subcutaneously. However, in terms of all-cause mortality, patients who were administered PIPC/TAZ subcutaneously had higher all-cause in-hospital mortality compared with those who received it intravenously.

Therefore, subcutaneous PIPC/TAZ administration can be used safely, and it has a similar incidence of adverse events as other antibiotics and similar in-hospital mortality due to infectious disease.

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Comment on "Polypharmacy and Kidney Function in Community-Dwelling Adults Age 60 Years and Older: A Prospective Observational Study"

Dear Editor:

We read with interest the study by Rahel Ernst et al in which they aimed to investigate whether there was a relationship between the total intake of drugs or nonsteroidal anti-inflammatory drugs (NSAIDs) and kidney function. The authors found that each additional medication taken cumulatively for 24 months decreased renal function and, in a high-risk subgroup, per NSAID taken cumulatively for 24 months, the renal function decreased by 1.21 mL/min/1.73 m^2 estimated glomerular filtration rate.[1] In the present study, the cumulative uptake of NSAIDs was found to be associated with a nearly 3-fold reduction in renal function. We think that some methodological issues should be taken into consideration while determining the relationship between long-term NSAID use and renal disease in older adults.[1]

NSAIDs are used frequently in older people, both in acute pain and mainly in cases such as knee osteoarthritis, which causes chronic pain.[2] However, NSAIDs have numerous adverse side effects, such as hypertension, congestive heart failure, electrolyte imbalance, and edema. According to the Beers criteria, long-term use of NSAIDs due to gastrointestinal complications, including gastroduodenal ulcer, gastrointestinal bleeding, and perforation, should be avoided; however, it is emphasized that NSAIDs should be used in combination with proton-pump inhibitors (PPIs) if pain cannot be controlled by other alternative analgesics.[3] This means that in Ernst et al's study, the patients who used NSAIDs for more than 24 months had been probably or should have been receiving PPI at the same time.[1]

PPIs are one of the most commonly prescribed drugs in older people, and it is estimated that between 25% and 70% of the prescriptions have no appropriate indication.[4] The use of chronic NSAIDs is on the top of the indications for which PPIs are recommended. However, in recent years, increasing evidence has shown that PPIs are not innocent drugs and, like NSAIDs, cause both acute and chronic kidney damage.[4] For example, in a large sample-based population-based cohort study, PPI increased the incidence of chronic kidney disease by 20% to 50%. In that study, the NSAID intake was higher in PPI users than non-PPI users; however, it was found that PPIs increased the risk of chronic kidney disease by 1.35-fold after adjustment to NSAIDs.[4] Therefore, in the study by Ernst et al, who investigated the effect of polypharmacy and NSAIDs on renal function, it is an important limitation that PPIs, which are the most common drugs to cause polypharmacy, were not evaluated simultaneously with NSAIDs.[1,5] In that study, it should have been checked whether PPI use contributed to the 3-fold cumulative

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deterioration in renal function or to what extent it was responsible. In order to establish a clear relationship between NSAIDs and kidney damage, especially in older adults, the simultaneous evaluation of other drugs, particularly PPIs, which affect renal function, and their potential impact on outcomes, should be statistically neutralized.

In conclusion, the study contributes valuable data to medical literature; however, given the above-mentioned issue, they ought to have expanded their analyses in order to provide a clearer picture to the readers.

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Proton Pump Inhibitors and Kidney Function Decline in Community-Dwelling Older Adults

To the Editor:

We thank Drs Soysal and colleagues for their important comment that proton pump inhibitors (PPIs), often given in combination with nonsteroidal anti-inflammatory drugs (NSAIDs), may have added to the decrease in kidney function observed with NSAID use. We therefore performed additional analyses in our data set to explore this important concern.

Table 1
Prospective Association Between Continuous Values of Baseline or Cumulative NSAID Intake and Kidney Function Over 24 Months

NSAIDs	Overall Kidney Function (eGFR) Over 24 mo	
	Adjusted Analysis Beta (95% CI)	*P*
At baseline	−2.29 (−5 to 0.41)	.19
Cumulative over 24 mo	−1.34 (−2.51 to −0.17)	.01

CI, confidence interval; eGFR, estimated glomerular filtration rate.
Values are unstandardized regression coefficients (beta) of multivariable linear repeated-measures models adjusted for age, sex, body mass index, treatment groups of the original randomized controlled trial, prevalence of diabetes, prevalence of hypertension, regular use of PPI at baseline, and the baseline value of the eGFR.

First, confirming Dr Soysal's comment on frequent combination of the drugs, we found that 46.5% (20/43) of NSAID users at baseline (43/270) also reported the regular use of PPIs at baseline.

Second, we performed the same analyses as reported in our article[1] plus adjustment for PPI use over time. Similar to our previous results,[1] with every additional NSAID taken cumulatively over 24 months, kidney function decreased by 1.34 mL/min/1.73 m^2 estimated glomerular filtration rate independent of PPI use (Table 1). Further, regular use of PPI at baseline (vs no PPI and no NSAID use) was not associated with kidney function decline over 24 months (beta = 0.74, 95% confidence interval −3.24 to 4.72, $P = .83$).

In summary, although other studies have found an association between PPI use and a decline in kidney function,[2,3] we cannot confirm such an association in our study. In our study, NSAID use, independent of PPI use, contributed to a worsening of kidney function over 24 months among the relatively healthy older adults aged 60 years and older enrolled in our study.

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