to 64%]; and (7) in a single study involving HIV-infected TB patients, the sensitivity of the SDHO test was 16% (95% CI 5% to 34%).

For extrapulmonary tuberculosis, 25 unique studies were identified, including 10 studies from low- and middle-income countries. None of these studies evaluated the tests in children. The results demonstrated that (1) for all commercial tests, sensitivity (0% to 100%) and specificity (59% to 100%) values from individual studies were highly variable; (2) pooled sensitivity was 64% (95% CI 28% to 92%) for lymph node tuberculosis and 46% (95% CI 29% to 63%) for pleural tuberculosis; (3) for Anda-TB IgG, the pooled sensitivity and specificity were 81% (95% CI 49% to 97%) and 85% (95% CI 77% to 92%) respectively while sensitivity (26% to 100%) and specificity (59% to 100%) values from individual studies were highly variable; and (5) in one study involving HIV-infected TB patients, the sensitivity of the MycoDot test was 33% (95% CI 19% to 39%).

The vast majority of studies were either sponsored by industry, involved

commercial test manufacturers, or failed to provide information on industry sponsorship."

The WHO added that the commercial serological tests that are currently available on the market are not approved or regulated by any recognized body, and that most are manufactured in Europe and North America.

"Blood tests for TB are often targeted at countries with weak regulatory mechanisms for diagnostics, where questionable marketing incentives can override the welfare of patients," Dr. Karin Weyer, coordinator of TB diagnostics and laboratory strengthening for WHO's Stop TB department, said in a press release (www.who.int/mediacentre/news/releases/2011/tb_20110720/en/index.html). "It's a multi-million dollar business centred on selling substandard tests with unreliable results."

Some 1.7 million people die from TB every year, and the WHO pegs it the major killer of people living with HIV.

The new policy does not apply to blood tests for latent TB infection, which are currently under WHO review. — Lauren Vogel, *CMAJ*

Free birth control urged as preventive health measure

Birth control pills and devices should be covered by all health insurance plans so as to reduce unintended pregnancies, the United States Institute of Medicine (IOM) says.

In a report, Clinical Preventive Services for Women: Closing the Gaps, commissioned by the US Department of Health and Human Services, the IOM identifies eight essential women's health services for expanded coverage under the 2010 Patient Protection and Affordable Health Act, including "the full range of Food and Drug Administration-approved contraceptive methods, sterilization procedures, and patient education and counselling for all women with reproductive capacity" (http://books.nap.edu/openbook.php?record_id=13181).

The recommendation was based on systematic reviews and other peer-reviewed studies which indicate that contraception and contraceptive counselling are effective at reducing unintended pregnancies. Many US women already receive some level of coverage for birth control through private insurance or federal reimbursement programs, but copayments can be prohibitive, particularly for low-income women. Full inclusion would make birth control more affordable for all American women.

Privately insured women using oral contraceptives whose plans cover prescription drugs paid more than half the cost of the pills in 2010, amounting to an average US$14 per pack, the Guttmacher Institute, a New York City, New York-based reproductive health research group testified to the IOM (www.guttmacher.org/pubs/CPSW-testimony.pdf). Brand-name versions of the pill, patch or ring can cost upwards of US$60 per month if paid entirely out of pocket, while long-acting or permanent methods of contraception can entail hundreds of dollars in upfront costs.

Not using contraception can be considerably more costly, however. Unintended pregnancies cost taxpayers about US$11.1 billion annually, the IOM stated, and the costs associated with nearly two-thirds of unwanted pregnancies — about one million births — are covered by Medicaid and other government programs (www.guttmacher.org/pubs/psrh/full/4309411.pdf).

Meanwhile, demand for abortions among low-income women has spiked over the past decade, increasing 18% among poor women between 2000 and 2008 (http://journals.lww.com/greenjournal/Fulltext/2011/06000/Changes_in_Abortion_Rates_Between_2000_and_2008.14.aspx).

The other services the IOM recommended for coverage without cost-sharing:

- Screening for gestational diabetes in pregnant women between 24 and 28 weeks of gestation, and at the first prenatal visit for pregnant women at high risk of diabetes;
- High-risk human papillomavirus DNA testing, in addition to conventional cytology testing in women with normal cytology results;
- Annual counselling about sexually transmitted infections;
- Annual counselling and screening for HIV;
- Comprehensive lactation support, counselling and equipment for all pregnant women and those in the postpartum period;
- Screening and counselling for interpersonal and domestic violence for all women and adolescent girls;
- At least one annual preventive care visit for all adult women. — Lauren Vogel, CMAJ

Health records lost in delivery debacle

Ontario's privacy commissioner is investigating the disappearance of the personal health information of thousands of participants in the province's colon cancer screening program.

Canada Post cannot confirm the delivery of 15 reports containing the names, dates of birth, health card numbers and colorectal cancer screening results of some 6500 people who took part in Ontario's ColonCancerCheck program, commissioner Ann Cavoukian revealed in a press release (www.newswire.ca/en/releases/archive/July2011/26/c7471.html). The delivery status of an additional 11 reports is still under investigation.

"Medical test results rank among the most sensitive personal information about an individual. I am astounded that such a loss could take place," Cavoukian said.

The reports were sent by Cancer Care Ontario to primary care physicians across the province in February and March via Canada Post's Xpresspost courier service. As part of that service, Canada Post was supposed to confirm delivery of the reports by obtaining the signatures of recipients.

Investigations by Cancer Care Ontario and the privacy commissioner's office initiated in late June when it was discovered that some of the packages had been delivered without obtaining the required signatures. The investigations included site visits to physicians' clinics to search for the lost reports.

"The first step is to minimize any harm by locating as many of these

reports as possible," Cavoukian said. "As part of our investigation, we will be looking at steps that can be taken to ensure that this type of breach doesn't happen again."

People whose health information is listed in the missing reports will be notified via mail (at least theoretically), or by their primary care physician, in coming weeks. — Lauren Vogel, *CMAJ*

FDA says its must strengthen its scientific base to regulate drug safety

Improved access to postmarket drug data, a better understanding of how patients use unapproved drugs and stronger risk assessment capabilities are needed within the United States Food and Drug Administration's (FDA) Center for Drug Evaluation and Research (CDER) if it is to fulfill its regulatory responsibilities, an internal agency report concludes.

The report, "Identifying CDER's Science and Research Needs Report," identifies seven major areas in which the FDA believes it must bolster its capabilities (www.fda.gov/downloads/Drugs/ScienceResearch/UCM264594.pdf). Those seven categories:

- "Improve access to post-market data sources and explore feasibility of their use in different types of analyses
- Improve risk assessment and management strategies to reinforce the safe use of drugs
- Evaluate the effectiveness and impact of different types of regulatory communications to the public and other stakeholders
- Evaluate the link among product quality attributes, manufacturing processes and product performance
- Develop and improve predictive models of safety and efficacy in humans
- Improve clinical trial design, analysis and conduct
- Enhance individualization of patient treatment."

The articulation of research needs and priorities is intended to feed into the FDA's forthcoming strategic plan, which is being developed in response to widespread criticism that the agency has become too cozy with industry. Among the criticisms that have been levied are accusations that the agency does not adequately regulate the reporting of adverse events, that it does not quantify risk accurately and that it does not follow up on company failures to produce postmarket surveillance data. The FDA has argued that it lacks the authority to pursue regulatory violations and the resources to enforce all regulations.

The report appears to be generally aimed at strengthening the FDA's capacity to evaluate and monitor "real world" drug use, particularly within specific population groups, and particularly with respect to long-term health consequences. The information CDER now receives from manufacturers, health care providers and patients with regard to adverse events is incomplete and limited "which often hampers the effective use of these reports in detecting signals and making regulatory decisions," the report states. "They are also subject to reporting bias. Efforts need to continue to improve the quality, quantity, and utility of these reports to enhance the detection and understanding of rare adverse events."

The agency also needs to bolster its capacity to regulate and monitor the use of "unapproved, compounded, fraudulent, and counterfeit products," as well as screen for adulterants in products and assess the risks of combination drug therapies being used to treat complex chronic diseases, the report states. — Wayne Kondro, *CMAJ*

US regulation of medical devices "flawed," report says

The United States government's fast-track process for vetting medical devices should be scrapped because it cannot assure the safety and efficacy of the products it clears for sale, according to a July 29 report by the US Institute of Medicine (IOM).

The Food and Drug Administration (FDA) is responsible for evaluating medical devices before they are made available to US consumers, but currently exempts so-called moderate-risk devices, such as wheelchairs and artificial hips, from rigorous review if they are deemed "substantially equivalent" to existing products on the market.

However, reliance on substantial equivalence cannot guarantee that devices cleared for sale are safe and effective, particularly as the majority of existing devices used as the basis for comparison have never been reviewed for these factors, the IOM argues in the report "Medical Devices and the Public's Health: the FDA 510(k) Clearance Process at 35 Years" (www.nap.edu/openbook.php?record_id=13150&page=R1).

The report, which was commissioned by the FDA in 2009, urges the agency to abandon rather than modify its existing fast-track process, known as the 510(k) process, and develop a new approval system that would use both premarket clearance and improved postmarket surveillance of device performance to ensure the safety and effectiveness of medical devices throughout the duration of their use.

The report also highlights weaknesses in the FDA's current postmarket oversight of medical devices, and calls on the agency to develop a comprehensive strategy to collect, analyze and act on information about devices' performance after clearance.

The FDA is planning a public meeting in the coming weeks to discuss recommendations made in the report, but argues an overhaul of its medical device review program is unnecessary and would likely require congressional approval.

"FDA believes that the 510(k) process should not be eliminated but we are open to additional proposals and approaches for continued improvement of our device review programs," Dr. Jeffrey Shuren, director of the FDA's Center for Devices and Radiological Health, said in a press release (www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm265908.htm). "Any major modifications made to the agency's premarket review programs should be based on sound science and through thoughtful and transparent discussion." — Lauren Vogel, *CMAJ*

America must brush up dental coverage for vulnerable populations, report says

Millions of Americans are not receiving needed dental work because of "persistent and systemic" barriers that limit their access to oral health care, the United States Institute of Medicine (IOM) revealed in a report that calls for expanded dental coverage for vulnerable populations.

While most Americans regularly visit the dentist, oral health care eludes many marginalized populations, "including racial and ethnic minorities, people with special healthcare needs, older adults, pregnant women, populations of lower socioeconomic status, and rural populations, among others," the IOM reported in "Improving Access to Oral Health Care for Vulnerable and Underserved Populations" (www.nap.edu/openbook.php?record_id=13116&page=1).

Economic, geographic and cultural factors are among the major contributors to this problem, the report says. In 2008, some 4.6 million children were unable to access needed dental care because their families could not afford it. Meanwhile, the IOM estimates that 33.3 million people live in areas with shortages of dental health professionals.

Although all states must provide comprehensive dental benefits for children enrolled in Medicaid or the Children's Health Insurance Program, they are not required to provide such benefits for adults. Because publicly funded programs are the primary source of health coverage for vulnerable and underserved populations, including dental benefits for all Medicaid beneficiaries is a critical and necessary goal, the report concludes.

The consequences of insufficient access to oral health care are "far-reaching," Dr. Frederick Rivara, chair of the committee that wrote the report, said in a press release (www.iom.edu/Reports/2011/Improving-Access-to-Oral-Health-Care-for-Vulnerable-and-Underserved-Populations/Press-Release.aspx).

Those consequences include increased risk of respiratory disease, cardiovascular disease and diabetes, as well as inappropriate use of hospital emergency departments for preventable dental diseases.

"As the nation struggles to address the larger systemic issues of access to health care, we need to ensure that oral health is recognized as a basic component of overall health," Rivara said. — Lauren Vogel, *CMAJ*

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