Fecal Escherichia coli (n = 555) were isolated from 115 residents on 43 farrow-to-finish swine farms to determine the prevalence of antimicrobial resistance and associated risk factors. Susceptibility to 21 antimicrobials was determined and the overall prevalence of antimicrobial resistance was 25.8%. Pair-wise difference in prevalences of resistance to individual antimicrobials was significant between isolates from residents on farms that fed medicated swine rations compared to those that did not (p = 0.013). Cross-resistance among antimicrobials of same class and multidrug-resistance were observed. Logistic regression models revealed the following risk factors positively associated with antimicrobial resistance: use of antimicrobials in pigs on farms; number of hours per week that farmers spent in their pig barns; handling of sick pigs; and intake of antimicrobials by farm residents. This study indicates that occupational exposure of farmers to resistant bacteria and use of antimicrobials in pig farming may constitute a source of resistance in humans, although the human health impacts of such resistance is unknown. The consumption of antimicrobials by farmers appeared to constitute a significant risk for resistance development. Fecal E. coli from farm residents may act as a reservoir of resistance genes for animal and/or human pathogens.