**CIPARS Farm Program: Surveillance of antimicrobial use and antimicrobial resistance in Canadian swine herds.**

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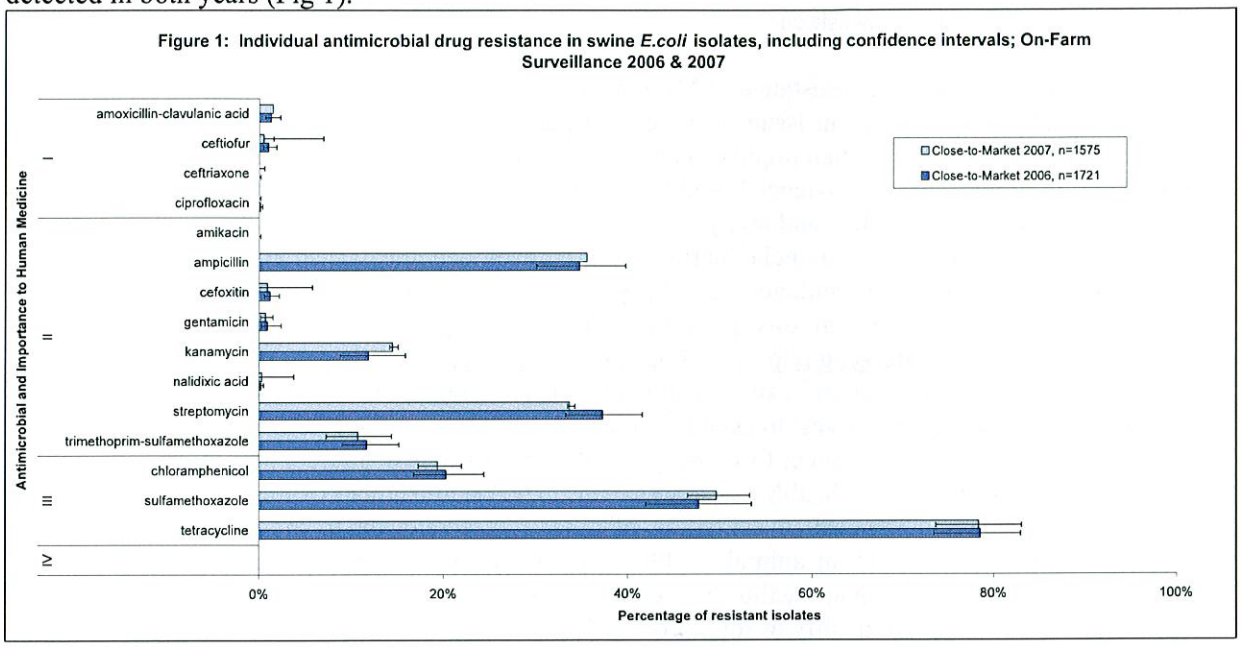
**Introduction:** Antimicrobial resistance (AMR) reduces our ability to effectively treat bacterial infections in animals and humans and is an issue of increasing public concern. AMR has been associated with the misuse of antibiotics in the human population but there is also concern with antimicrobial use in agri-food production. In order to provide science based information on antimicrobial use and resistance in the swine industry, it is essential to collect and analyze information at the farm level. The Public Health Agency of Canada and its federal and provincial partners have developed the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) to monitor AMR and antimicrobial use (AMU) in Canada. Further information on this program and annual reports are available at http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php and http://www.phac-aspc.gc.ca/cipars-picra/index-fra.php. The active Farm surveillance program in swine is the most recent component of CIPARS and began in January 2006 with the following objectives: to establish a national farm surveillance infrastructure; to provide data on antimicrobial use and resistance; to investigate associations between antimicrobial use and resistance; and to provide data for human health risk assessments. The establishment of this network will also allow for the surveillance and targeted investigation of other issues relevant to the swine industry including those with both a public and an animal health focus. These objectives are consistent with the broader objective of protecting human health by reducing exposure to potential hazards while increasing confidence in the safety and quality of food produced in Canada.

**Materials and Methods:** The CIPARS On-Farm program was implemented in 108 sentinel swine herds across the five major pork producing provinces in Canada (QC, ON, MB, SK and Alberta). In each of the 5 participating provinces, the number of CIPARS sentinel sites is proportional to the national total of grower-finisher units. To provide producer anonymity, herd veterinarians select the producers and participate in the sample and data collection. Swine veterinarians were purposively selected from provincial sampling frames to enrol representative herds within their practices. Twenty-nine swine veterinarians from private and corporate practice have enrolled client producers that are CQA® validated, produce more than 2000 market hogs per year, and are representative of the demographic and geographic distribution of herds in the veterinarian's swine practice. Criteria for exclusion were; herds that were regarded to be organic pertaining to animal husbandry, herds that were feeding edible residual material or herds that were pasture-raised. The inclusion/exclusion criteria helped ensure that the herds enrolled were representative of the majority of hog production in Canada. Pooled fecal samples are collected from pens of close-to-market weight (>175 lbs) finisher hogs three times annually in each participating herd. All fecal samples are cultured for generic *E. coli, Enterococcus* and *Salmonella* using standard CIPARS methodology[2]. Susceptibility testing is performed on 3 *E. coli*, 3 *Enterococcus* spp. and, if isolated, 1 *Salmonella* spp. isolate per sample. Minimum inhibitory concentrations (MIC) for 15 antimicrobials are established for all isolates using the Sensititre® Microbiology System (Trek Diagnostic Systems, Cleveland, OH, USA). Ongoing antimicrobial use data for feed, water and injectables are collected for each batch of pigs using questionnaires. Additional management and production information is also collected through the questionnaires. Descriptive analyses were conducted using commercially available software (Microsoft Excel 2003; Microsoft Corporation, Redmond, Washington, USA). All statistical

analyses accounted for clustering of resistance within herds through generalized estimating equations (GEE) (PROC GENMOD, SAS for Windows version 9.1; SAS Institute, Cary, North Carolina, USA). All models had a binary outcome, logit-link function, and an exchangeable correlation structure. Null binomial response models estimated the prevalence of resistance to each drug. For each model the intercept ($\beta_0$) and 95% confidence intervals (CI) were used to calculate population-average prevalence estimates using the formula $[1 + \exp(-\beta_0)]^{-1}$ .[1]

**Results and Discussion:** For both 2006 and 2007 similar resistance levels and patterns were detected. In both years 87% of the *E. coli* isolates were resistant to at least one antimicrobial in the test panel. Resistance to drugs classified as Very Important to Human Health (Class 1) [9] including; amoxicillin-clavulanic acid (AMC), ceftiofur (TIO), ceftriaxone (CRO) and ciprofloxacin (CIP), was rare or not detected in both years (Fig 1).

**Figure 1: Individual antimicrobial drug resistance in swine *E.coli* isolates, including confidence intervals; On-Farm Surveillance 2006 & 2007**

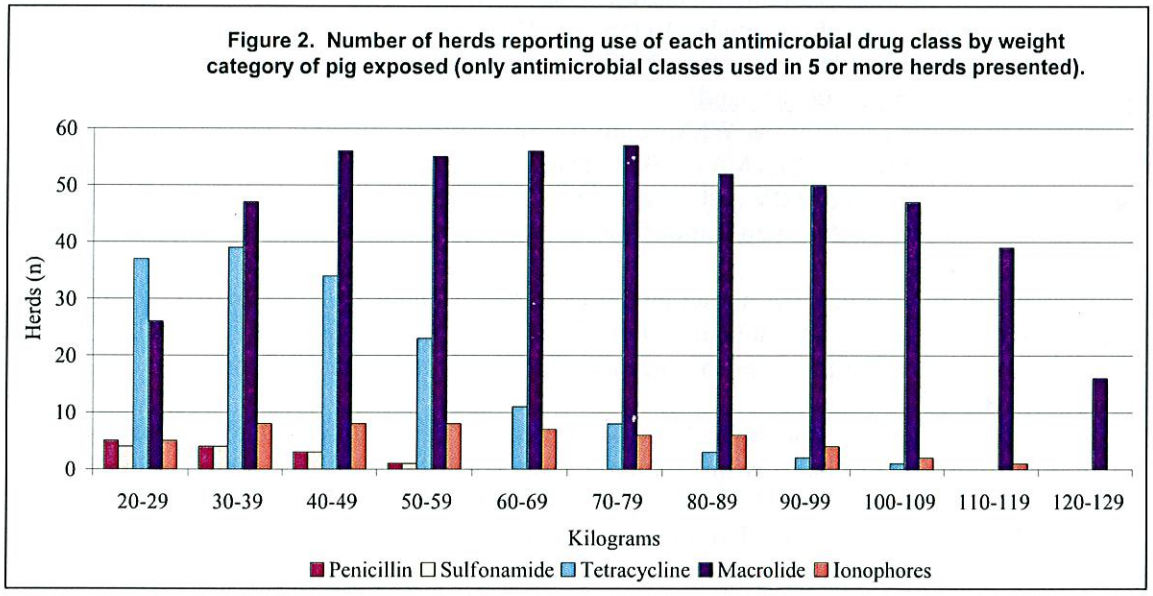



In 2006 and 2007, respectively, 98 and 136 *Salmonella* were isolated. These are small isolate numbers for understanding AMR in *Salmonella*, since different serovars have a propensity to carry different resistance genes.[5,7,8] These datasets were not robust enough to account for variation at the serovar level in the statistical analyses which must be considered when interpreting the data. However, the frequency of resistance to each drug was similar to previous reports from CIPARS abattoir surveillance and regional research projects from western Canadian swine farms[2,5,7]. The only exception to this was resistance to ampicillin (AMP) (23% in 2006 and 35% in 2007) which was higher than the 8-13% previously reported in Canada. Future years will clarify the importance of this finding. Resistance to one or more antimicrobials was detected in 66% and 61% of the *Salmonella* spp. isolates in 2006 and 2007 respectively. No resistance was identified to the Class 1 antimicrobials CIP and CRO and infrequent resistance was observed to AMC and TIO in 2006. As well, no resistance was seen to naladixic acid (NAL). In 2007 no resistance to any of the above antimicrobials was detected. Susceptibility to the quinolones and 3rd generation cephalosporins are important findings because fluoroquinolones are used to treat invasive *Salmonellosis* and 3rd generation cephalosporins are indicated for severe *Salmonella* infections in children.[9,10] In both years the most frequent serovars were Typhimurium var. 5 and Derby. Canadian and American Surveillance programs have not monitored AMR in *Enterococci* from pigs although a cross-sectional study from pigs in Ontario and British Columbia was conducted in 1999-2000[3,11]. It must be noted that bias introduced by different sampling strategies, age of pig sampled, isolation techniques, and susceptibility testing methods cannot be differentiated from true differences caused by geography, management or antimicrobial use. In both years of monitoring none of the *Enterococci* from these Canadian swine farms were resistant to vancomycin (VAN); this concurs with the

report from Ontario and British Columbia in 2000 [3] and with CIPARS Abattoir surveillance.[2] Avoparcin, a glycopeptide antimicrobial, is related to VAN and its utilization for growth promotion in animals has been associated with VAN resistant enterococci (VRE).[13] Avoparcin was never licensed for use in Canada or the United States. Quinupristin-dalfopristin (QDA) is a streptogramin antimicrobial that has been used to treat VAN resistant enterococci (VRE). Of the CIPARS On-farm swine isolates, 42% and 46% were resistant to this drug combination in 2006 and 2007 respectively. This is markedly higher than the 1.4% resistance reported in Denmark in 2006.[12] QDA resistance may partially be explained by the common use of macrolides and lincosamides in Canadian pigs.[5,6] Cross-resistance occurs between lincosamides, macrolides and streptogramin antimicrobials.[14] The common use of macrolides is also a possible explanation for the frequent resistance to tylosin and erythromycin observed in these isolates.

Preliminary qualitative analysis has been completed on the 2007 antimicrobial use data. Seventy-three percent of the batches were exposed to at least one antimicrobial through feed, and 81% of the batches were exposed to antimicrobials through feed or water (185/229). We assume that reporting feed or water AMU indicates that all pigs in the batch were exposed. Therefore, the majority of samples tested for antimicrobial susceptibility were collected from pigs that had been exposed to an antimicrobial at some point in the 20 weeks preceding sampling. Seventy-six percent of herds reported injectable antimicrobial use. The most commonly reported antimicrobials used in feed were macrolides and tetracyclines (Fig 2). Penicillins were the most commonly reported antimicrobials provided through both water and injection. Unmedicated rations were more common during the latter part of the grower-finisher period. Additional analysis of the antimicrobial use data is ongoing.

**Figure 2. Number of herds reporting use of each antimicrobial drug class by weight category of pig exposed (only antimicrobial classes used in 5 or more herds presented).**




The development, implementation and continuation of an on farm surveillance program has provided valuable information for the industry, provinces and Canada as a whole on antimicrobial resistance and use in this sector. It has demonstrated the ability to develop an infrastructure for a national surveillance program which could be used to monitor many other diseases or trends important to the swine industry. The Canadian swine industry has continued to demonstrate its pro-active stance on food safety through the support of this program.

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