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Livestock Density as Risk Factor for Livestock-associated MRSA, the Netherlands

To the Editor: We challenge the conclusions of Feingold et al. that "regional density of livestock is a notable risk factor for nasal carriage of LA-MRSA for persons with and without direct contact with livestock" (*1*). They did not study nasal carriage of methicillin-resistant *Staphylococcus aureus* (MRSA), but they retrospectively analyzed 87 culture-confirmed MRSA cases reported to a reference laboratory. These were a mixture of clinical disease isolates and screening (nose, throat, and perineum) isolates that were unevenly distributed between the groups (*2*). Because their analysis aimed to assess exposure risk by residential location, they should have excluded the 5 persons who acquired MRSA outside the Netherlands.

Table. Pig density in the Netherlands, United States (excluding Alaska), and major pig-producing states

Location	No. pigs	Area, km^2	Pig density, pigs/km^2	Relative pig density*
The Netherlands	12,100,000†	41,518	291.4	1
United States	67,500,000†	8,108,782‡	8.3	35.0
Iowa	19,700,000	145,744	135.2	2.2
North Carolina	8,600,000	139,393	61.7	4.7
Minnesota	7,600,000	225,174	33.8	8.6

*Pig density in the Netherlands divided by pig density in other locations.
†US data were obtained from a quarterly US Department of Agriculture report (http://usda01.library.cornell.edu/usda/nass/HogsPigs//2010s/2012/HogsPigs-09-28-2012.pdf).
‡Alaska was excluded because of minimal swine industry.

Retrospective case–control studies preclude direct estimation of incidence, prevalence, or risk. However, because of the symmetric property of odds ratios, disease odds ratios can be inferred indirectly from the estimated exposure odds ratios in case–control studies (*3*). However, this case–case study design has no true controls, precluding valid inferences of absolute or relative risks. The higher ratio of livestock-associated (LA)–MRSA to a typeable strain of MRSA (T-MRSA) in rural cases could be attributable to higher risk for LA-MRSA in rural areas, lower risk for T-MRSA in rural areas, or both.

To illustrate this point, suppose urban dwellers had equal prevalence rates of LA-MRSA and T-MRSA of 5%, and rural dwellers had prevalence rates of 2% for LA-MRSA and 1% for T-MRSA. The ratio approach used would indicate that rural dwellers had twice the risk for LA-MRSA than urban dwellers, when the absolute risk is 2.5 times higher in the urban group. At best, their conclusion could be viewed as a hypothesis that should be tested.

Three large community-based studies with better methods collectively refute this hypothesis. Across these studies, LA-MRSA prevalence (44%) was >180 times higher in 352 occupationally exposed persons than in 2,094 rural residents without farm exposure (0.24%) (*4–6*). Prevalence in family members of livestock workers was intermediate (5.2%). These consistent observations indicate that exposure to LA-MRSA in livestock-dense regions is a common occupational risk for livestock workers, a lesser indirect risk to their family members, and a negligible risk to persons without livestock or farm contact.

Finally, the contention of Feingold et al. that pig production in the Netherlands is "greatly overshadowed by the density of pig-farming operations in the United States" is mistaken (*1*) (Table). Pig density in the Netherlands is 35 times higher than in the United States, and more than twice that in Iowa.

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In Response: We thank Davies et al. for their letter (*1*) responding to our report (*2*). We appreciate the opportunity to address their comments, some of which raise appropriate concerns.

Davies et al. correctly note that the original methicillin-resistant *S. aureus* (MRSA) registry data were derived from swab specimens and clinical isolates; the distribution of anatomic sites differed between the cases and controls in our study. However, all study participants were proven MRSA carriers. As per their comment in their letter (*1*), we reran multivariate models excluding 5 persons who acquired MRSA outside the Netherlands. We found odds ratios (and $p<0.05$) similar to those originally reported for covariates of municipality-level livestock densities.

Davies et al. apparently pooled data from 3 studies and stated that there is negligible risk for livestock-associated–MRSA among persons who do not have livestock or farm contact. Each of these studies was designed differently and had different comparison groups, and each report conceded that factors such as indirect human or environmental transmission could have exposed study participants who lacked known farm risk factors.

In addition, Davies et al. state that our observed association of increased odds of livestock-associated–MRSA compared with a typeable strain of MRSA in regions with higher livestock densities should be limited to hypothesis generation. We agree, as stated in the final sentence of our report (*2*). However, a similar association was confirmed in a recent study in the Netherlands that included MRSA-negative controls (*3*).

To clarify our statement comparing pig densities in the United States and the Netherlands (*2*), we referred to density in terms of animals per operation, a relevant parameter for other zoonotic diseases, including swine and avian influenzas. To state this information in a different manner, in 2007, a total of 60% of the 67.7 million pigs raised in the United States were raised on farms with >5,000 pigs, but only 22% of the 11.66 million pigs raised in the Netherlands were raised on farms with >5,000 pigs (*4*,*5*).

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