Comparing Active and Passive Surveillance of Antimicrobial Resistance: Are We Getting the Whole Story?

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ABSTRACT

Antimicrobial resistance (AMR) represents a threat to animal and human health and, therefore, surveillance and monitoring of AMR are important. The two main types of surveillance, passive (PS) and active (AS), have different characteristics which affect the type and strength of inference that can be drawn from their results. Using animal and foods-of-animal origin data, the two surveillance types were compared using phenotypic AMR data for chicken *Salmonella* Heidelberg isolates, and porcine *Salmonella* Typhimurium var. 5- isolates, to determine if the two methods were sampling from common pools of bacteria, respectively. Examination of the connectivity of the profiles sampled by PS and AS, and determination of whether the numbers of profiles observed by each type were as expected if the methods had sampled from single bacterial populations, showed there were no significant differences between the porcine data collected by PS and AS. In the chicken data, the number of profiles obtained by PS was higher than expected, and the number of profiles obtained by AS was lower than expected. Thus, a combination of passive and active surveillance may be optimal for antimicrobial resistance, where the balance between two may differ for each host/bacteria combination.

KEYWORDS

Antimicrobial resistance, *Salmonella*, active surveillance, passive surveillance

INTRODUCTION

Bacterial infections which are resistant to antimicrobial drugs are increasingly common, and arguably provide one of the greatest threats to animal and human health (Tenover, 2006). As a consequence, the surveillance and monitoring of antimicrobial resistance (AMR) are important activities, and are required to assess the prevalence of AMR, identify critical points that may be targeted to control AMR, and detect new or emerging resistances. Surveillance and monitoring are also necessary to assess the impact of any mitigation strategies (Aarestrup, 2004).

Passive surveillance (PS) is generally less costly and widely used but, as the data are derived primarily from diagnostic samples from clinically ill individuals, they are unlikely to represent the characteristics of the general animal and microbial populations. Active surveillance (AS) is more costly, because it involves the planned collection of targeted and often representative samples, from normal healthy individuals. As a result, samples collected through AS should better reflect the characteristics of the general population. Therefore, there are two potential sources of bias with PS with respect to AS – clinically ill individuals versus well individuals, and clinician submission of samples versus population-based sampling.

Comparisons of AMR data obtained using different surveillance methods frequently occurs, and may not be valid if the data obtained through the various methods are biased in different ways. The purpose of this study was to

compare AMR data obtained through AS and PS in order to determine whether the surveillance methods are equivalent in terms of the target microbial populations sampled. Specifically, we wanted to determine whether the isolates collected by each method are similar and derived from the same pool of bacteria.

MATERIALS AND METHODS

Description of the Data

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is a national surveillance program which monitors trends in antimicrobial use and AMR in selected bacteria from animal, human, and food sources across Canada (Public Health Agency of Canada, 2007). This monitoring programme includes components of both active and passive surveillance.

Animal and foods-of-animal-origin data from *Salmonella* Typhimurium var. 5- porcine isolates (porcine), and *Salmonella* Heidelberg chicken isolates (chicken), were selected as case studies for these analyses. Passive surveillance data comprised primarily diagnostic samples submitted by producers or veterinarians. Active surveillance data primarily comprised samples obtained by CIPARS through their on-farm, abattoir, and retail surveillance components; a small number of isolates derived from other government monitoring in Canada were also included. Antimicrobial susceptibility testing was performed using the Sensititre® automated microdilution method (Public Health Agency of Canada, 2007), and isolates were classified as susceptible or resistant to each antimicrobial. Information on 15 antimicrobials was available. The resistance profile for each isolate was compiled. As each isolate could be either susceptible (0) or resistant (1) to each antimicrobial examined, the profile in this context was the ordered combination of 0s and 1s describing the resistance of each isolate.

Connectivity of the PS and AS Profiles

To determine whether the PS and AS methods were sampling from the same microbial community, data were analysed using the eBurst algorithm (Imperial College London, 2006). Using the most stringent conditions, with all members of a group having identical resistance outcomes for $\geq$ 14 of the 15 antimicrobials with at least one other member in the group, the connectivity of the PS and AS profiles for each case study was examined.

Observed and Expected Numbers of PS and AS Profiles

To investigate further whether the two surveillance methods sampled from a common microbial community, a bootstrapping approach was used. At each of 10,000 iterations, the isolates were randomly relabelled without replacement as obtained by PS or AS, and the number of profiles in each category tabulated. The observed numbers of profiles obtained by each method were compared to the bootstrapped distributions of expected numbers for each case study.

RESULTS

There were 499 porcine isolates, of which 52% were collected by PS and 48% by AS. There were 42 profiles obtained by PS and 38 by AS; overall, 54 profiles were observed in the porcine data. Of the 765 chicken isolates, 25% were collected by PS and 75% by AS. There were 24 profiles obtained by PS, 28 by AS, with 39 profiles overall observed in the chicken data.

The eBurst diagrams for both case studies demonstrated that most of the profiles (98% of porcine, 79% of chicken) from both PS and AS could be connected in a web generated by either an addition or loss of resistance to a single antimicrobial.

In the porcine data, the observed numbers of profiles obtained by both PS and AS were well within the distribution of expected results. In the chicken data, the number of profiles obtained by PS was much higher than expected and the number of profiles obtained by AS was much lower than expected (Figure 1).

a) b)

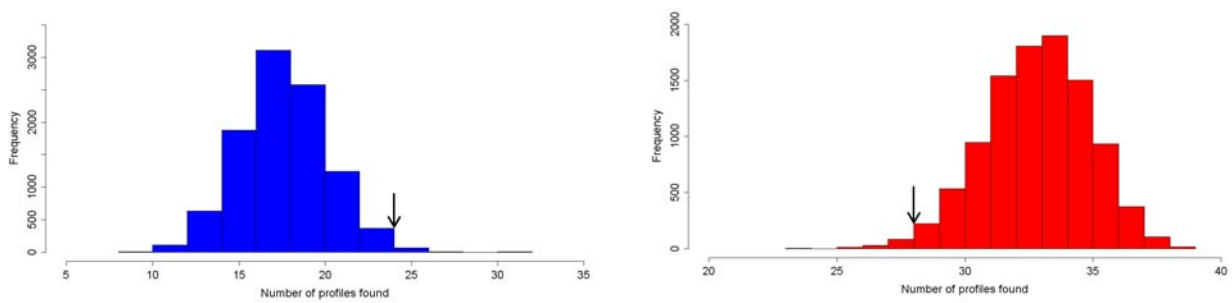

Figure 1 a) Distribution of the expected number from bootstrapping of chicken resistance profiles found by PS, b) Distribution of the expected number from bootstrapping of chicken resistance profiles found by AS. Arrows represent observed number of profiles (24 PS, 28 AS).

CONCLUSION

The results of the eBurst analysis suggest that in both case studies, but especially in the porcine data, both surveillance methods are potentially sampling from a pool of related bacteria, as the majority of the profiles can be connected to each other by the gain or loss of resistance to a single antimicrobial. However, there were differences in the results of the porcine and chicken data in terms of consistency of inference between PS and AS. In the case of the porcine data, the numbers of profiles detected by PS and AS were as expected, given the null hypothesis that both surveillance methods are sampling from the same microbial community, supporting the conclusion from the eBurst connectivity diagram. For the chicken data, the number of profiles detected by PS was higher than expected and, conversely, the number of profiles detected by AS was lower than expected.

Why these differences exist between the species is a matter for speculation. It may be due to variations in AMR patterns between different *Salmonella* serovars (Aarestrup, 2004), inherent differences in the biology of the two animal species, chicken and swine, or in the process, methods, and motivation of AS and PS between the two species, or disparities in animal management and husbandry practices within the two production systems. This would include heterogeneity of antimicrobial use. With genotypic or management information, it may be possible to determine further the cause of the differences observed in our study.

Previous studies have shown that a combination of passive and active surveillance may be optimal for the detection of rare or emerging diseases (Cantón, 2005; Doherr & Audigé, 2001), and this may also be the case for antimicrobial resistance. However, our results suggest that the optimal balance between the two methods may vary depending on the host and bacterial species. Determining this optimal balance for each host/bacteria combination will be critical if antimicrobial resistance is to be assessed accurately.

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ACKNOWLEDGEMENTS

This study was funded by the William Stewart Fellowship, University of Glasgow.