To the Editors:

We read with interest the recent report by KORNUM *et al.* [1] investigating the link between community-acquired pneumonia and obesity in a large cohort of Danish patients. The authors observed that the increased risk of pulmonary infection no longer existed for obesity when other major chronic diseases were included in the regression model. Cohort studies that describe comorbid associations become more meaningful when one can assign an underlying pathophysiological process. In this context, we would suggest that there are a number of plausible mechanisms that are confounders with obesity. Insulin resistance and hyperglycaemia are more prevalent amongst obese individuals. Airway surface fluid glucose is normally strictly maintained at low levels, which may be as much as 20 times lower than that of plasma, by means of a process of active transport. Elevation of glucose in airway surface fluid, which can occur with even mild hyperglycaemia, promotes bacterial growth within the airway in a dose-dependent manner and predisposes to pneumonia [2].

It was also suggested that gastro-oesophageal reflux related to obesity increases the risk of community-acquired pneumonia by the aspiration of gastric contents into the lung. The situation may be rather more complex, as gastric contents by nature of their acidity are usually sterile. However, the use of acid-suppressing drugs, such as proton pump inhibitors and, to a lesser extent, H_2-antagonists, raise gastric pH and promote the survival and growth of bacteria colonising the aerodigestive tract [3]. Use of the more potent proton pump inhibitors has increased in obese patients [4] and this group of drugs is strongly associated with the development of community-acquired pneumonia. One may also consider other drugs that are more frequently prescribed in the obese; for example, the statins. This class of drug may be beneficial in both preventing and reducing the severity of community-acquired pneumonia, thus decreasing the need for hospitalisation [5]. Improving the outcome of community-acquired pneumonia will require exploration of these and other mechanisms where plausible risk factors are identified by cohort studies.

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REFERENCES

1 Kornum JB, Nørgaard M, Dethlefsen C, *et al.* Obesity and risk of subsequent hospitalisation with pneumonia. *Eur Respir J* 2010; 36: 1330–1336.
2 Baker EH, Wood DM, Brennan AL, *et al.* Hyperglycaemia and pulmonary infection. *Proc Nutr Soc* 2006; 65: 227–235.
3 Herzig SJ, Howell MD, Ngo LH, *et al.* Acid-suppressive medication use and the risk for hospital-acquired pneumonia. *JAMA* 2009; 301: 2120–2128.
4 Friedenberg FK, Hanlon A, Vanar V, *et al.* Trends in gastroesophageal reflux disease as measured by the National Ambulatory Medical Care Survey. *Dig Dis Sci* 2010; 55: 1911–1917.
5 Chalmers JD, Short PM, Mandal P, *et al.* Statins in community acquired pneumonia: evidence from experimental and clinical studies. *Respir Med* 2010; 104: 1081–1091.

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From the authors:

We thank our colleagues for their interest in our recent study in the *European Respiratory Journal* on the risk of pneumonia hospitalisation in obese individuals [1].

I. Schreter and colleagues present interesting data on body mass index (BMI) as a predictor of pneumonia in a cohort of patients hospitalised with influenza. Their findings suggest that increased BMI (reference value not stated) is related to higher odds for the presence of pneumonia among hospitalised influenza patients, after adjustment for age, sex and comorbidity. Pneumonia was present at the time of admission in most influenza patients with pneumonia, suggesting that obesity may have worsened the pre-hospital course of influenza. This association may be biological, *i.e.* due to impaired immune response, risk of aspiration, or an altered ventilation pattern in obesity. However, it may also be that obese persons are, on average, less likely to seek timely medical advice and antiviral medication treatment. The challenge in such observational epidemiological studies (including our own) is the risk of uncontrolled confounders associated with being obese, such as a less healthy lifestyle, a possible increase in substance abuse, fewer immunisations, and altered healthcare-seeking behaviour.

C.D. Hingston and colleagues suggest two pathophysiological mechanisms that may have increased the risk of pneumonia in our obese study participants: hyperglycaemia leading to bacterial growth in airway surface fluid, and acid-suppressing drug use leading to bacterial growth in the gastric contents that may be aspirated. Unfortunately, there were no available medication data in our dataset to examine the latter mechanism. However, we observed a higher occurrence of gastro-oesophageal reflux diagnoses in severely obese individuals (3% among those with a BMI $\geqslant$35 kg·m^2) than in normal-weight participants (1% of those with a BMI 22.5–24.9). Concerning hyperglycaemia, we observed that 17% of severely obese *versus* only 1% of normal-weight participants in our study developed new uncomplicated diabetes during follow-up, and 6% *versus* 0.3%, respectively, developed complicated diabetes. Development of any comorbidity was a strong predictor of subsequent pneumonia in our cohort (hazard ratio (HR) 4.4 (95% CI 4.0–4.8) for a Charlson comorbidity index score of 1–2, and HR 11.5 (95% CI 9.4–14.2) for a Charlson index score of $\geqslant$3), and associations between baseline obesity and pneumonia risk vanished when adjusting for subsequent comorbidity [1]. Diabetes is known to increase pneumonia risk by 25–75%, particularly when long-term glycaemic control is poor [2]. We therefore find it likely that diabetes mediated some of the effect of obesity in our study, perhaps by the mechanisms suggested by C.D. Hingston and