FOR THE RECORD

WHO identifies barriers to elimination of malaria

Progress in eliminating malaria is being threatened by inadequate funding and growing resistance to drugs and insecticides, according to the World Health Organization's (WHO) annual report on the mosquito-borne infection.

"In 2011, no one should die of malaria for lack of a $5 bed net, a 50-cent diagnostic test, and a $1 antimalarial treatment," Dr. Robert Newman, director of the WHO's malaria program, said in a press conference posted online (http://terrance.who.int/mediacentre/audio/press_briefings/VPC_Malaria_Report_13DEC2011.mp3).

Current funding is well below the amount WHO estimates is required to eliminate malaria (more than US$5 billion), states the *World Malaria Report 2011* (www.who.int/entity/malaria/world_malaria_report_2011/9789241564403_eng.pdf). Annual funding is expected to peak this year at US$2 billion but is projected to fall to US$1.5 billion by 2015. The report proposes that certain cost-cutting measures, such as developing longer-lasting bed nets, could lessen the impact of reductions in funding, and suggests that some countries where malaria is endemic could invest more in controlling the infection based on global economic growth over the past decade.

But inadequate funding isn't the only block to eliminating malaria worldwide, according to Dr. Margaret Chan, WHO's director-general. "Parasite resistance to antimalarial medicines remains a real and ever-present danger to our continued success," Chan wrote in the report's foreword.

The recommended treatment for the infection caused by the most deadly type of malaria parasite includes the drug artemisinin, based on a compound extracted from a Chinese herb. Resistance to artemisinin-based treatments was found along the Cambodia–Thailand border and has been identified in Vietnam and Myanmar, though efforts to contain the spread have reduced the cases of malaria reported in these regions, the report states.

Parasite resistance often develops when a drug is used alone rather than in combination with other drugs. WHO has recommended that all countries ban the sale of treatments using only artemisinin. These products, however, were still on the market in all 25 countries in 2010, though the number of pharmaceutical companies selling them dropped from 39 to 28.

The report also cited mosquito resistance to insecticides used on bed nets as a growing threat. There is widespread use of nets containing a single kind of insecticide, which increases the risk of mosquitoes developing immunity. Resistance has been reported in 41 countries around the world, including 27 in Africa. The report states that WHO is working with various stakeholders to create a resistance-management plan to be released next year.

Despite concerns over funding and parasite and mosquito resistance, there has been considerable progress in the global fight against malaria, states the report. Since 2000, deaths attributed to malaria have fallen by 26% (an estimated 655 000 people died from malaria in 2010), and reported cases have decreased by 17%.

Still, this falls far short of the goals of reducing both cases of malaria and deaths caused by the infection by 50% from 2000 levels by 2010 (set by the Roll Back Malaria Partnership, an international initiative with more than 500 partners that WHO helped launch in 1998). Now, those targets have been replaced by even more ambitious goals: to reduce malaria deaths to near zero and cases from 2000 levels by 75% by 2015.

The reports suggests these targets will be met by "achieving and sustaining universal access to and utilization of preventative measures; achieving universal access to case management in the public and private sectors and in the community (including appropriate referral); and accelerating the development of surveillance systems." — Julia Sisler, Ottawa, Ont.

Fewer deaths in Canada's hospitals

The death rate in most major hospitals has declined over the past seven years, according to the latest hospital standardized morality ratio report from the Canadian Institute for Health Information (CIHI).

Overall, there has been a significant decrease in the mortality ratio for more than half of Canadian facilities since a baseline year of 2004. The results have remained about the same for 44% of hospitals and significantly increased for 3% of facilities, according to a CIHI release (www.cihi.ca/CIHI-ext-portal/internet/en/Document/health+system+performance/quality+of+care+and+outcomes/hsmr/RELEASE_08DEC11).

The quality indicator measures the number of actual deaths in a hospital or health region against the a national average of 'expected' deaths, adjusted for factors like age, sex, length of stay, diagnoses, comorbidities, reason for admission and transfer from another institution, according to the CIHI report, *2011 HSMR Results*, on 75 large acute care facilities in eight provinces (www.cihi.ca/cihi-ext-portal/internet/en/document/health+system+performance/quality+of+care+and+outcomes/hsmr/hsmr_results_canada).

A hospital standardized mortality ratio of 100 means the number of actual deaths was equal to the national average. In 2011, there are more hospitals with a ratio below that average, and only a handful with a ratio above it. The baseline national average has been unchanged since 2004–05, allowing

results from one year to be compared to those of another.

The central region in Newfoundland has the highest ratio in Canada at 120, which is down from 123 in 2004–2005, but up from 114 in 2010. The mortality ratios in all regions of Newfoundland and Labrador have gone up in the past year, and all are greater than the national average.

In Ontario, hospitals with ratios over 100 include the Sudbury Regional Hospital (112), the Kingston General Hospital (102) and the London Health Sciences Centre (101). Across Canada, other facilities with high ratios include the Chinook Regional Hospital in Lethbridge, Alberta (109), and the Nanaimo Regional General Hospital in British Columbia (103).

The hospitals with the lowest mortality ratios in 2011 were the Saint John Regional Hospital in New Brunswick (62), the Brant Community Healthcare System — Brantford General Site in Ontario (66) and the St. Mary's General Hospital in Kitchener, Ont. (69).

The provinces of Saskatchewan, New Brunswick and British Columbia have the lowest mortality ratios, based on the average of all the health regions in each province. But Ontario is improving its rates, as evidenced by indications that all hospitals in the Toronto region have reduced their ratios from 2004–2005.

The results are not intended to allow comparisons between hospitals, the report states. Each institution can track its own data over time and use the results to improve in-patient experiences. "The potential benefits of HSMR [hospital standardized mortality ratio] data are clearly demonstrated when individual organizations use the data and tie it to actions to make a difference in quality of care."

The standardized mortality ratio is not a specific measure of preventable deaths in any hospital. The factors that affect the number of "expected" deaths are complex. For example, there are about 65 diagnostic groups that account for 80% of in-patient deaths in Canada, including malignant neoplasm of the liver, lung, brain or breast, septicemia, Alzheimer disease, stroke, acute myocardial infarction, pneumonia or heart failure.

Results are only provided for eight provinces because there are inadequate data to support ratios derived from smaller provinces, while Quebec is excluded "due to differences in data collection." — Julia Sisler, Ottawa, Ont.

Confusion over interventions for mothers and babies stymies progress, study finds

A global review has identified 56 essential interventions to reduce mother–child mortality rates and replace the current "hodge-podge" of interventions now being used across jurisdictions.

The 56 interventions, produced by the World Health Organization (WHO), Aga Khan University and the Partnership for Maternal, Newborn & Child Health, are intended to be implemented as "packages" at different stages in a mother and child's life.

"What's new is putting together information in a different way and building consensus among physicians, scientists and professional organizations to lay out an evidence-based path to help women before, during and after birth and their children. Everyone now agrees on the 56 essential interventions," Dr. Elizabeth Moon, author of the study and director of WHO's department of Maternal, Newborn, Child and Adolescent Health, said in a press release (www.who.int/pmnch/media/press_materials/pr/2011/20111215_essential_interventions_pr/en/index.html).

Measures to prevent postpartum hemorrhage, including the use of prophylactic uterotonics, uterine massage and active management of third-stage labour featured prominently among the interventions recommended for mothers by the report, *Essential Interventions, Commodities and Guidelines for Reproductive, Maternal, Newborn and Child Health* (www.who.int/pmnch/topics/part_publications/essentialinterventions14_12_2011low.pdf).

Worldwide, some 358 000 women die during pregnancy and childbirth every year, and the majority of those deaths occur immediately after childbirth, most often as a result of bleeding, high blood pressure, prolonged and obstructed labour, infections and unsafe abortions, the study states.

Other interventions for mothers highlighted by the study include

- Screening for maternal illnesses, hypertensive disorders of pregnancy and anemia
- Counselling on family planning, birth and emergency preparedness
- Prevention and management of HIV, malaria and postpartum sepsis
- Smoking cessation.

Birth is equally dangerous for newborns, according to the study. A child's risk of dying is highest during the first 28 days of life. About three million children die each year in the first month of life, with about one-half of those occurring within 24 hours of birth, and 75% of those occurring within a week of birth.

Interventions to manage infections and prevent asphyxia comprise the majority of recommended interventions for newborns, including

- Hygienic cord and skin care
- Neonatal resuscitation with bag and mask by a professional health worker
- Case management of neonatal sepsis, meningitis and pneumonia
- Surfactant to prevent respiratory distress syndrome in preterm babies
- Continuous positive airway pressure to manage babies with respiratory distress syndrome
- Presumptive antibiotic therapy for newborns at risk of bacterial infection.

The study also calls for the commencement of breastfeeding within an hour of birth, as well as exclusive breastfeeding for six months, Vitamin A supplementation from six months of age and improved management of severe acute malnutrition.

To date, few efforts have been made to integrate such mother–child interventions across the continuum of care, the study asserts. Confusion and inconsistency in implementation of such recommendations mean that many countries, particularly those in sub-Saharan Africa and Southern Asia, are unlikely to achieve Millennium Development Goals related to reductions in maternal, neonatal and under-five mortality rates by 2015, it adds. — Lauren Vogel, *CMAJ*

United States limits use of cephalosporins in animals

The United States Food and Drug Administration (FDA) has announced a crackdown on the extralabel use of cephalosporin antimicrobial drugs in most food-producing animals because of the threat antibiotic resistance poses to human health.

The order, which takes effect Apr. 5, prohibits the use of cephalosporins in cattle, swine, chickens and turkeys unless "they follow the dose, frequency, duration, and route of administration that is on the label" (www.ofr.gov/OFRUpload/OFRData/2012-00035_PI.pdf). But it does not apply to ducks, rabbits or other minor species of food producing-animals.

It also prohibits the use of cephalosporin drugs for disease prevention and thus essentially outlaws injections of chicken eggs or the use of "biobullets" in cattle.

"We believe this is an imperative step in preserving the effectiveness of this class of important antimicrobials that takes into account the need to protect the health of both humans and animals," Michael R. Taylor, FDA's deputy commissioner for foods, stated in a press release (www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm285704.htm).

Alarms have long been sounded over Canadian management of antibiotic resistance (www.cmaj.ca/lookup/doi/10.1503/cmaj.109-3109). Critics have charged that the federal government has failed to tighten off-label drug usage on farms (www.cmaj.ca/lookup/doi/10.1503/cmaj.091009) or to close a legal loophole that allows massive imports of unapproved drugs (www.cmaj.ca/lookup/doi/10.1503/cmaj.090525). But while even officials within Health Canada's Veterinary Drugs Directorate have urged action, the Conservative government has been silent on the issue (www.cmaj.ca/lookup/doi/10.1503/cmaj.109-4055).

FDA originally issued an order for a prohibition on the extralabel use of cephalosporin antimicrobial drugs for all food-producing animals in 2008 but revoked that prior to implementation after trade organizations representing food producers and animal drug manufacturers argued that the agency had "failed to meet the legal standard for issuing a prohibition order" and was imposing conditions that were too broad.

The agency says that its review of regulatory law indicates that it has the authority under the Animal Medicinal Drug Use Clarification Act of 1994 "if it finds that extralabel use of a drug in animals presents a risk to public health" and particularly, if there is "evidence demonstrating that the use of the drug has caused, or likely will cause, an adverse event."

"At this time, FDA is concerned that certain extralabel uses of cephalosporins in food-producing major species are likely to lead to the emergence and dissemination of cephalosporin-resistant strains of foodborne bacterial pathogens. If these drug-resistant bacterial strains infect humans, it is likely that cephalosporins will no longer be effective for treating disease in those people. The Agency is particularly concerned about the extralabel use of cephalosporin drugs that are not approved for use in food-producing major species because very little is known about their microbiological or toxicological effects when used in food-producing animals," the agency states in the order.

Meanwhile, the scientific evidence indicates that "extralabel use of cephalosporins in certain food-producing animals species is contributing to the emergence of cephalosporin-resistant zoonotic foodborne bacteria," the agency states, arguing that if cephalosporins become less effective in treating pathogens in humans, physicians will have little choice but to turn to drugs that have a greater incidence of adverse effects or aren't as effective.

Cephalosporins annually account for more than 50 million prescriptions in the US, the agency adds. Although most commonly used to treat pneumonia, they are also used to treat skin and soft tissues infections, as well as "intra-abdominal infections, pelvic inflammatory disease, and diabetic foot infections. Approved indications for newer cephalosporins include the treatment of lower respiratory tract infections, acute bacterial otitis media, skin and skin structure infections, urinary tract infections (complicated and uncomplicated), uncomplicated gonorrhea, pneumonia (moderate to severe), empiric therapy for febrile neutropenic patients, complicated intra-abdominal infections, pelvic inflammatory disease, septicemia, bone and joint infections, meningitis, and surgical prophylaxis." Third-generation cephalosporins are now being used to treat gastrointestinal tract infections in hospitals, along with *Salmonella* and *Shigella* infections.

Just two cephalosporin drugs, ceftiofur and cephaprin, are approved for use in food-producing animals, specifically for certain diseases, including; "(1) The treatment of respiratory disease in cattle, swine, sheep, and goats; (2) the treatment of acute bovine interdigital necrobacillosis (foot rot) and acute bovine metritis; (3) the control of bovine respiratory disease; and (4) the control of early mortality associated with *E. coli* infections in day-old chicks and poults. In addition, ceftiofur is approved as an intramammary infusion for the treatment of clinical mastitis in lactating dairy cattle associated with coagulase-negative staphylococci, *Streptococcus dysgalactiae*, and *E. coli*. Cephapirin is only approved as an intramammary infusion for the treatment of lactating cows having bovine mastitis caused by susceptible strains of *Streptococcus agalactiae* and *Staphylococcus aureus*." — Wayne Kondro, *CMAJ*

A moral duty to assist dying

Terminally ill people with less than a year to live should be entitled to receive lethal doses of medication from physicians if they wish to end their lives, recommends the United Kingdom's independent Commission on Assisted Dying.

"There is a strong case for providing the choice of assisted dying for terminally ill people," the Commission states in its report, *The current legal status of assisted dying is inadequate and incoherent...* (www.demos.co.uk/files/CoAD_-_web.pdf?1325710486). "Even with skilled end of life care, the Commission finds that a comparatively small number

of people who are terminally ill experience a degree of suffering towards the end of their life that they consider can only be relieved either by ending their own life, or by the knowledge that they can end their life at a time of their own choosing."

Current law and policy is unjust to the terminally ill and health care professionals, the report argues. "There is significant concern that assisting suicide remains an amateur activity, and that no prospective safeguards are in place to protect those who seek assistance, or who might feel themselves under pressure from others to seek assistance."

The report follows on the heels of a recent recommendations from a Royal Society of Canada expert panel that assisted suicide and voluntary euthanasia be legalized on the grounds that there is no valid philosophic distinction between them and withholding and withdrawal of life-sustaining treatment from competent adults (www.cmaj.ca/lookup/doi/10.1503/cmaj.109-4059).

The Commission, chaired by former labour minister Lord Charles Falconer, urged the creation of a statutory framework for assisted dying that includes the following elements:

- "a good level of care and support services with properly trained health and social care staff
- clearly defined eligibility criteria
- the person concerned requests an assisted death on his or her own behalf, and has the capacity to make the request
- a doctor who, where possible, knows the person well and supports the person and their family through the process
- the person who requests an assisted death is fully informed of all the options available to them for treatment, care and support and still wishes to proceed
- an assessment to determine if the person meets the eligibility criteria is provided by at least two doctors who are wholly independent of one another
- detailed guidance on how lethal medication to be used for an assisted death should be stored, transported and administered in such a way as to ensure, as far as possible, no risk of abuse, constituting a danger to the public, or being stolen
- the patient must take the final action that will end their own life
- certification of the death expressly records it as an assisted death
- correct reporting of the assisted death to a national monitoring commission that reviews all cases and has retrospective powers to investigate whether individual cases complied with the law."

The two physicians would have to independently certify that the patient met specified eligibility criteria. "The first criterion requiring a diagnosis of terminal illness would need each doctor to certify that the person had an advanced, progressive, incurable condition that is likely to lead to the patient's death within the next 12 months. The second criterion, requiring that the person requesting an assisted death made this request voluntarily and without coercion, would require both doctors to explore thoroughly the individual's motivation for requesting an assisted death and to provide evidence of this voluntariness. The third criterion would require that the individual has the mental capacity to make an informed choice. We received evidence to the effect that capacity assessments are part of every doctor's usual responsibilities. If assisted dying were to be legally permitted in this country, it would be the role of the relevant professional bodies to develop a detailed code of practice for the assessment of mental capacity to safeguard decisions about assisted dying. Such a code of practice would need to include specific measures to identify people experiencing depression, or other psychological disorders that could potentially impair that person's judgement," the report states.

Other safeguards urged by the commission include the following:

- "Ensure the person has been fully informed of all other treatment and end of life care options that are available and still wishes to proceed.
- Ensure that the eligibility criteria are met.
- Ensure that the person has a settled intention to die.
- Ensure the safe storage and transportation of lethal medication.
- Ensure the person has a reliable and supported assisted death.
- Ensure that assisted deaths are reported correctly.
- Provide monitoring and regulatory oversight by a national monitoring commission with powers to investigate cases suspected of noncompliance retrospectively."

Physicians would also be obliged to ensure that a person with a "settled intention to die" receives timely, but not too hasty, lethal medication. To that end, the commission urges that a minimum time period of two weeks passes before a patient receives lethal medication, except in cases where the patient has less than a month to live, in which case the waiting period should be reduced to six days.

Doctors administering the lethal medication should also be responsible for directing friends and relatives of the patient to suitable local bereavement support services.

The report also urges that the National Institute of Health and Clinical Excellence provide guidance on appropriate lethal medications to use in assisting a suicide. — Wayne Kondro, *CMAJ*

***CMAJ* 2012. DOI:10.1503/cmaj.109-4094**