

*Conflicts of interest:* Dr Chong has received research grants (paid to his institution) from Biogen and Daavlin Corp, is an investigator for Pfizer Inc and Biogen Inc, and has received honoraria from Celgene Corp and Viela Bio as a consultant. Authors Prasad, Raman, and Ogun-sanya have no conflicts of interest to declare.

*IRB approval status:* Approved by University of Texas Southwestern Medical Center Institutional Review Board.

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<https://doi.org/10.1016/j.jaad.2020.01.010>

### Association between uremic pruritus and long-term outcomes in patients undergoing dialysis



*To the Editor:* Uremic pruritus (UP) is common in patients receiving chronic dialysis and has been associated with unfavorable outcomes and survival. The cause of death among patients with UP has been controversial.<sup>1,2</sup> We designed this prospective open cohort study using retrospectively collected data from the Taiwan National Health Insurance Research Database (NHIRD). The NHIRD contains the deidentified information regarding diagnosis, prescriptions, examinations, operations, and expenditures in both inpatient and outpatient services of 99.8% (23 million) of residents in Taiwan since March 1995.

The diagnosis of UP was defined in patients who received more than 42 daily doses of antihistamine or who received ultraviolet B phototherapy within 1 year after dialysis initiation. To eliminate

indications for antihistamine or phototherapy other than UP, we excluded patients who were diagnosed with allergic rhinitis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code: 477.xx), urticaria (ICD-9-CM code: 708), psoriasis (ICD-9-CM code: 696), mycosis fungoides (ICD-9-CM code: 202.1), or Sezary disease (ICD-9-CM code: 202.2) during the first year of follow-up. The primary outcome was all-cause mortality, and the secondary outcomes were cardiovascular- and infection-related death. The clinical characteristics of UP and non-UP groups were balanced through propensity score matching.

Data were analyzed after 25,048 patients with UP and 50,096 patients without UP were matched (Table 1). A mean follow-up of 5 years revealed that the UP group had a higher risk of all-cause mortality (hazard ratio, 1.05; 95% confidence interval, 1.03-1.07), cardiovascular death (subdistribution hazard ratio, 1.06; 95% confidence interval, 1.02-1.09), and infection-related death (subdistribution hazard ratio, 1.08; 95% confidence interval, 1.05-1.11) than the other group. The cumulative risk of all-cause mortality is presented in Fig 1.

UP contributes to worse long-term outcomes through several ways. The presence of UP is frequently associated with inadequate uremic toxin removal, hyperphosphatemia, and fluid overload.<sup>3,4</sup> Moreover, these factors can contribute to increased cardiovascular events. A high level of uremic toxin can impair immunity through the inhibition of granulocyte or lymphocyte function and activation. Frequent scratching may disrupt the skin barrier, which can lead to cutaneous infections.

The limitation of this study is that its claims database does not contain laboratory data or pruritus severity information. Our effort on using a treatment-based criterion to identify patients with UP can sort out the group with more intense pruritus, and this may be similar to those with a high visual analog score of itching. However, the previously reported association between a higher visual analog score regarding pruritus intensity and worse outcome was not observed in a recent cohort study in Taiwan.<sup>1,2,5</sup> This implies the need for developing a better scoring system.

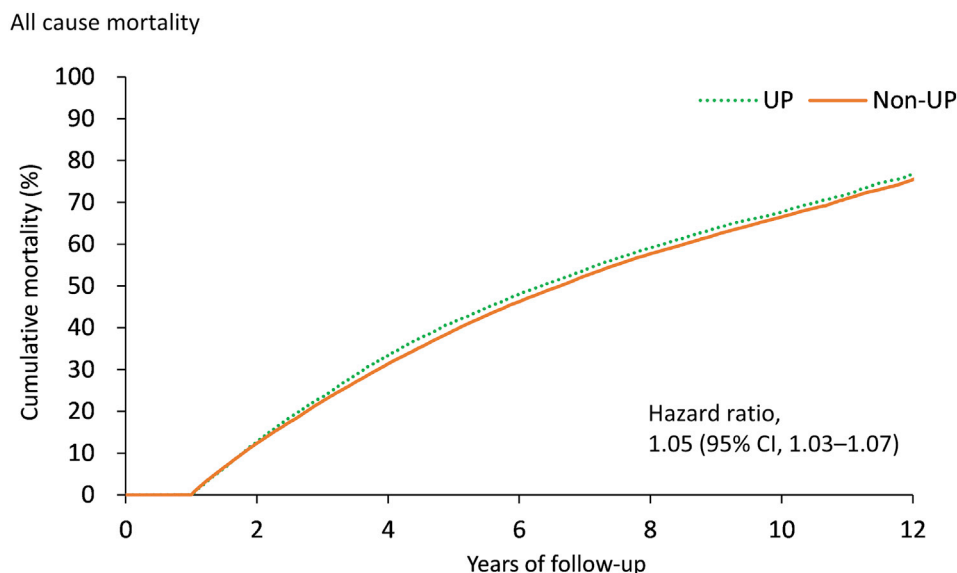
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**Table I.** Outcomes in patients undergoing dialysis with and without uremic pruritus

Outcome	Events, No. (%)		UP vs non-UP	
	UP (n = 25,048)	Non-UP (n = 50,096)	HR or SHR (95% CI)	P value
All-cause mortality	13,086 (52.2)	25,271 (50.4)	1.05 (1.03-1.07)	<.001
Infection death	6,002 (24.0)	11,190 (22.3)	1.08 (1.05-1.11)	<.001
Cardiovascular death	6,366 (25.4)	12,137 (24.2)	1.06 (1.02-1.09)	.001

CI, Confidence interval; HR, hazard ratio; No., number; SHR, subdistribution hazard ratio; UP, uremic pruritus.



Number of patient at risk:							
UP	25048	20069	12569	7925	4873	2889	955
Non-UP	50096	40190	25761	16241	10036	5824	1822

**Fig 1.** The cumulative mortality rate during follow-up in patients with and without uremic pruritus (UP). CI, Confidence interval.

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**Funding sources:** This work was supported by a grant from the Taiwan Ministry of Science and Technology (grant number: 106-2314-B-182A-118-MY3). The funder had no role in study design, data analysis and interpretation, and manuscript drafting.

**Conflicts of interest:** None disclosed.

**IRB approval status:** This study is approved by IRB of Chang Gung Memorial Hospital (IRB No.: 201901097B1).

Reprints not available from the authors.

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