evidence regarding the effects of these drugs on pneumonia. The randomised design of PROGRESS greatly reduced the likelihood of confounding of the analyses and provided an excellent opportunity to explore the validity of the associations reported in observational studies [2, 3]. Thus, the key issue is the selection of elderly subjects in terms of ethnicity, post-stroke state, performance status, type of ACE inhibitor and swallowing function.

The clinical epidemiology research group of ETMINAN *et al.* [8] recently reported that no association was found between the use of ACE inhibitors or angiotensin II receptor blockers (ARBs) and risk of hospitalisation secondary to CAP. The study further confirmed the limited efficacy of ACE inhibitors on the risk reduction of hospitalisation due to pneumonia in a white population. As we speculated, ARBs did not have any role in the prevention of aspiration pneumonia.

Stroke and post-stroke patients often exhibit a normal cough reflex, but not swallowing reflex, and the small volume of aspirated materials due to impaired swallowing during night is a key factor for the risk of pneumonia [9, 10]. Hence, a ten times higher rate of pneumonia in post-stroke patients without significant neurological deficit, compared with the rate of pneumonia in normal elderly [5]. Furthermore, the age-dependent impairment of upper airway reflexes should be carefully considered for the mechanism of CAP in the elderly irrespective of the history of stroke.

Finally, we emphasise that aspiration and silent aspiration are very important mechanisms of aspiration pneumonia. Silent aspiration is very common in patients with stroke and frail elderly patients, and nasogastric tube feeding without swallowing rehabilitation or oral care cannot reduce the pneumonia risk in patients with swallowing disorders [11].

We believe that angiotensin-converting enzyme inhibitors could prevent aspiration pneumonia in selected elderly patients. Post-stroke and the frail elderly are the best candidates for the pneumonia risk reduction by angiotensin-converting enzyme inhibitors [12]. However, these merits may not be consistently observed in Caucasian elderly patients with or without stroke.

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From the authors:

I would like to thank S. Teramoto and co-workers for their response to the study my co-workers and I performed on the effects of angiotensin-converting enzyme (ACE) inhibitors on the risk of acquiring pneumonia. Indeed, we could not confirm an association between the use of ACE inhibitors and the risk of pneumonia in a general population. This, however, does not exclude any beneficial effects of ACE inhibitors in specified patient subgroups.

As mentioned in our introduction and by S. Teramoto and co-workers, it is known that patients with a history of stroke do have a higher risk of acquiring pneumonia, which is particularly due to a reduced cough and swallowing reflex [1, 2]. That ACE inhibitors can be beneficial in these patients is already widely reported [3–5]. We aimed to study whether this protective effect can also be extended to the general population. Unfortunately, we were not able to test modification of the association through stroke, as data on stroke history were sparsely available in the database.

Concerning ethnicity, the reason why the association could not be confirmed in the non-Asian participants of the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) is still subject to speculation. Genetic differences should certainly be considered. However, OHKUBO *et al.* [4] were unable to show an influence of the ACE I/D polymorphism on the protective

association. Another explanation could be the higher prevalence of ACE inhibitor-induced cough in Chinese subjects, as shown by CHAN *et al.* [6]. It is possible that ACE inhibitors are also protective in non-Asian populations. However, larger populations may be necessary to confirm such an effect.

Further studies on the relationship between angiotensin-converting enzyme and pneumonia in predominantly white populations are currently being undertaken in our department.

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PDE-5 inhibitors lower portal and pulmonary pressure in portopulmonary hypertension

To the Editors:

Several studies have proved that inhibitors of phosphodiesterase (PDE)5 are potent compounds for lowering pulmonary pressure in pulmonary arterial hypertension. With great interest we read the study conducted by REICHENBERGER *et al.* [1] about the effect of sildenafil on portopulmonary hypertension (PPHTN). This is a specific condition characterised by an elevated pulmonary arterial pressure (PAP), increased pulmonary vascular resistance and a normal wedge pressure in a setting of underlying portal hypertension. Effective medical therapy is of great importance, as a markedly increased pulmonary pressure has a very poor prognosis in cirrhotic patients and is a contraindication for liver transplantation. The results of the studies by REICHENBERGER *et al.* [1] and others [2, 3] show that in these patients, inhibitors of PDE5 also lower PAP. However, REICHENBERGER *et al.* [1] focused on the effect of sildenafil on PAP; the potential effect of this drug on portal pressure was not investigated.

In a recent study, we showed that the PDE5 inhibitor vardenafil lowers portal pressure and increases portal blood flow in healthy subjects as well as in patients with liver cirrhosis [4]. We also found that sildenafil and tadalafil had similar effects (unpublished data). Recently, we investigated the acute effect of tadalafil on portal and pulmonary haemodynamics simultaneously in a patient with PPHTN.

In the 55-yr-old patient, alcoholic Child A cirrhosis had been diagnosed 7 yrs before. Alcohol consumption had stopped since cirrhosis was diagnosed. The reason for admission was increasing dyspnoea at physical exercise. The patient was taking no medication at the time of the study. The patient was obese (186 cm, 108 kg, body mass index 31.2), his blood pressure was 140/105 mmHg and his cardiac frequency was 79 bpm. ECG and Doppler echocardiogram showed right heart enlargement with systolic PAP ~75 mmHg. Spirometry showed a normal vital capacity (5.3 L, 103%) and forced expiratory volume in one second (3.3 L, 86%). Abdominal duplexsonography showed a slow (9 $cm \cdot s^{-1}$) and reduced portal flow, ~0.15 $L \cdot min^{-1}$ with intrahepatic retrograde perfusion. The umbilical vein was reopened and a large splenorenal shunt was detected. Second-grade oesophageal varices were found on endoscopy.

After counselling the local ethics committee, we investigated the effect of tadalafil, a selective inhibitor of PDE5, on portal and pulmonary haemodynamics. Catheters were introduced into the pulmonary artery and one of the liver veins simultaneously. Haemodynamic parameters were recorded every 15 min for 75 min. After 10 mg tadalafil, mean PAP was reduced from 45 to 38 mmHg (fig. 1). Cardiac index increased from 3.02 to 3.24 $L \cdot min^{-1} \cdot m^{-2}$ and pulmonary vascular resistance decreased from 459 to 351 $dynes \cdot s \cdot cm^{-5}$, while arterial oxygen pressure increased from 70.5 to 78.2 mmHg. Hepatovenous pressure gradient decreased from 10 to 7 mmHg and systemic arterial pressure decreased from 167/89 to 152/87 mmHg. Our results show, that PDE5 inhibition reduces portal venous and PAP in this patient with PPHTN.

Portal hypertension in liver cirrhosis is caused by multiple factors, *e.g.* regenerative nodules and sinusoidal fibrosis, hyperdynamic splanchnic circulation, vasoactive substances and increased sinusoidal tonus due to diminished nitric oxide production and increased cyclic guanosine monophosphate (GMP) degradation [5, 6]. Inhibitors of PDE5 increase portal venous flow and lower portal pressure by inhibiting the degradation of cyclic GMP [4]. Pulmonary arterial hypertension has