Prescribing and guidelines: both must improve to combat antimicrobial resistance

To the Editors:

In a recent *European Respiratory Journal* editorial, WOODHEAD [1] provided an interesting examination of the contribution of inappropriate antibiotic prescribing for lower respiratory tract infections (LRTIs) in the community to the development and spread of antimicrobial resistance in common bacterial pathogens.

The discussion reports that the heterogeneous antibiotic prescribing across Europe seen in the GRACE (Genomics to Combat Resistance against Antibiotics in Community-acquired LRTI in Europe) network data was associated with no clinically important outcome differences. Yet WOODHEAD [1] goes on to note that other research, such as our own study examining outcomes of antibiotic-treated LRTIs using the UK General Practice Research Database (GPRD), came to different conclusions. We reported that antibiotic prescribing on the day of an LRTI diagnosis was associated with a reduction in hospital admissions and mortality related to LRTI [2]. Our study (an independent academic project, which received absolutely no pharmaceutical company support), used individual patient data, from a single database in order to avoid the ecological fallacy. We included all known potentially confounding variables in regression modelling to minimise bias and ensure the statistical robustness of the analysis. The suggestion made by WOODHEAD [1] that the data were compromised by use of unlinked databases is, therefore, mistaken. Indeed, our findings were replicated in another study, again from an independent group unassociated with antibiotic-marketing companies [3]. We agree with the need to find ways of using antibiotics appropriately in the community, but there are arguments (from recognised academic units) in favour of their use in selected, at-risk patient groups with LRTIs in terms of reducing complications and improving outcomes [2, 3]. Their timely use in community-acquired pneumonia is vital [4].

There is a tendency to dismiss observational database studies due to ill-defined methodological limitations or lack of statistical robustness, but well-designed observational studies contribute valuable information [5]. Due to the typically short duration and strict inclusion criteria used in randomised clinical trials (RCTs), it can be difficult to evaluate rare, but serious, outcomes unless prohibitively large numbers are enrolled. In addition, patients recruited to respiratory RCTs

tend to be poorly representative of the true patient population, limiting external validity.

It is true that some older observational studies in LRTIs were compromised by the ecological fallacy, but it should also be noted that the LRTI RCT evidence is inconclusive, as no adequately powered trials have been undertaken. Observational data using large, high-quality databases (such as the GPRD) and appropriate statistical techniques are a valid data source, and can contribute to the evidence base and to hypothesis generation. All data (whether observational or RCT in origin) should be interpreted within the context of the wider evidence base.

M. Thomas*, D.B. Price# and A. Chisholm#

*Academic Primary Care, University of Aberdeen, Aberdeen, and #Research in Real Life, Cambridge, UK.

Correspondence: D.B. Price, Research in Real Life, 5a Coles Lane, Oakington, Cambridge, CB24 3BA, UK. E-mail: david@rirl.org

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