

# Residual Urine Volume in Hemodialysis Patients: International Trends, Predictors and Outcomes in the DOPPS

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## Background / Goal

- Background**
  - Residual urine volume (RUV) decline after hemodialysis initiation has received limited attention in hemodialysis, and preventive actions are matter of debate
- Goal**
  - Describe international trends in RUV from 2002-2015
  - Analyze the effect of potentially modifiable predictors on the association between RUV and mortality

## Methods

- Sample**
  - 21,199 hemodialysis patients from 12 countries in DOPPS phases 2-5 (2002-2015)
    - Europe: Belgium, France, Germany, Italy, Spain, Sweden, United Kingdom
    - North America: United States, Canada

- Analysis**
  - Model:** Cox regression models
  - Outcome:** Patient all-cause mortality
  - Exposure:** Reported RUV at study baseline
  - Adjustments:** age, sex, race (Black v. non-Black), vintage (continuous + indicator for vintage <1), body mass index, region (North America, Europe, Japan), serum creatinine, and thirteen comorbidities: congestive heart failure, cancer, other cardiovascular, cerebrovascular disease, coronary artery disease, diabetes, gastro-intestinal bleeding, hypertension, lung disease, neurologic disease, psychiatric disorder, and recurrent cellulitis or gangrene.

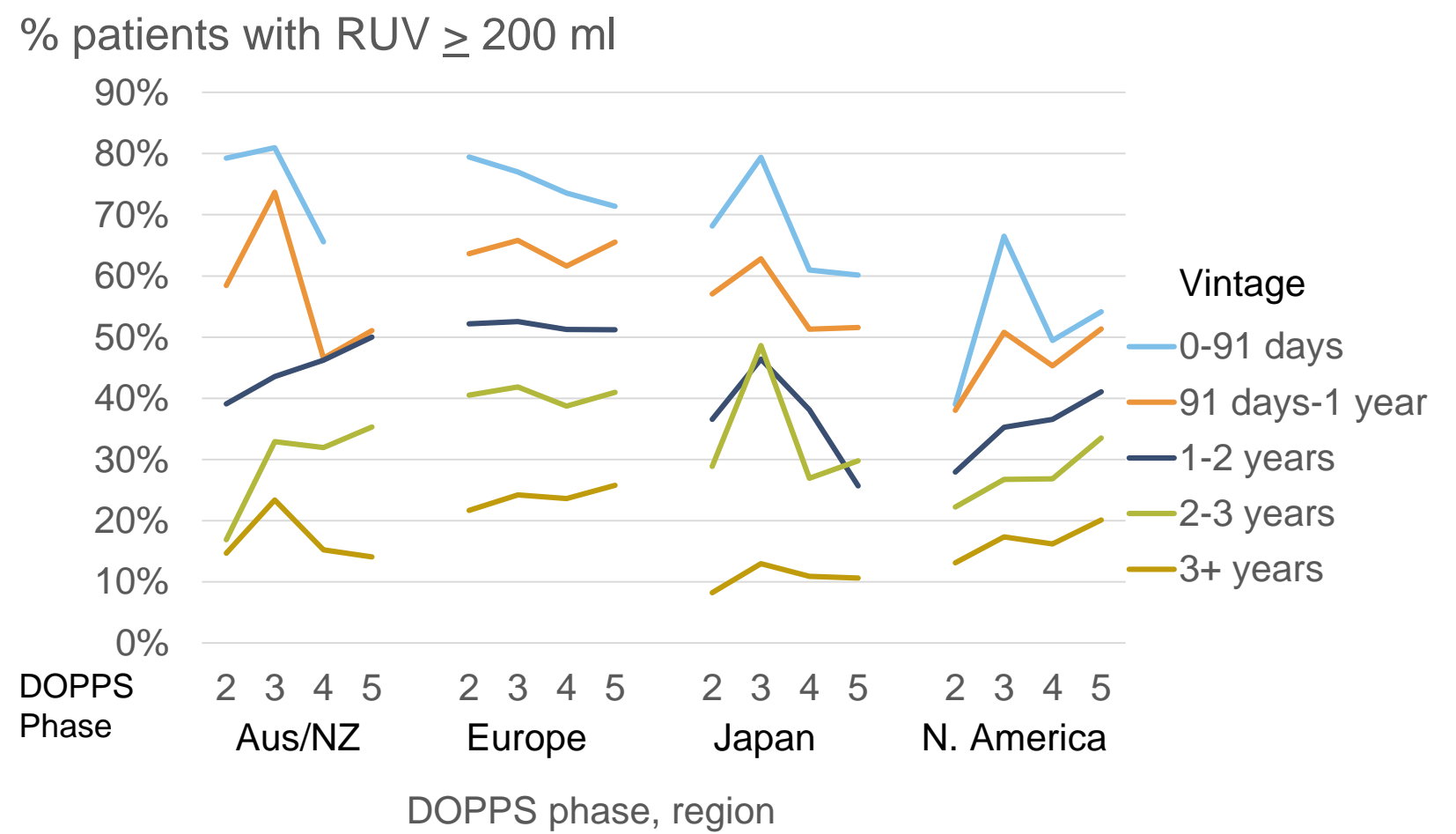
## Results

**Table:** Distributions of patient factors by vintage, region and reported RUV (<200 ml/day versus ≥200 ml/day)

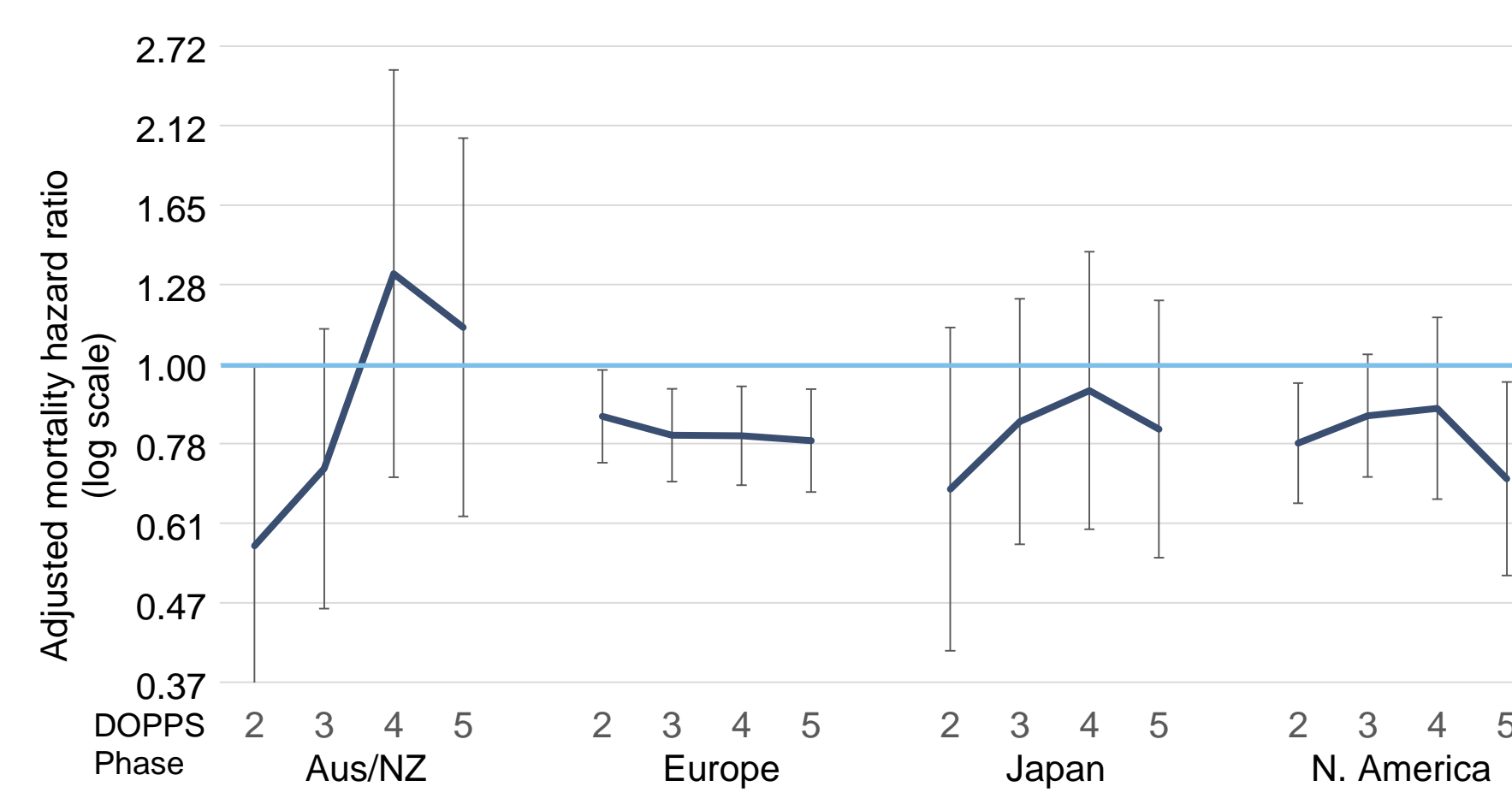
Residual urine volume (ml/day)	Vintage	Region		All										Australia/New Zealand										Europe										Japan										North America									
				<90 days		90 days - 1yr		1-1.9 years		2-2.9 years		≥3 years		<90 days		90 days - 1yr		1-1.9 years		2-2.9 years		≥3 years		<90 days		90 days - 1yr		1-1.9 years		2-2.9 years		≥3 years		<90 days		90 days - 1yr		1-1.9 years		2-2.9 years		≥3 years											
		<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200	<200	≥200														
N		465	845	1584	1889	2378	1704	2148	1084	11559	2255	12	51	95	120	149	115	155	58	759	143	202	456	699	1067	1030	1010	957	629	4660	1284	62	124	197	228	354	171	349	156	3717	394	189	214	593	474	845	408	687	241	2423	434		
Age		65.4	63.3	64.8	63.6	65.0	64.3	65.9	64.0	63.3	63.2	56.0	58.7	63.7	61.3	65.4	57.8	65.8	59.2	63.0	59.3	65.9	65.4	66.3	64.1	66.1	65.8	66.6	65.3	64.7	64.9	67.0	61.8	64.0	64.5	65.2	64.7	66.2	63.9	62.9	62.3	64.8	60.9	63.6	62.8	63.5	62.1	64.8	61.9	61.4	60.5		
Male		59%	62%	58%	63%	57%	61%	59%	62%	57%	60%	67%	61%	63%	59%	62%	60%	62%	67%	60%	57%	56%	62%	56%	65%	58%	62%	58%	62%	56%	62%	81%	65%	71%	72%	62%	64%	70%	62%	59%	59%	55%	60%	55%	55%	53%	58%	53%	60%	53%	56%		
Vintage (years)		0.1	0.1	0.6	0.6	1.5	1.5	2.5	2.5	9.3	6.3	0.2	0.1	0.7	0.6	1.5	1.5	2.5	2.5	8.2	6.3	0.1	0.1	0.6	0.6	1.5	1.5	2.5	2.5	9.1	6.4	0.1	0.1	0.6	0.6	1.5	1.5	2.5	2.5	11.3	6.4	0.1	0.1	0.6	0.6	1.5	1.5	2.5	2.4	7.1	5.9		
Cause of ESRD: diabetes II		31%	28%	32%	27%	30%	27%	31%	27%	20%	22%	25%	29%	34%	32%	30%	26%	34%	29%	22%	27%	17%	22%	22%	19%	19%	23%	21%	21%	12%	16%	42%	43%	43%	39%	38%	44%	40%	41%	22%	30%	41%	33%	39%	38%	39%	31%	40%	36%	31%	31%		
Cause of ESRD: polycystic disease		3%	5%	4%	6%	5%	6%	4%	7%	6%	6%	0%	2%	4%	2%	3%	2%	3%	4%	3%	5%	9%	2%	3%	2%	3%	2%	3%	3%	4%	0%	4%	4%	3%	3%	5%	3%	3%	5%	4%	1%	0%	1%	1%	0%	1%	1%	2%	4%	3%			
Cause of ESRD: IGA nephropathy		1%	2%	2%	3%	2%	3%	2%	3%	4%	4%	0%	4%	2%	3%	2%	3%	4%	3%	5%	9%	2%	3%	2%	3%	2%	3%	3%	4%	0%	4%	4%	3%	3%	5%	3%	3%	5%	4%	1%	0%	1%	1%	0%	1%	1%	2%	4%	3%				
Interdialytic weight gain (%)		2.8%	2.3%	3.4%	2.7%	3.4%	2.8%	3.4%	3.0%	3.9%	3.0%	3.6%	2.3%	3.2%	2.4%	3.1%	2.6%	2.6%	1.9%	3.0%	2.7%	2.6%	2.2%	3.2%	2.5%	3.2%	2.5%	3.2%	2.9%	3.5%	2.7%	2.9%	2.6%	4.1%	3.4%	4.1%	3.8%	4.3%	3.8%	4.6%	3.8%	2.9%	2.5%	3.4%	3.0%	3.5%	3.1%	3.4%	3.3%	3.8%	3.3%		
Congestive heart failure		33%	32%	36%	31%	33%	28%	32%	27%	28%	26%	50%	22%	28%	43%	34%	29%	32%	23%	41%	32%	25%	32%	30%	28%	28%	25%	29%	25%	26%	25%	29%	29%	30%	22%	19%	19%	21%	22%	19%	19%	41%	36%	47%	40%	45%	36%	42%	35%	41%	34%		
Hypertension		83%	87%	84%	85%	83%	87%	84%	87%	79%	85%	92%	92%	79%	91%	85%	93%	85%	79%	83%	78%	77%	86%	81%	84%	79%	85%	80%	87%	78%	84%	71%	86%	77%	82%	76%	80%	80%	81%	72%	81%	91%	91%	91%	87%	91%	93%	91%	92%	91%	90%		
Pre-dialysis systolic blood pressure (mmHg)		142.4	144.8	142.4	142.9	144.6	143.2	143.7	144.3	143.7	144.4	155.7	148.7	143.6	144.7	148.9	144.3	141.8	147.7	146.5	147.9	138.6	141.6	137.7	139.6	139.9	139.5	139.1	140.1	136.9	140.7	149.2	151.0	150.0	148.3	147.7	151.4	151.5	150.6	149.1	150.9	143.2	146.6	145.2	147.2	148.3	148.4	146.4	150.5	147.4	148.3		
Post-dialysis systolic blood pressure (mmHg)		140.9	143.6	134.9	136.6	134.5	136.0	133.4	135.6	131.7	136.3	156.7	139.0	136.7	136.1	134.0	136.3	131.8	136.9	133.8	138.2	137.8	141.7	130.6	134.5	130.3	133.9	129.4	133.8	127.0	134.1	148.8	150.7	140.3	142.2	137.3	142.3	139.9	141.5	135.7	142.9	140.5	144.2	137.7	138.6	138.4	136.0	136.4	134.0	136.4			
Prescriptions of diuretics - any (%)		33%	48%	29%	50%	24%	46%	19%	48%	10%	42%	20%	44%	23%	35%	16%	20%	10%	23%	6%	20%	26%	54%	29%	58%	25%	55%	20%	58%	11%	51%	64%	51%	46%	50%	39%	49%	27%	48%	12%	41%	30%	35%	24%	35%	18%	30%	15%	29%	9%	23%		
Calcium channel blocker (%)		42%	49%	40%	42%	37%	39%	34%	41%	36%	39%	30%	46%	43%	35%	31%	37%	22%	33%	30%	27%	35%	44%	30%	35%	29%	34%	27%	39%	26%	33%	62%	68%	59%	67%	46%	56%	48%	55%	48%	57%	43%	48%	44%	46%	44%	45%	39%	39%	39%	43%		
Angiotensin-converting-enzyme inhibitor (%)		20%	24%	23%	24%	22%	23%	22%	23%	18%	24%	10%	23%	40%	27%	25%	24%	30%	21%	23%	18%	17%	28%	20%	25%	18%	22%	24%	20%	25%	5%	8%	5%	6%	9%	11%	8%	11%	9%	9%	28%	26%	30%	28%	32%	29%	30%	27%	30%	27%			
Angiotensin receptor blocker (%)		17%	20%	16%	20%	17%	21%	17%	21%	20%	22%	10%	15%	10%	13%	8%	8%	7%	13%	13%	17%	17%	18%	14%	18%	15%	19%	13%	18%	13%	18%	41%	48%	38%	46%	35%	40%	38%	40%	34%	41%	10%	11%	13%	15%	14%	21%	16%	17%	15%	16%		
Antihypertensives (#)		1.9	2.3	1.9	2.2	1.8	2.1	1.7	2.2	1.6	2.1	1.4	2.2	1.8	1.8	1.3	1.4	1.2	1.4	1.2	1.5	1.6	2.3	1.5	2.1	1.5	2.1	1.4	2.2	1.3	2.1	2.4	2.3	2.2	2.4	2.0	2.3	2.0	2.2	1.8	2.2	2.1	2.2	2.3	2.1	2.3	2.1	2.2	1.9	2.1			

Bolded cells indicate p < 0.05 for a comparison between patients with residual urine volume <200 v. ≥200 ml/day. Shaded cells indicate that p remains < 0.05 after using the Hochberg correction for multiple comparisons

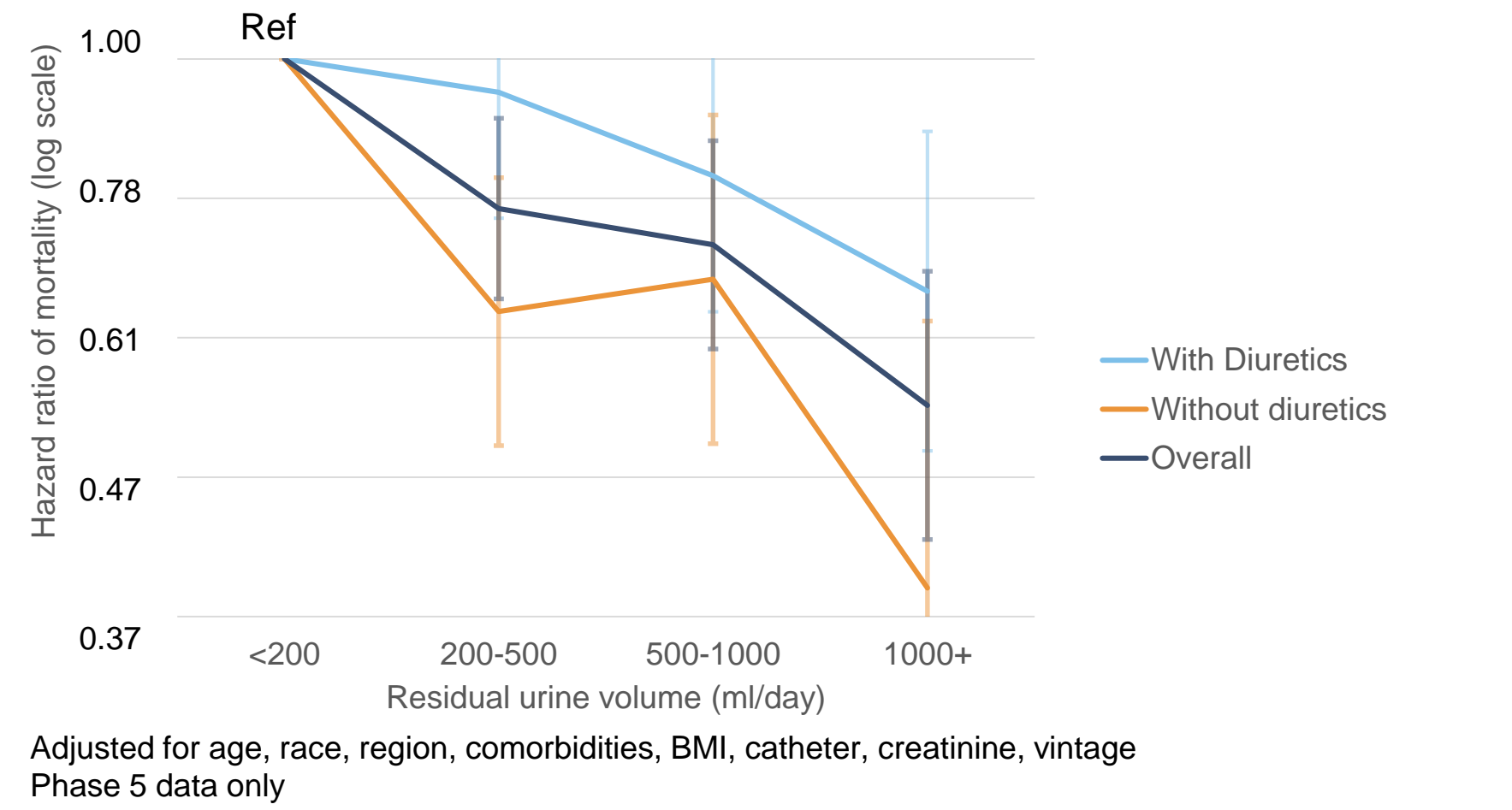
**Figure 1:** % patients with reported RUV ≥200 ml/day, among prevalent cross-section of patients at the start of each DOPPS phase



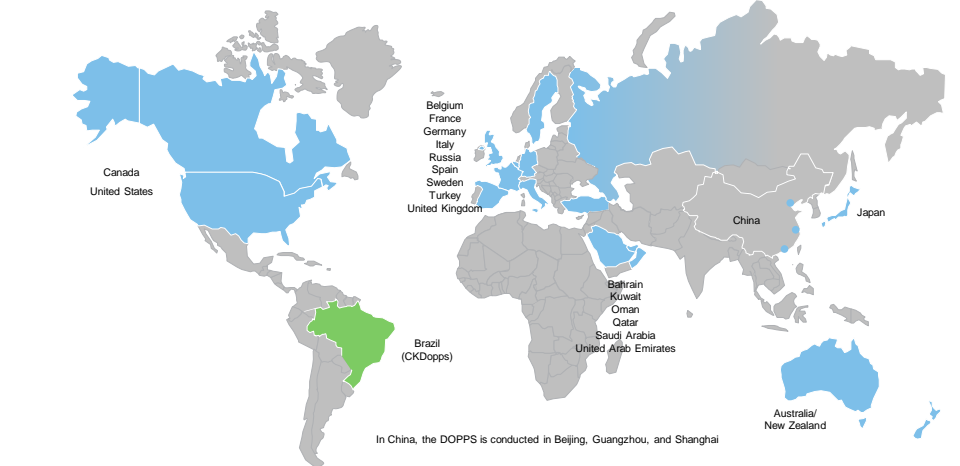
**Figure 2:** Adjusted mortality hazard ratio of reported RUV ≥200 ml/day (versus <200 ml/day), by region and by DOPPS phase



**Figure 3:** Interaction between diuretic use and reported RUV's effect on mortality (p = 0.05)



## DOPPS The Dialysis Outcomes and Practice Patterns Study



Support for the DOPPS Program (including CKDopps, DOPPS, and PDOPPS) is provided by Amgen (founding sponsor, since 1996), Kyowa Hakko Kirin (since 1999, in Japan), and Baxter Healthcare (since 2011). Additional support is provided for specific projects and/or countries by Amgen, AstraZeneca, Hexal AG, Janssen, Kenex, Proteon, Relypsa, Roche, Vifor Fresenius Renal Pharma, ERA-EDTA, Japanese Society for PD, Societies for Nephrology in Germany, Italy, and Spain. Public funding is provided by a number of institutions. Support for the DOPPS Program is provided without restrictions on publications. The [DOPPS.org](http://DOPPS.org) website has full details.

The DOPPS Program is coordinated by Arbor Research Collaborative for Health, Ann Arbor, MI USA.

- The DOPPS is an international prospective cohort study of hemodialysis treatment and patient outcomes:**
  - DOPPS 1 (1996-2001):** 308 dialysis facilities and 17,034 patients in 7 countries (France, Germany, Italy, Japan, Spain, UK, and US)
  - DOPPS 2 (2002-2004), DOPPS 3 (2005-2008), DOPPS 4 (2009-2011):** ≥300 facilities and 11,000 - 13,000 patients per study phase in 12 countries (DOPPS 1 countries + Australia, Belgium, Canada, New Zealand, and Sweden)
  - DOPPS 5 (2012-2015), DOPPS 6 (2015-2017):** ~500 facilities and 30,000 patients in nine new countries (Bahrain, China, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, Russia, and Turkey) in addition to the 12 countries represented in DOPPS 4

- In prevalent patients with median vintage of 3.5 years, 31% reported RUV ≥ 200 ml/day, at a wide geographical range (19% in Japan to 58% Germany), without a substantial time trend identified over DOPPS phases (Figure 1).
- Among patients on dialysis less than 1 year, 59% reported RUV ≥200 ml/day, decreasing to 45%, 36% and 17% of patients on dialysis 1-1.9 years, 2-2.9 years, and ≥3 years, respectively (Figure 1).
- Table: In this largest international analysis to date, few of the analyzed variables seemed to be consistently associated with the presence of reported RUV ≥200 ml/day, across regions and vintage categories. Statistical significance was not consistently reached throughout all region and vintage categories, even for the 'obvious association' between diuretic use and presence of reported RUV ≥200 ml/day.
- However, polycystic kidney disease as primary cause of ESRD seemed to be more common among patients who reported RUV ≥200 ml/day (compared with <200 ml, while congestive heart failure as a comorbidity seemed to be less common among patients who reported RUV ≥200 ml/day (compared with <200 ml/day). Patients who reported RUV ≥200 ml/day more commonly had Angiotensin Converting Enzyme inhibitors and Angiotensin-II Receptor Blockers prescribed (compared with <200 ml/day).
- Prevalent patients who reported RUV ≥200 ml/day had lower adjusted mortality than patients with RUV <200 ml/day, and the association seemed to be fairly consistent across regions, with the exception of Australia/New Zealand (Figure 2).
- The mortality risk associated with reported RUV tended to decline with increasing RUV, and the interaction test for whether this association differed among patients who were prescribed (versus not prescribed) diuretics resulted in a p value of 0.05, (Figure 3).

## Summary / Conclusions

- Maintenance of RUV differs by region and vintage, but has remained relatively stable in the DOPPS since 2002
- Many patients on dialysis for two years or more have RUV; this may previously have been under-recognized
- The relationship between RUV and survival appears to be dose-dependent
- RUV seems to be beneficial among patients on diuretics and patients without diuretics; however, there may be differences in the effect sizes
- Dose and the choice of diuretics and other means to potentially preserve RUV deserve more focused investigation.