

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Supplementary Materials:

Links to the following videos are also available online underneath the article abstract.

- 1. Supplementary Video 1: Itching due to kidney failure – A patient’s experience**
(vimeo.com/49458473)
- 2. Supplementary Video 2: Gabapentin treatment for itching – A patient’s experience** (vimeo.com/49455976)

Supplementary Table 1: Patient characteristics according to the extent to which patients were bothered by itchy skin. (Expanded Table 1 showing categories of lab measures and p-values)

	To what extent were you bothered by itchy skin during the past 4 weeks?					AOR ^A [95% CI]
	Not at all	Somewhat	Moderately	Very much	Extremely	
Total sample, N	2111	1840	1188	692	425	
Total sample, %	34	29	19	11	7	
Patient characteristics:						
Male	60	59	60	60	59	1.01 [0.91, 1.12]
Age, years	62(15)	62(15)	63(15)	63(15)	64(15)	1.06 [1.02, 1.10]
Time on dialysis, years						
< 0.25	8	5	6	6	7	0.98 [0.83, 1.15]
0.25 - <1	12	11	11	14	12	1.01 [0.88, 1.15]
1 - <5	45	45	47	46	48	1.00 [reference]
5 - <10	19	23	22	19	19	1.03 [0.92, 1.15]
≥ 10	16	17	14	15	14	0.97 [0.85, 1.09]
BMI, kg/m²	26(6)	25(6)	26(7)	26(6)	26(7)	1.05 [1.00, 1.11]
Treatment time (min)	237(34)	237(35)	235(31)	232(32)	232(28)	0.99 [0.97, 1.00]
Hemodiafiltration (HDF)^B						
Non-HDF	82	85	84	85	84	1.00 [reference]
HDF 4-15 L	3	4	5	3	5	1.04 [0.78, 1.37]
HDF 15-20 L	5	3	4	4	3	1.01 [0.77, 1.32]
HDF >20 L	11	8	8	9	8	0.92

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						[0.72, 1.17]
Smoker ^c	19	21	22	24	21	1.15 [0.97, 1.35]
Hepatitis B/C	6	8	9	9	9	1.26 [1.06, 1.50]
Labs:						
Hemoglobin, g/dL	11.0(1.4)	11.0(1.4)	11.0(1.4)	11.0(1.4)	10.9(1.5)	0.99 [0.95, 1.03]
PTH, pg/mL	355(416)	348(449)	346(496)	322(345)	349(430)	0.99 [0.98, 1.01]
White Blood Cell count						
<5400	29	30	28	27	27	1.00 [reference]
5400 - <6700	24	25	27	27	24	1.07 [0.98, 1.18]
6700 - <8400	28	25	25	27	22	0.93 [0.85, 1.03]
≥ 8400	19	20	20	20	26	1.08 [0.98, 1.19]
Albumin (g/dL)						
< 3.5	23	23	26	28	34	1.14 [1.04, 1.25]
3.5 - <4.0	42	44	43	44	40	1.00 [reference]
≥ 4.0	34	33	30	28	26	0.87 [0.80, 0.95]
Albumin (g/dL) continuous	3.8(0.5)	3.7(0.5)	3.7(0.5)	3.7(0.5)	3.7(0.5)	0.86 [0.75, 0.98]
Ferritin (ng/mL)						
< 100	17	24	18	18	18	0.92 [0.79, 1.06]
100 - <400	32	30	33	33	32	1.00 [reference]
400 - <800	29	28	30	30	31	1.03 [0.92, 1.15]
≥ 800	23	18	19	19	19	1.01 [0.89, 1.14]
Calcium (mg/dL)						
< 8.4	21	22	24	23	21	1.02 [0.91, 1.15]

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8.4 - <9.5	57	56	55	53	58	1.00 [reference]
9.5 - <10.2	18	17	16	19	19	1.02 [0.89, 1.15]
≥ 10.2	4	5	5	4	3	0.98 [0.80, 1.21]
Phosphorus (mg/dL)						
< 3.5	11	11	13	11	13	1.00 [0.88, 1.14]
3.5 - <5.5	56	51	52	51	50	1.00 [reference]
5.5 - <6.7	20	23	21	22	20	1.01 [0.91, 1.13]
≥ 6.7	13	15	14	15	16	1.07 [0.95, 1.21]
Calcium x Phosphorus product (mg²/dL²)	43[36,52]	45[36,55]	44[35,52]	44[36,53]	44[36,54]	1.02 [0.98, 1.06]
Single Pool Kt/V						
< 1.2	14	18	17	18	19	1.00 [reference]
1.2 - <1.5	33	34	34	35	34	1.02 [0.92, 1.13]
≥ 1.5	53	49	49	47	47	0.95 [0.86, 1.04]
CRP (mg/L) ^D						
< 1	24	24	23	25	17	1.00 [reference]
1 - <3	25	28	22	19	20	0.77 (0.65, 0.91)
3 - <5	13	13	9	10	8	0.68 (0.52, 0.90)
5 - <10	17	18	22	21	18	1.18 (0.94, 1.47)
10 - <15	7	5	8	7	10	1.39 (1.06, 1.83)
≥ 15	14	13	16	18	26	1.31 (1.05, 1.64)
CRP (mg/L) ^D continuous	3.0 [1.0,8.0]	2.7 [1.0,7.0]	4.0 [1.0,9.7]	4.0 [1.0,10.5]	5.3 [1.7,15.8]	1.00 [1.00, 1.01]

Footnote: Data shown as mean (standard deviation), median [interquartile range], or column percent.

Non-response rate was 27% overall, varying from 9% in Turkey to 46% in Canada.

A. Each variable tested in separate logistic regression model with moderately to severely being bothered by itchy skin as the outcome accounting for facility clustering and adjusting for age, sex, vintage, 13 summary comorbidities (coronary artery disease, cancer, other cardiovascular disease, cerebrovascular disease, congestive heart failure, diabetes mellitus, gastrointestinal bleeding, hypertension, lung disease, neurologic disorder, psychological disorder, peripheral vascular disease, recurrent cellulitis), and country. Adjusted odds ratio (95% confidence interval) shown for age per 10 years, BMI per 5 kg/m², treatment time per 10 minutes, calcium phosphorus product per 10 mg²/dL².

B. Hemodiafiltration (HDF) measure excludes US and Canada due to lack of use; n=4774

C. Smoker defined as someone indicating being a current smoker or stopped smoking within past year

D. CRP is restricted to facilities that reported measurement in at least 50% of patients (excludes US), n=2066

Supplementary Table 2

What time of the day is the itch most bothersome?			When is the itch most bothersome in relation to your dialysis treatments?		
	%	N		%	N
1: Morning	5%	43	1: Soon before the dialysis session	2%	20
2: Afternoon	3%	31	2: During the dialysis session	15%	138
3: Evening	15%	145	3: Soon after the dialysis	9%	85
4: At night	30%	282	4: On non-dialysis days	14%	128
5: No specific time, or most all times	48%	454	5: No specific time, or most all times	61%	576
All	100%	955	All	100%	947

Time of day and timing in relation to dialysis treatment that itch is most bothersome in patients who answered 'Yes' to question 'Are you bothered at all by itchy skin?'

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Supplementary Table 3: Health care providers that patients spoke with about their itchy skin.

	Overall bothered by itchy skin	Nearly Always or Always bothered by itchy skin												
		All	Bel	Can	GCC	Ger	Ita	Jpn	Rus	Spa	Swe	Tur	UK	US
Nephrologist	42%	46%	59%	59%	70%	46%	84%	34%	62%	55%	71%	26%	46%	26%
Nurses or other staff	32%	37%	26%	51%	23%	33%	35%	44%	29%	36%	41%	31%	32%	39%
Skin doctor	18%	24%	26%	16%	31%	32%	38%	27%	11%	15%	18%	31%	16%	17%
Primary care doctor	16%	19%	4%	27%	2%	33%	24%	9%	29%	15%	9%	21%	44%	37%
None	25%	17%	11%	18%	12%	14%	8%	13%	12%	19%	21%	19%	19%	33%
Total responders:	2522	999	27	49	98	57	37	338	73	73	34	42	57	114

Footnote: Question wording: ‘What health care providers have you spoken with about your itchy skin (choose all that apply)?’; restricted to patients who answered ‘Yes’ to question ‘Are you bothered at all by itchy skin?’ (presented in ‘Overall’ column) and also selected 5 or 6 (‘Nearly Always or Always bothered’) on 0-6 scale in response to ‘During the past week, how often have you been bothered by: your itching?’.

ANZ = Australia and New Zealand, Bel = Belgium, Can = Canada, Chi = China, GCC = the six Gulf Cooperation Council countries (Bahrain, Qatar, Kuwait, Oman, Saudi Arabia, and United Arab Emirates), Ger = Germany, Ita = Italy, Jpn = Japan, Rus = Russia, Spa = Spain, Swe = Sweden, Tur = Turkey, UK = the United Kingdom, US = the United States of America.

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Supplementary Table 4: Health care providers that prescribed treatments/medications for patients with itchy skin.

	Overall bothered by itchy skin	Nearly Always or Always bothered by itchy skin												
		All	Bel	Can	GCC	Ger	Ita	Jpn	Rus	Spa	Swe	Tur	UK	US
Nephrologist	52%	52%	55%	59%	79%	49%	69%	46%	60%	68%	89%	33%	29%	27%
Nurses or other staff	23%	23%	18%	24%	11%	16%	0%	30%	13%	25%	18%	33%	7%	36%
Skin doctor	24%	26%	32%	26%	33%	33%	31%	28%	17%	17%	18%	33%	17%	21%
Primary care doctor	19%	18%	14%	26%	0%	21%	29%	8%	25%	13%	14%	20%	59%	46%
Total responders:	1927	832	22	34	91	43	35	314	53	53	28	40	41	78

Footnote: Question wording: ‘Which health care providers have prescribed treatments/medications for your itchy skin (choose all that apply)?’; restricted to patients who answered ‘Yes’ to question ‘Are you bothered at all by itchy skin?’ (presented in ‘Overall’ column) and also selected 5 or 6 (‘Nearly Always or Always bothered’) on 0-6 scale in response to ‘During the past week, how often have you been bothered by: your itching?’.

ANZ = Australia and New Zealand, Bel = Belgium, Can = Canada, Chi = China, GCC = the six Gulf Cooperation Council countries (Bahrain, Qatar, Kuwait, Oman, Saudi Arabia, and United Arab Emirates), Ger = Germany, Ita = Italy, Jpn = Japan, Rus = Russia, Spa = Spain, Swe = Sweden, Tur = Turkey, UK = the United Kingdom, US = the United States of America.

Supplementary Table 5: Medical Director’s ranking of therapeutic options for patients with severe pruritus.

% of Medical Directors	Rank of Importance				
	1 (most)	2	3	4	5 (least)
Increasing dialysis dose (in patients with low Kt/V)	15%	25%	29%	24%	6%
Phosphorus control (in patients with high serum phosphorus)	60%	16%	15%	8%	1%
Lowering PTH levels (in patients with high PTH)	2%	26%	21%	28%	23%
Use of prescription medications for pruritus	13%	15%	13%	14%	45%
Increasing prescribed treatment time (in patients with short treatment time)	11%	18%	21%	26%	24%

Footnote: Question wording: ‘Please rank the following therapeutic options for patients with severe pruritus in order of importance (from 1 to 5, with 1 being most important)’; restricted to complete responses, N=241

Supplementary Table 6: Treatments/medications patient was taking to relieve itchy skin.

	Overall bothered by itchy skin	Nearly Always or Always bothered by itchy skin												
		All	Bel	Can	GCC	Ger	Ita	Jpn	Rus	Spa	Swe	Tur	UK	US
Non-Rx topical	29%	30%	21%	51%	42%	51%	24%	17%	35%	29%	36%	12%	25%	45%
Rx topical	38%	44%	36%	31%	33%	25%	38%	72%	6%	26%	42%	36%	46%	23%
Non-Rx oral	7%	7%	4%	4%	14%	5%	11%	1%	17%	4%	3%	12%	4%	14%
Rx oral	19%	22%	29%	24%	24%	12%	38%	22%	7%	30%	45%	31%	15%	17%
Ultraviolet (UV) light treatment	1%	1%	0%	0%	3%	0%	0%	1%	1%	1%	0%	0%	0%	0%
None	25%	18%	21%	16%	9%	23%	19%	8%	45%	26%	9%	26%	29%	29%
Total responders:	2434	971	28	45	97	57	37	334	69	69	33	42	52	108

Footnote: Question wording: ‘What treatments/medications are you currently taking to relieve your itchy skin (choose all that apply)?’; restricted to patients who answered ‘Yes’ to question ‘Are you bothered at all by itchy skin?’ (presented in ‘Overall’ column) and also selected 5 or 6 (‘Nearly Always or Always bothered’) on 0-6 scale in response to ‘During the past week, how often have you been bothered by: your itching?’; Rx=prescription, non-Rx= non-prescription/over the counter, topical = topical (cream or ointment put on skin), oral = oral (medication taken by mouth). Among patients ‘nearly always or always bothered’, topical cream use (Rx or non-Rx) was 38%, and oral medication use (Rx or non-Rx) was 28%.

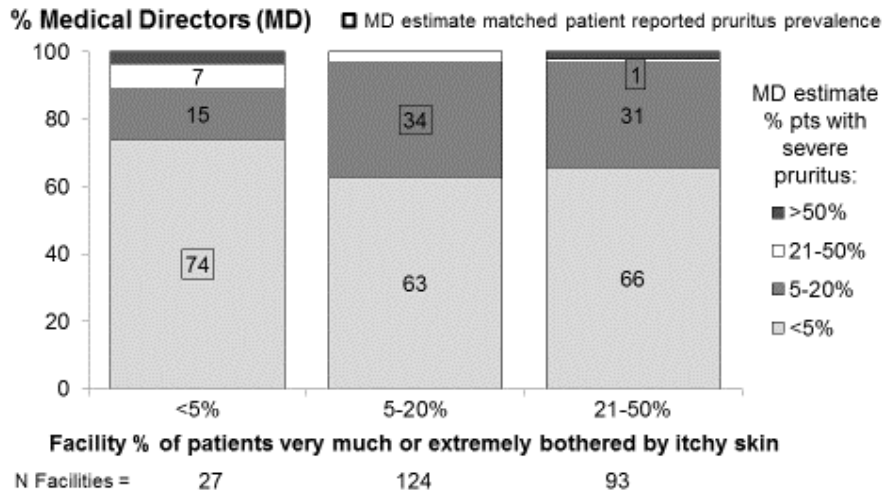
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Supplementary Table 7: Medical Directors' drug options for patients with pruritus who are not referred to a specialist.

	1: Chronic use, 1st line therapy	2: Chronic use, 2nd line therapy	3: Chronic use, 3rd line therapy	4: Acute use only (i.e., prescribe for 1 month or less)	5: I never prescribe for pruritus	N MDs
Topical antihistamines	23%	9%	7%	24%	36%	249
Oral antihistamines (over the counter)	32%	13%	3%	21%	31%	238
Oral antihistamines (prescription)	46%	24%	5%	19%	7%	259
IV antihistamines	2%	6%	9%	35%	48%	254
Topical corticosteroids	9%	11%	12%	39%	29%	256
Oral corticosteroids	2%	2%	4%	26%	66%	253
IV corticosteroids	1%	1%	1%	18%	79%	249
Gabapentin	5%	19%	21%	4%	52%	198
Antidepressants	2%	8%	21%	8%	60%	252
Anti-anxiolytics/sedatives	2%	6%	20%	19%	53%	251
Opioids	1%	5%	9%	6%	79%	249

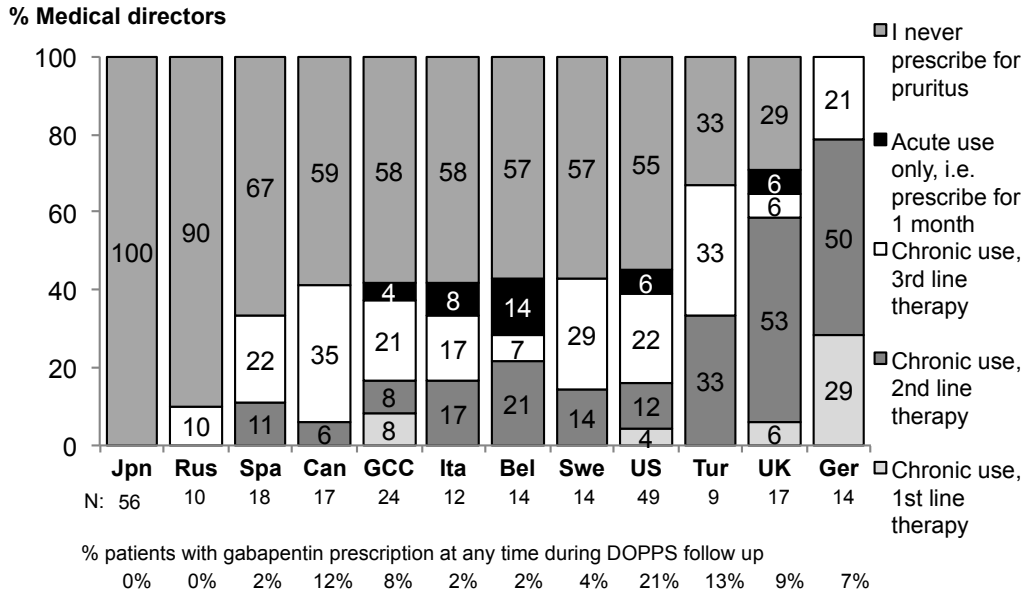
Footnote: Question wording: 'For chronic hemodialysis patients with pruritus whom you do not refer to a specialist, please describe your use of the following drugs options'. Medication use categories are not exclusive. Chronic use as 1st line therapy of prescription or non-prescription/over the counter oral antihistamines was 57%.

Supplementary Figure 1: Medical Directors’ estimates of the percentage of patients affected by severe pruritus in their unit, shown by percentage of patients reporting being very much or extremely bothered by itchy skin.



Footnote: Facilities were classified by categorizing % patients responding to question: “To what extent were you bothered by itchy skin during the past 4 weeks?” with ‘very much’ or ‘extremely’ at the time of facility recruitment into study (representative study cross section, facilities with <5 patient responses were excluded) and by medical director responses to question “Based on your current clinical practice, estimate the percent of patients with severe pruritus”.

Supplementary Figure 2: Variation between countries in Medical Directors' prescribing of gabapentin for pruritus.



Question text: “For chronic hemodialysis patients with pruritus whom you do not refer to a specialist, please describe your use of the following drug options: Gabapentin”.

ANZ = Australia and New Zealand, Bel = Belgium, Can = Canada, Chi = China, GCC = the six Gulf Cooperation Council countries (Bahrain, Qatar, Kuwait, Oman, Saudi Arabia, and United Arab Emirates), Ger = Germany, Ita = Italy, Jpn = Japan, Rus = Russia, Spa = Spain, Swe = Sweden, Tur = Turkey, UK = the United Kingdom, US = the United States of America.