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CKD-MBD in China

Current and Perspective

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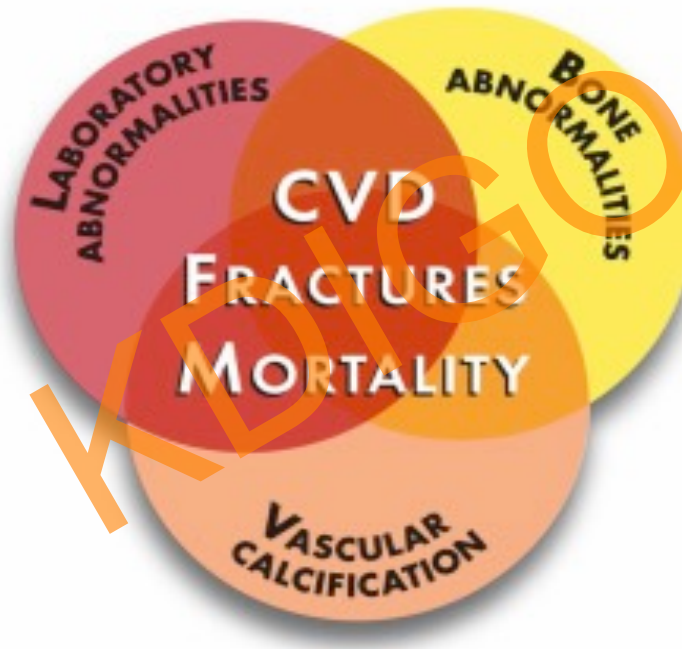


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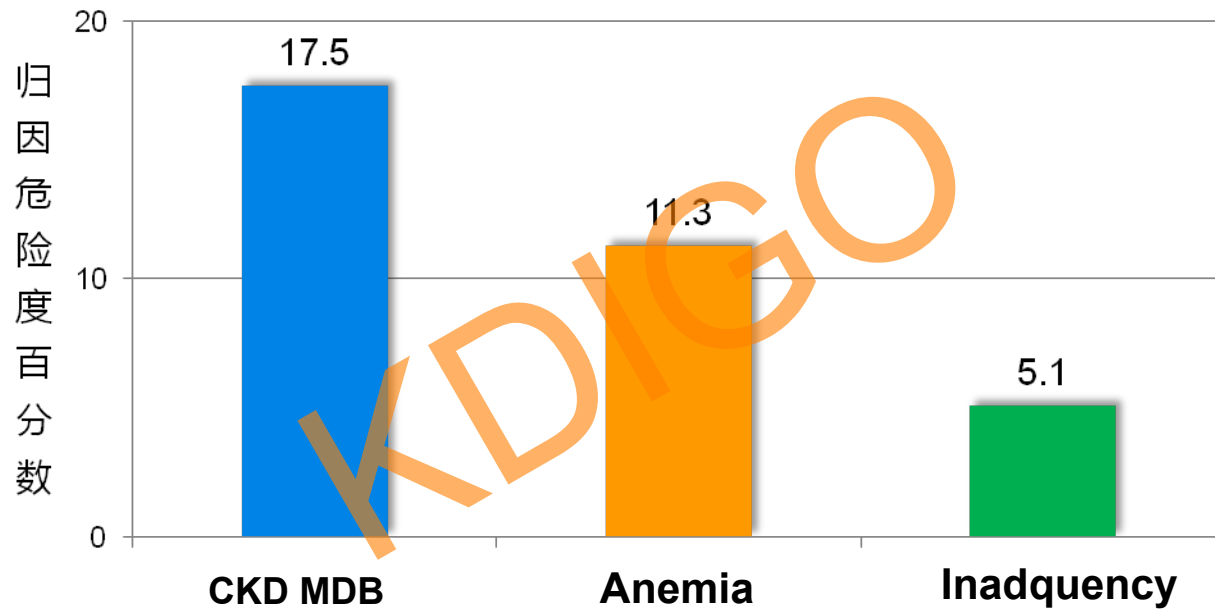
CHRONIC KIDNEY DISEASE— MINERAL AND BONE DISORDER



- P ↑, FGF-23 ↑, PTH ↑
- 1, 25 (OH) 2D3 ↓, Ca ↓



CKD-MBD: Common Cause of Death on dialysis patients



^a serum P \geq 5 mg/dL, serum calcium \geq 10 mg/dL, PTH \geq 600 pg/mL中的一项或多项

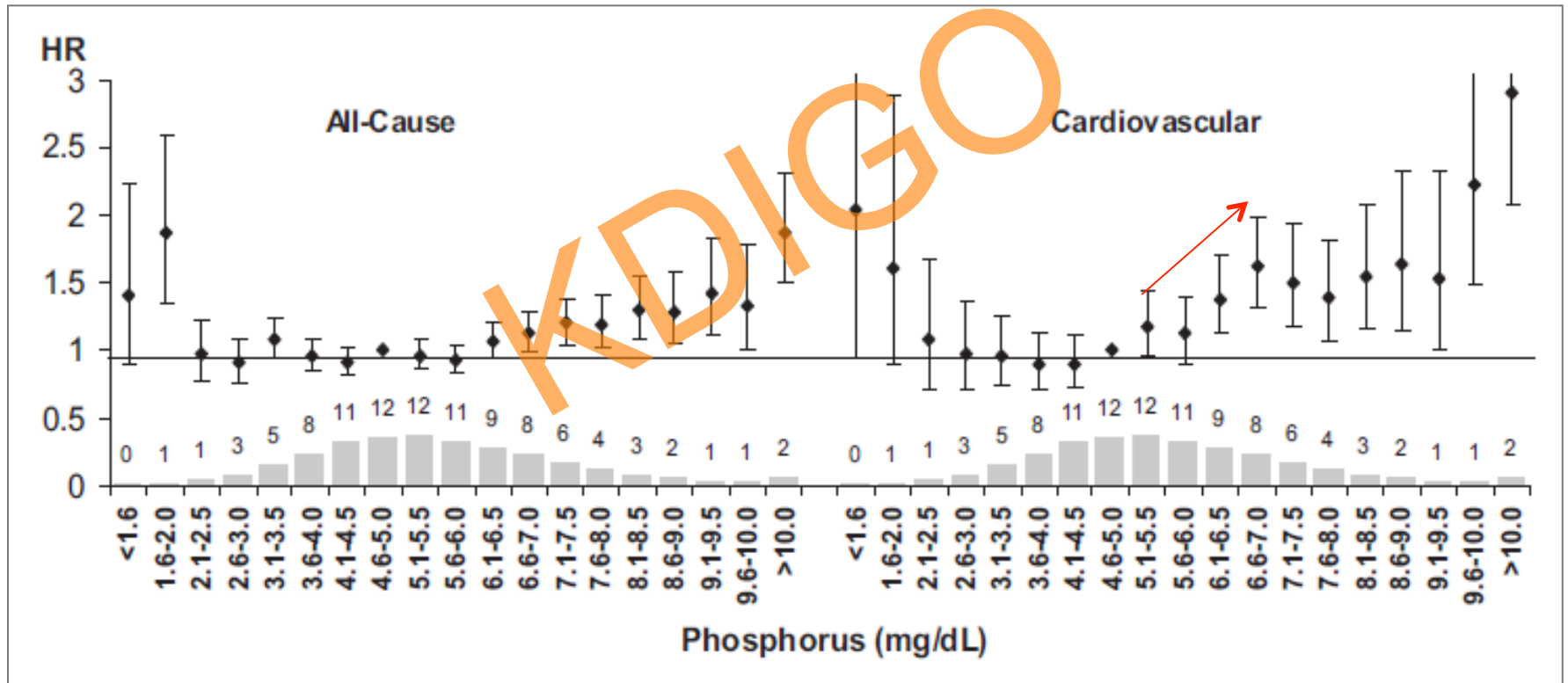
A retrospective study with 40,538 MHD patients and followed up 12-18 M

Conclusion: CKD-MBD caused death: **17.5%**, **3** times higher than inadequacy and **1.5** times than anemia



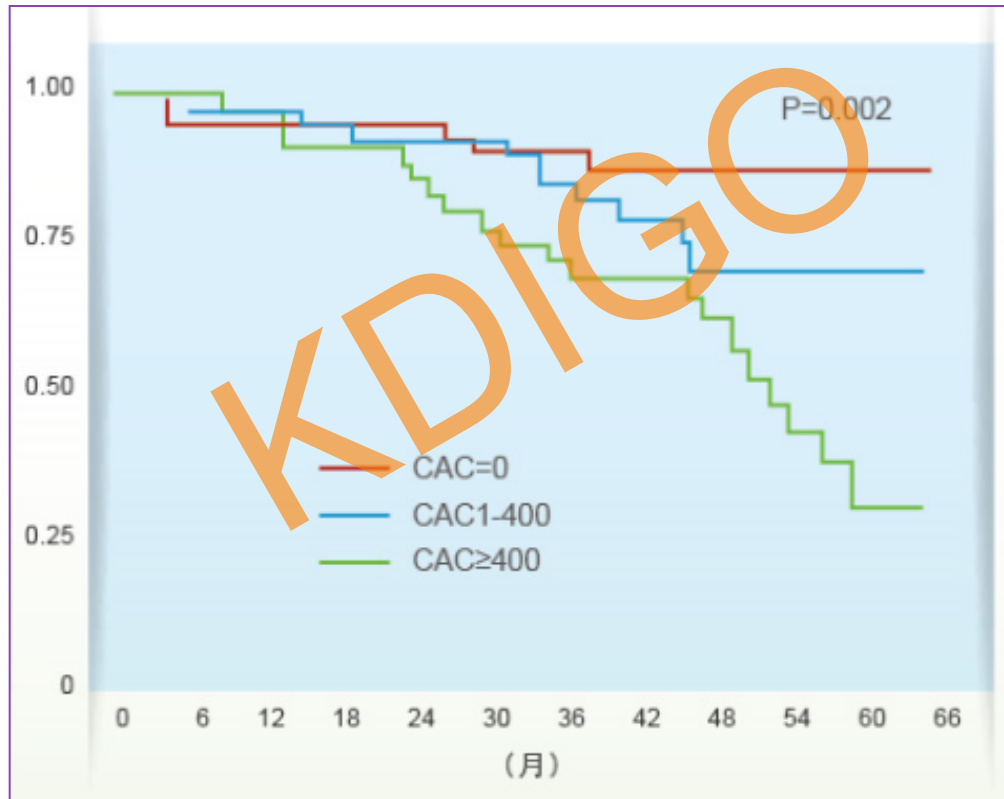
Phosphate Level on All cause and CVD mortality (2008)

925 units, 25,588 ESRD received dialysis more than 180 days





Vascular calcification remarkably increases the mortality of dialysis patients





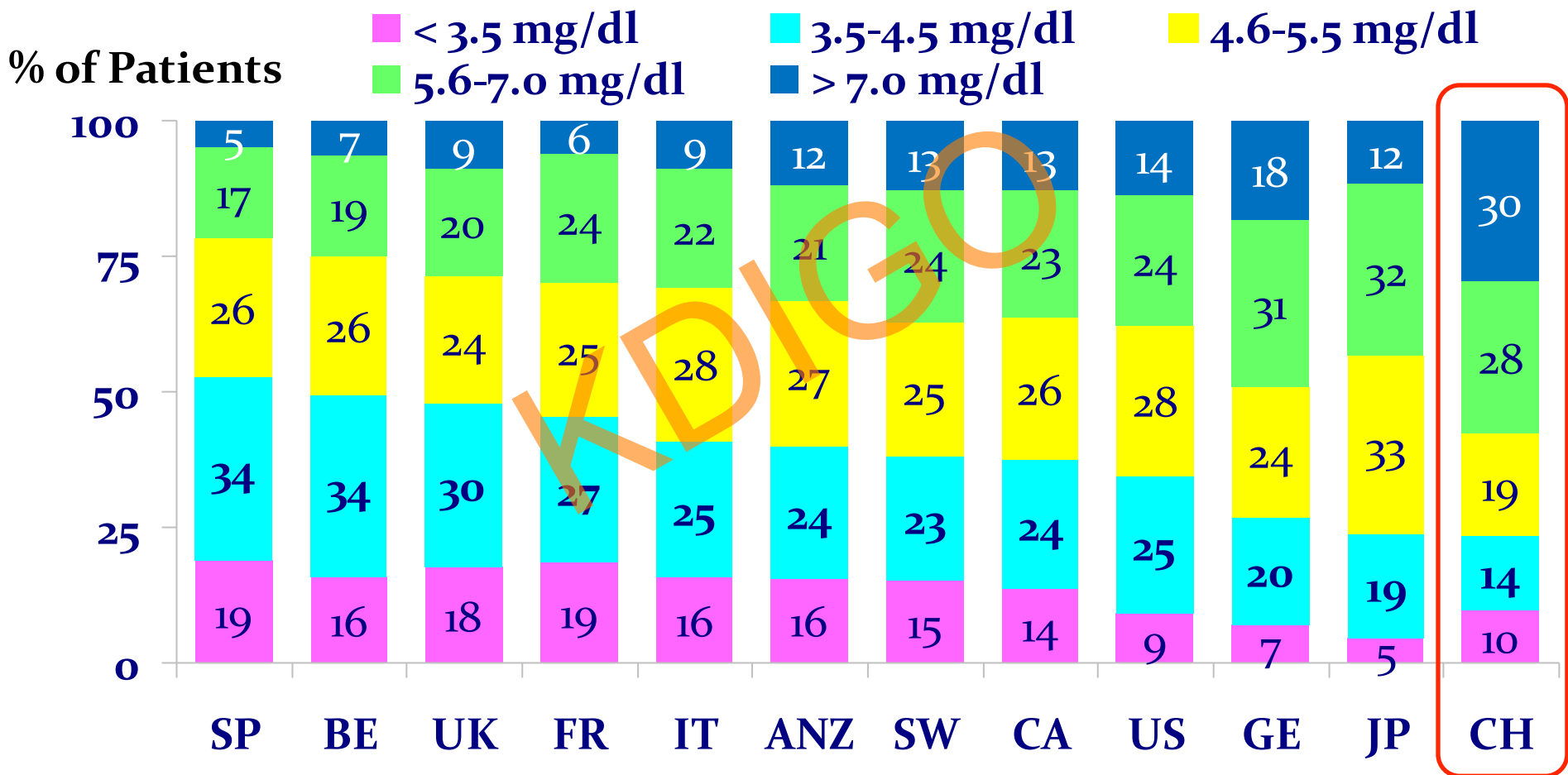
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Outlines

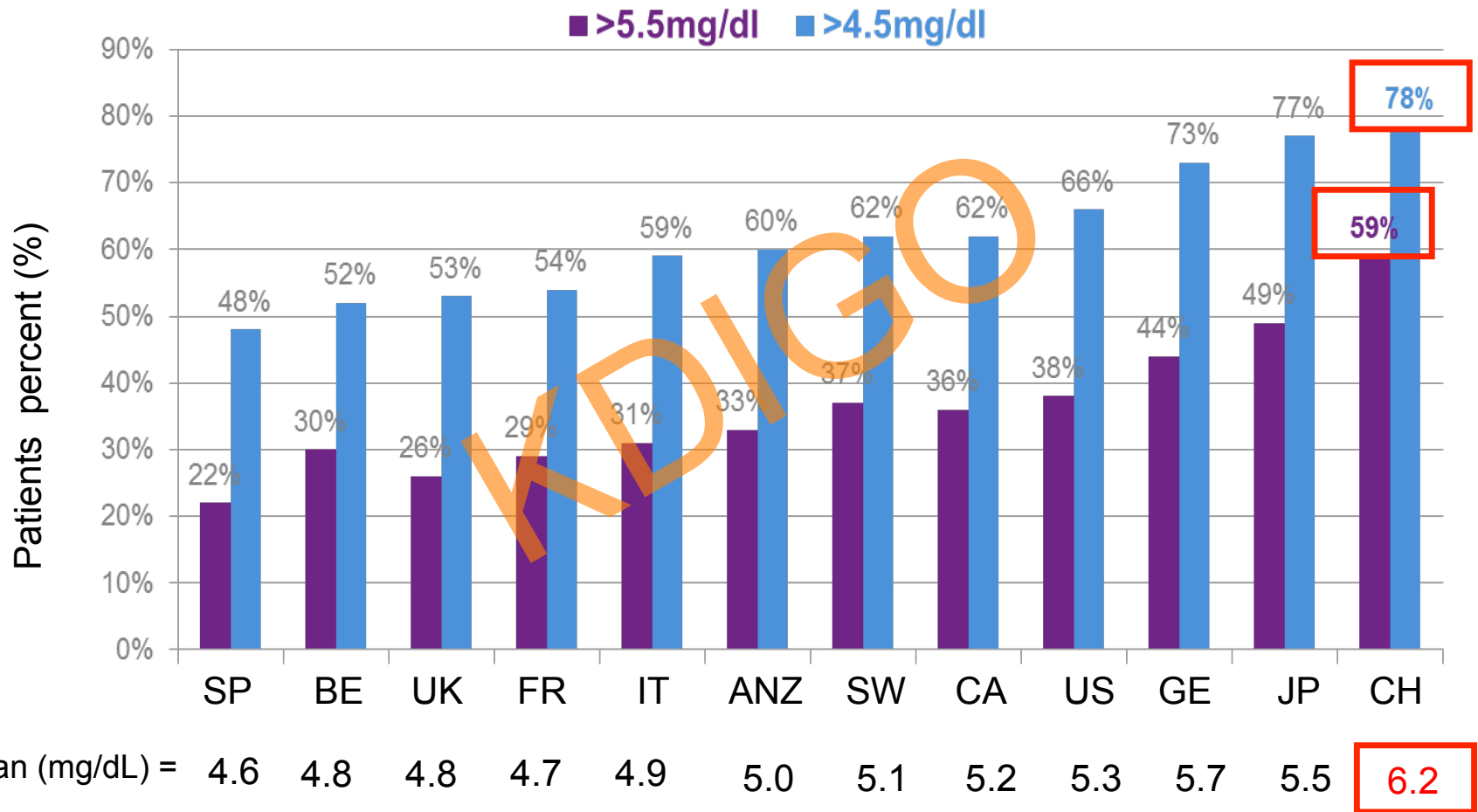
- The prevalence of CKD-MBD in CKD patients
- Risk factors and effects on patients' outcome
- Treatment of CKD-MBD: Current and challenge

Serum Phosphorus by Country – DOPPS 4 (2009-2011)*



* Data are from the initial prevalent cross-section of patients in each country

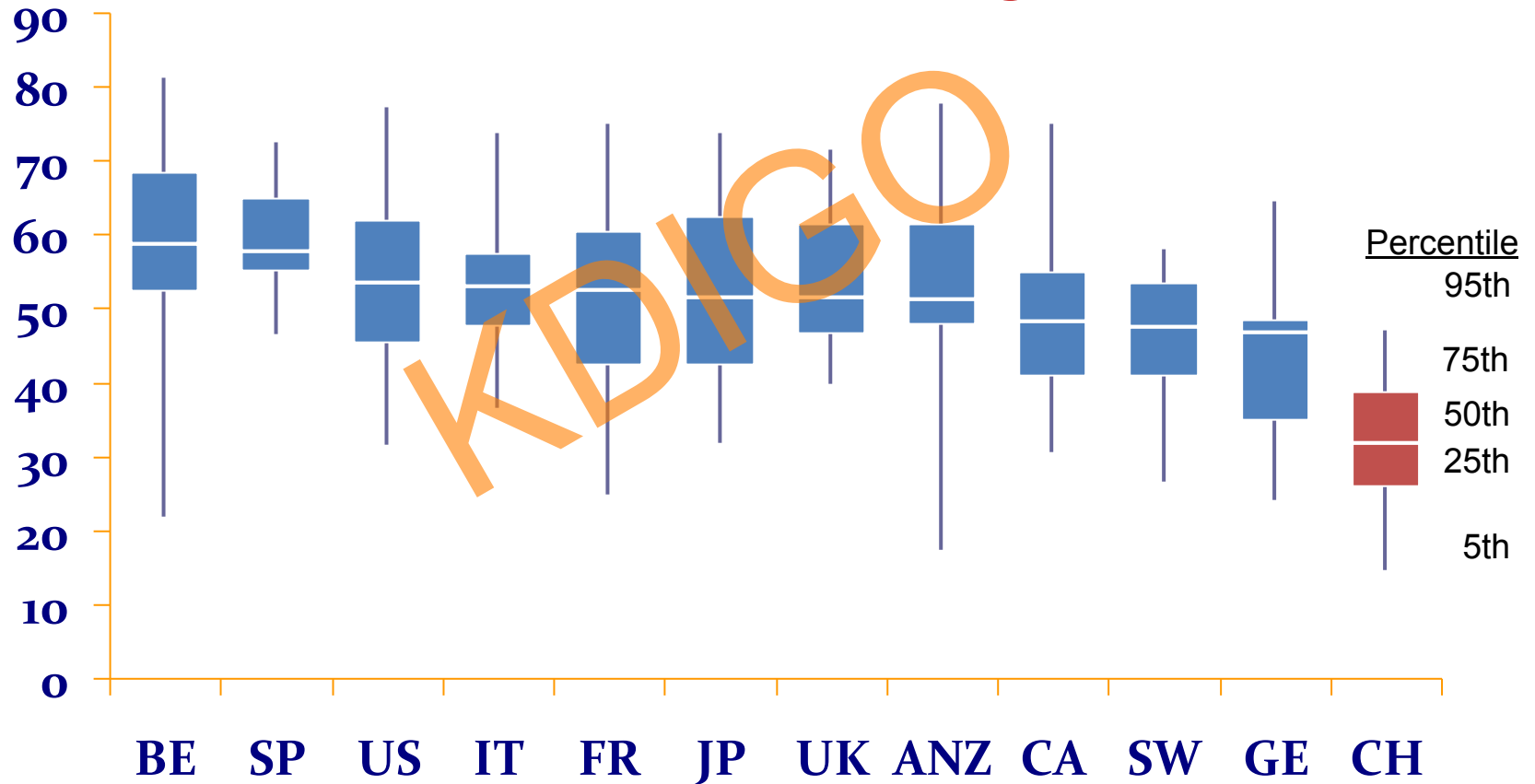
The Prevalence of Hyperphosphatemia of Dialysis Patients in China: 78%



* Data are from the initial prevalent cross-section of patients



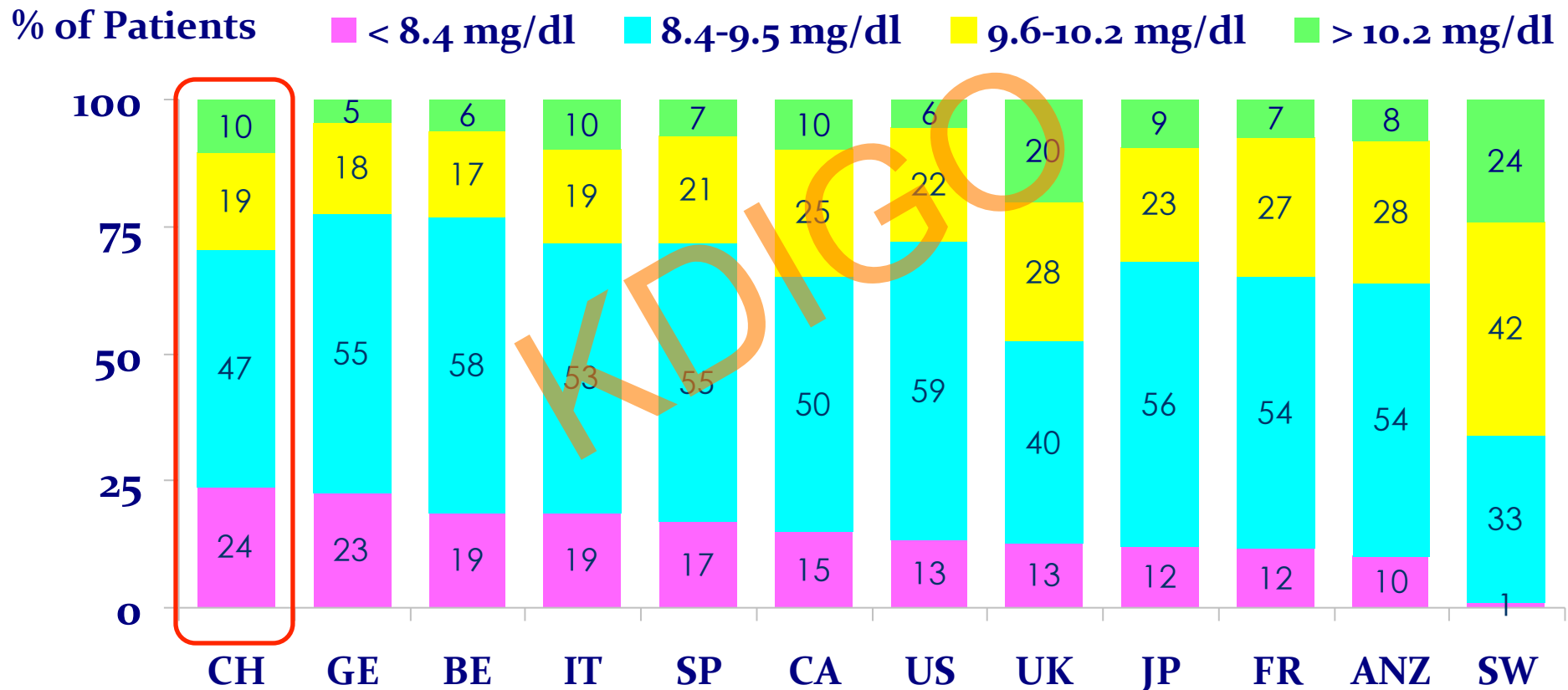
Distribution of facility % of patients with Phosphorus 3.5-5.5 mg/dL*



* KDOQI guidelines; Restricted to initial cross-section of patients in facilities with at least 5 patients with non-missing phosphorus data; DOPPS 4 (2009-2011)

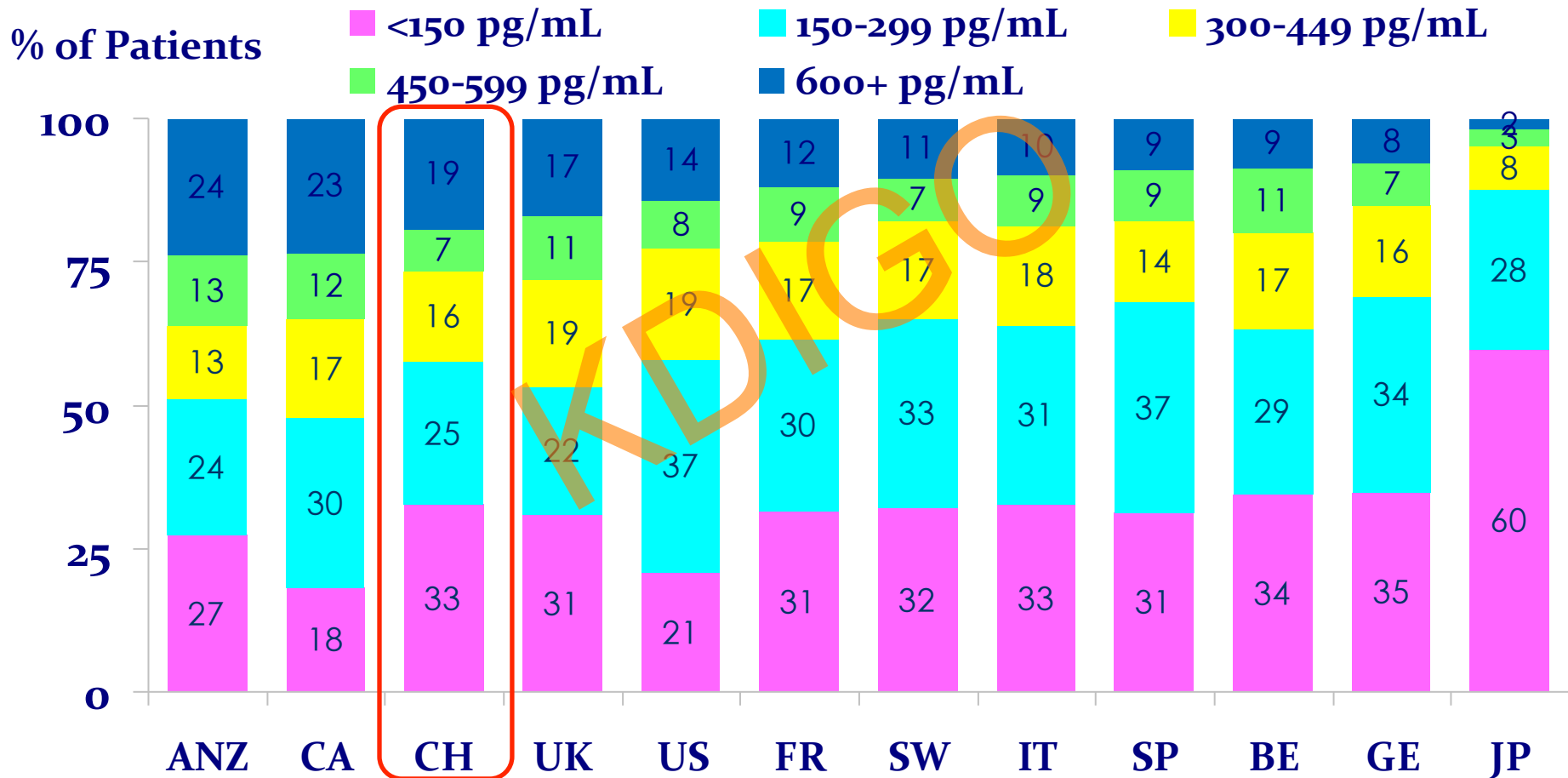


Serum Calcium by Country DOPPS 4 (2009-2011)*



* Data are from the initial prevalent cross-section of patients in each country; Calcium is albumin corrected

Serum PTH by Country DOPPS (2009-2011)*



* Data are from the initial prevalent cross-section of patients in each country

Serum PTH by Country DOPPS (2009-2011)*

High Percentage of Patients with PTH > 600pg/mL



Phosphate Binder Prescription by Country DOPPS (2009-2011)*

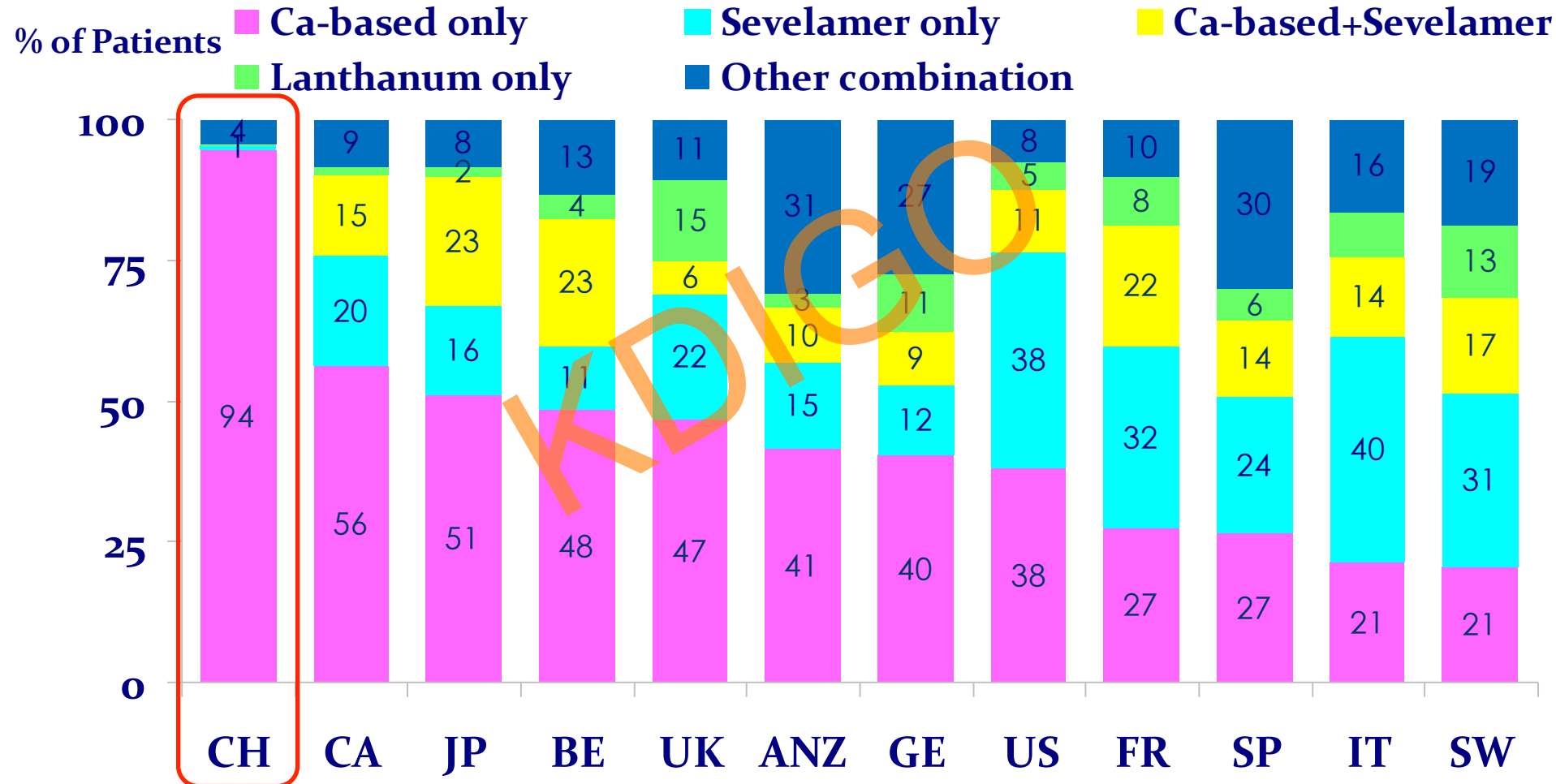
% of Patients



* Data are from the initial prevalent cross-section of patients in each country; Yellow bars extend to calculated prevalence if missing data classified as 'No' prescription (% missing for ESA ranges from 14.6% in China to 0.3% in Germany)

Phosphate Binder Formulations by Country

DOPPS 4 (2010-2011)*



* Data are from the initial prevalent cross-section of patients in each country; 'Other combination' includes all mono- or combination therapies not otherwise listed



Serum Phosphorus of PD Patients in SYSU

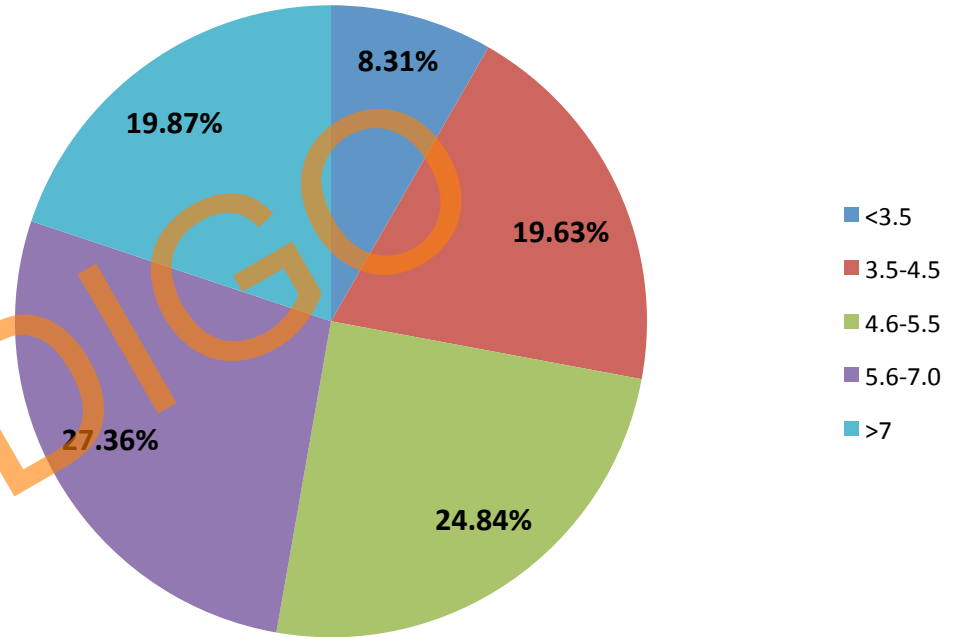
N=2456

P (Mean) = 5.64 ± 1.95 mg/dl

72.07% > 4.5 mg/dl

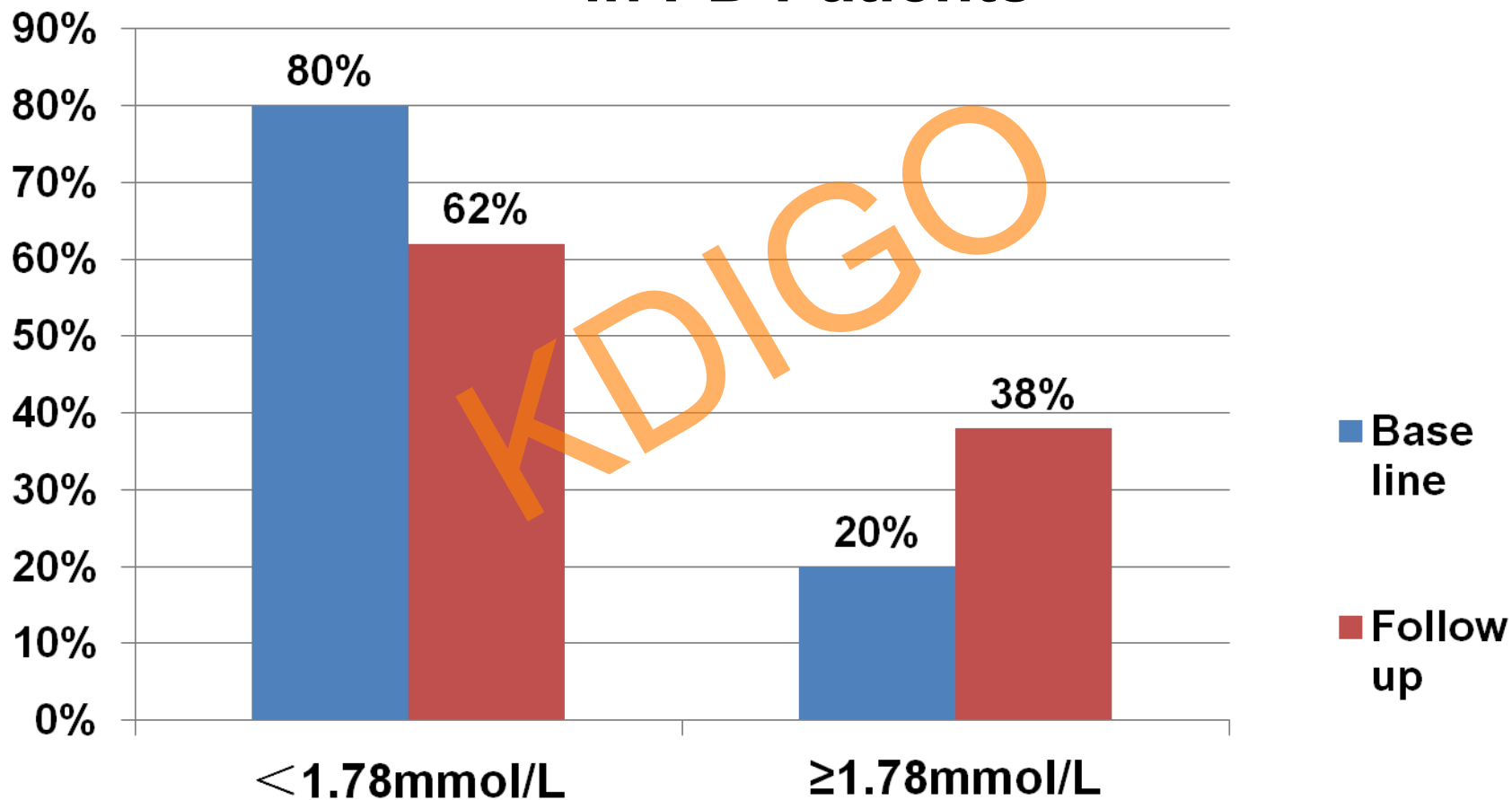
59.16% > 5.0 mg/dl

47.23% > 5.5mg/dL

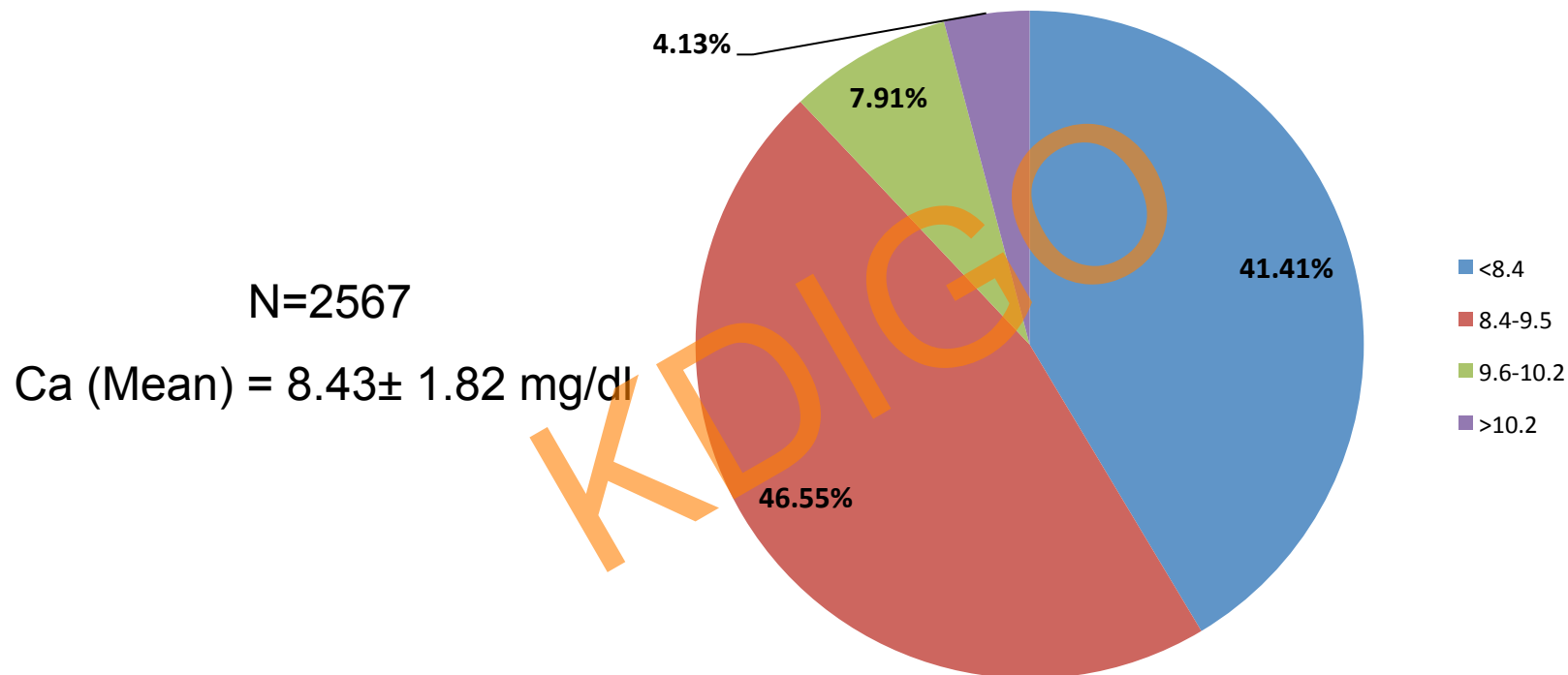


P (mg/dL)	<3.5	3.5-4.5	4.6-5.5	5.6-7.0	>7.0
Patient No.	204	482	610	672	488
(%)	8.31	19.63	24.84	27.36	19.87

Target Achievements of Serum Phosphorus in PD Patients

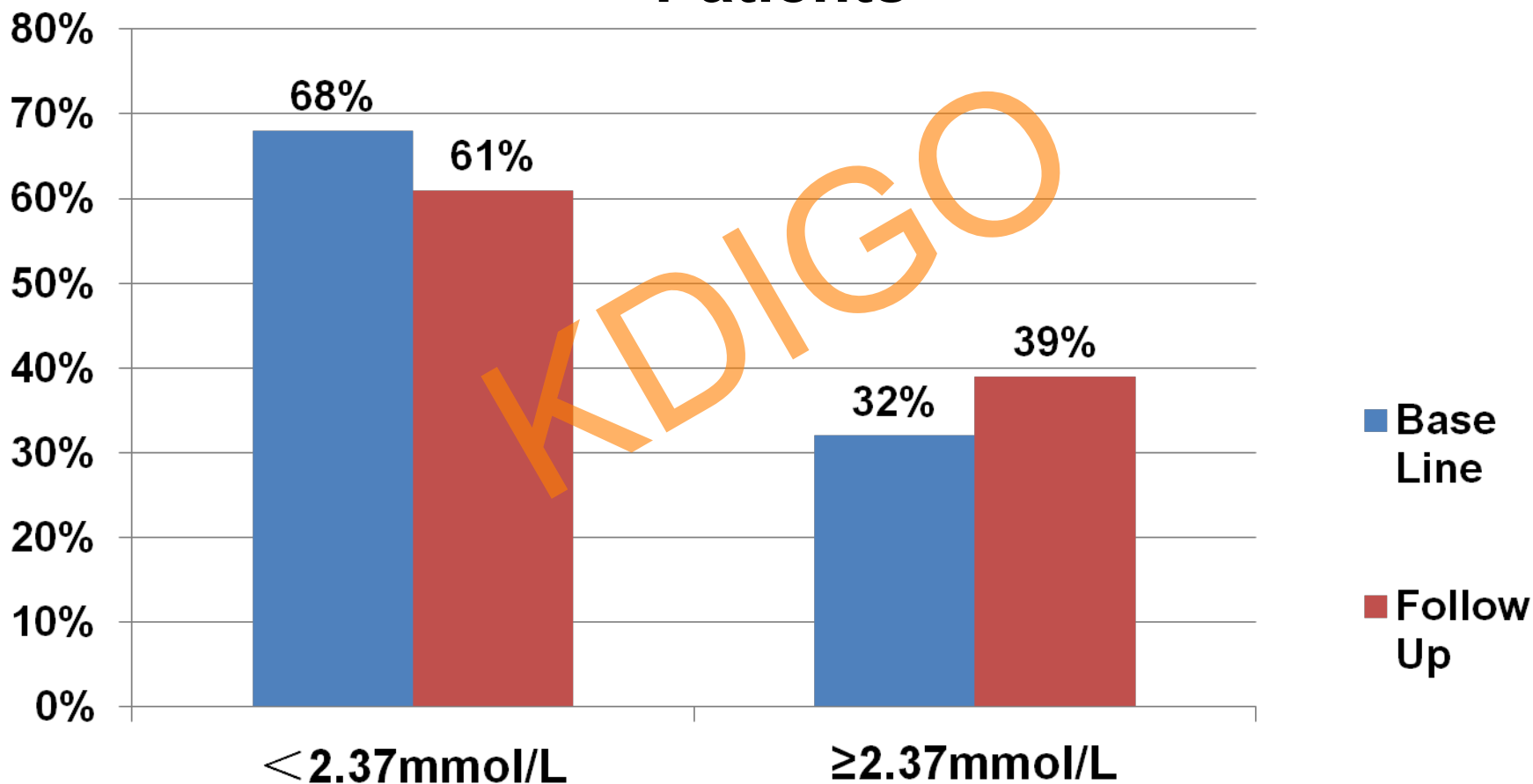


Serum Calcium of PD Patients in SYSU



Ca (mg/dL)	<8.4	8.4-9.5	9.6-10.2	>10.2
Patient No.	1063	1195	203	106
(%)	41.41	46.55	7.91	4.13

Target Achievements of Serum Calcium in PD Patients



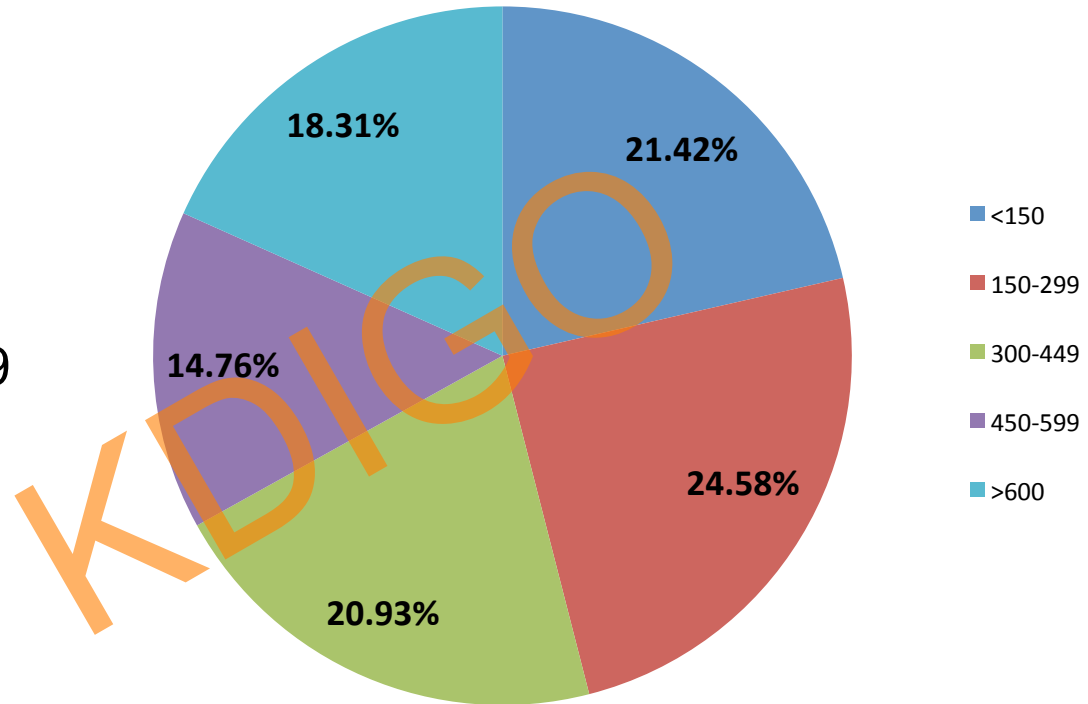


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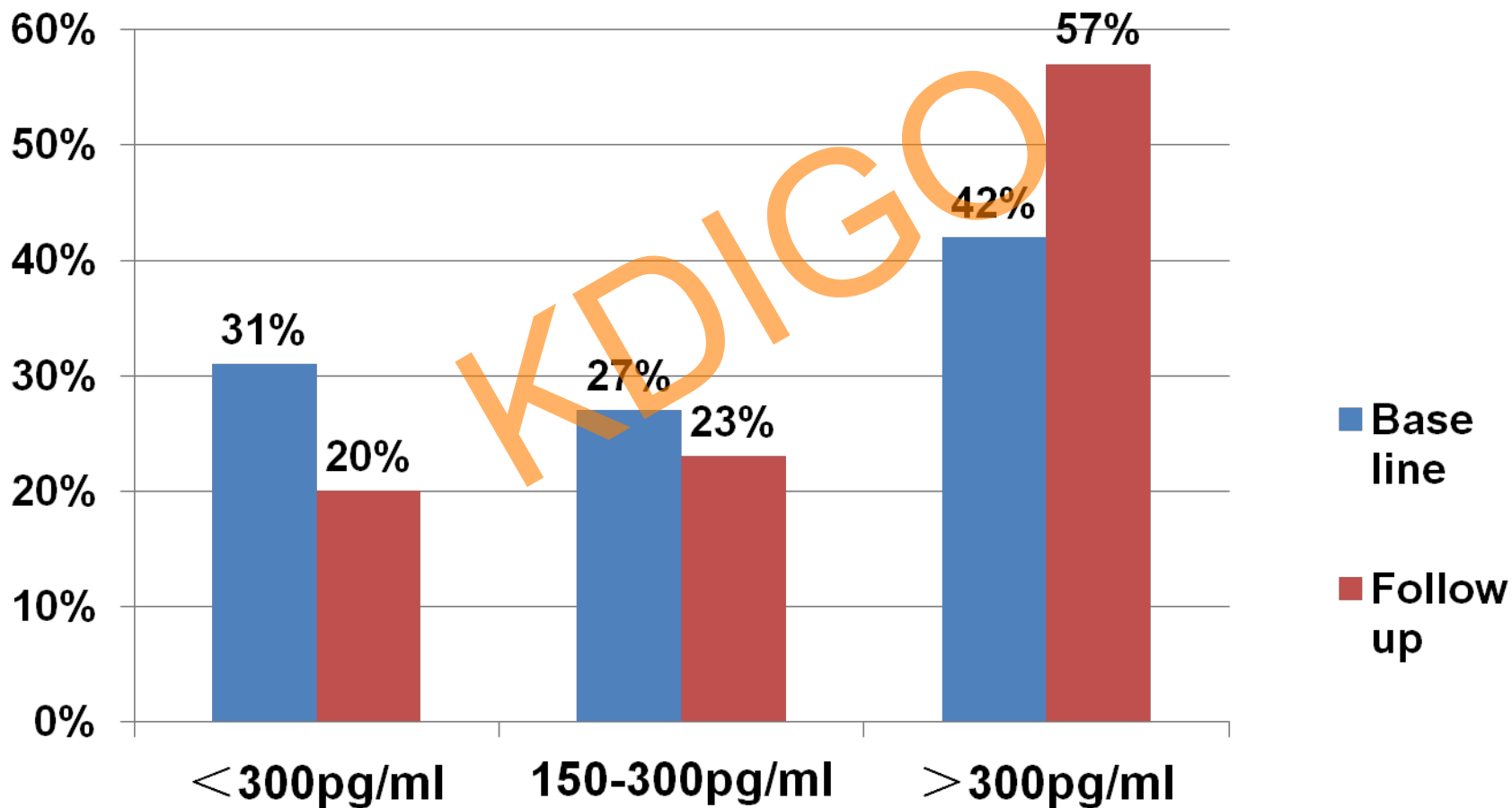
Serum PTH of PD Patients in SYSU

N=2026
Median PTH 329
(172,520)



PTH (pg/ml)	<150	150-299	300-449	450-599	>600
Patient No.	434	498	424	299	371
(%)	21.42	24.58	20.93	14.76	18.31

Target Achievements of iPTH in PD Patients



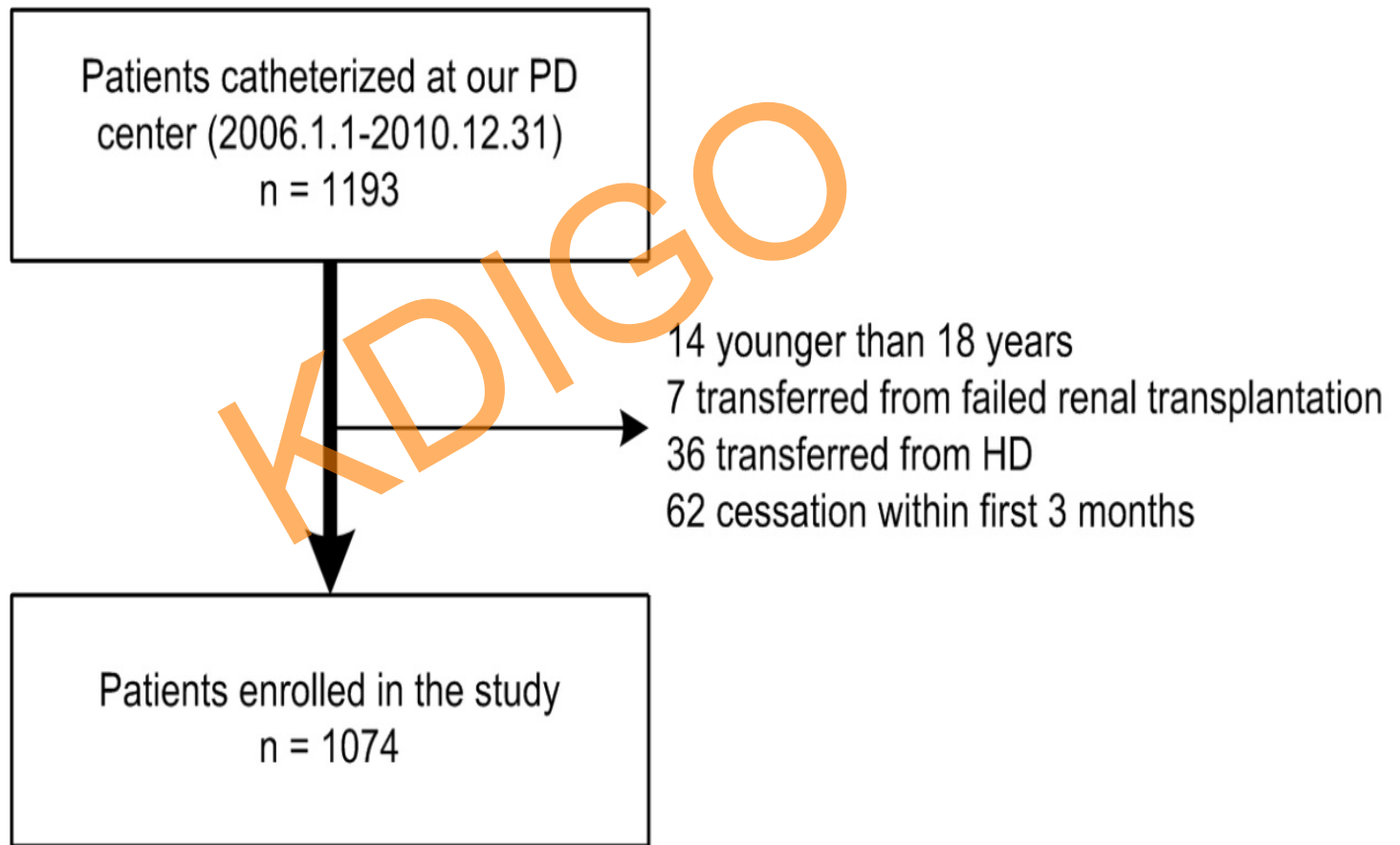
Risk Factors of Mortality in PD Patients

Cross section analysis

Risk factors	Odds ratio	95% CI	P-value
Age (per 1 year older)	1.05	1.03-1.06	< 0.001
Davies score of Comorbidities (per 1 point greater)	1.24	1.01-1.52	0.05
Hemoglobin (per 1g/dL greater)	0.76	0.68-0.85	< 0.001
Serum albumin (per 1g/dL greater)	0.48	0.30-0.74	0.001
Serum creatinine (per 1mg/dL greater)	0.88	0.82-0.95	0.001
Serum phosphorus (per 1mg/dL increasing)	1.27	1.06-1.51	0.01
Serum uric acid (per 1mg/dL greater)	1.16	1.06-1.27	0.001
Use of ACEI/ARB (yes/no)	0.66	0.47-0.94	0.021

Data from Sun Yat-sen University PD registration database

Effects of Ca, P, and Ca×P on outcomes of PD patients





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Baseline Characteristics of Serum Calcium, Phosphorus, Ca*P and iPTH of PD Patients

	Mean \pm SD	Median (interquartile range)
Ca(mg/dl)	8.73 \pm 1.01	8.74 (8.18-9.30)
P(mg/dl)	5.18 \pm 1.75	4.86 (4.03-6.04)
Ca*P	44.7 \pm 14.6	42.8(35.4-51.2)
iPTH(pg/ml)	351 \pm 301	284 (140-471)

Note: Calcium concentration means corrected serum calcium concentration

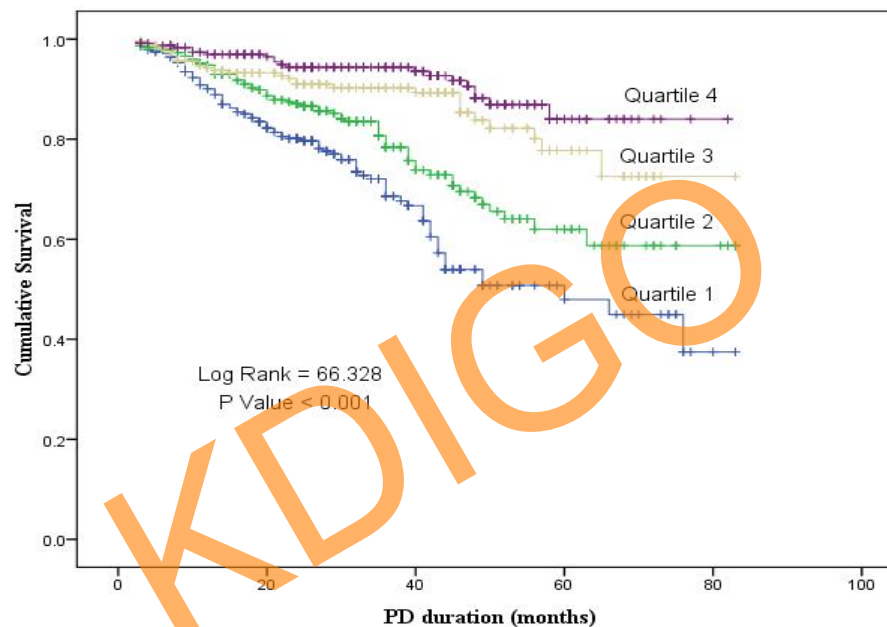
Correlation of Ca, P, Ca×P and iPTH at baseline in PD Patients

	Ca	P	Ca*P	iPTH	Residual Urinal Volume	Albumin	Active VD3	Calcium Agents	Phosphate binder
P	-0.305 ^a								
Ca×P	0.018	0.930 ^a							
iPTH	-0.414 ^a	0.288 ^a	0.157 ^a						
Residual Urinal Volume	-0.068 ^b	0.010	-0.012	0.096 ^a					
Albumin	0.395 ^a	-0.055	0.072 ^b	0.006	0.113 ^a				
Active VD3	0.027	-0.098 ^a	-0.103	0.213 ^a	0.081 ^a	0.135 ^a			
Calcium Agents	-0.032	0.021	0.010	0.119 ^a	0.044	0.039	0.319 ^a		
Phosphate binder	-0.013	0.037	0.031	0.113 ^a	0.040	0.060 ^b	0.316 ^a	0.950 ^a	
Low calcium dialysate	0.143 ^a	-0.067 ^b	-0.016	0.002	-0.017	0.142 ^a	0.244 ^a	0.151 ^a	0.196 ^a

^a Correlation is significant at the 0.01 level (2-tailed).

^b Correlation is significant at the 0.05 level (2-tailed).

The correlation between serum calcium level and all-cause mortality in PD patients



Number at risk

Q1	286	203	66	18	2	0
Q2	300	226	81	27	6	0
Q3	240	169	94	21	1	0
Q4	240	189	116	19	2	0

The correlation between serum calcium and all-cause mortality in PD patients

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Continuous Ca ^d	0.561 (0.494-0.638)	<0.001	0.748 (0.629-0.890)	0.001	0.793 (0.666-0.945)	0.01
Ca Quartile 1	1.0		1.0		1.0	
Ca Quartile 2	0.618 (0.448-0.852)	0.003	0.896 (0.611-1.314)	0.573	0.992 (0.674-1.461)	0.968
Ca Quartile 3	0.325 (0.213-0.495)	<0.001	0.781 (0.477-1.277)	0.324	0.889 (0.542-1.459)	0.642
Ca Quartile 4	0.197 (0.121-0.321)	<0.001	0.477 (0.271-0.840)	0.01	0.570 (0.323-1.008)	0.053

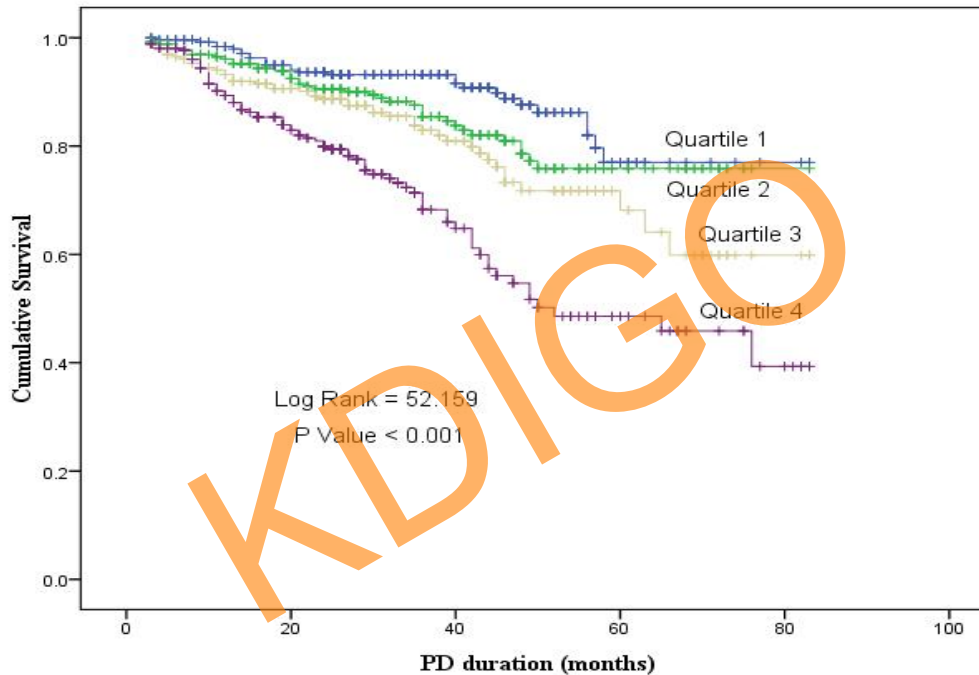
^aModel 1 : unadjusted

^bModel 2 : adjusted with gender , age , residual urine , comorbidity , Hb , P , iPTH

^cModel 3 : Model 2+ Rocaltrol , calcium and low calcium PD solution

^d per increased 1 mg/dl

The correlation between serum phosphorus and all-cause mortality in PD patients



Number at risk

Q1	262	212	119	20	2	0
Q2	266	200	102	24	1	0
Q3	259	193	77	20	3	0
Q4	259	172	56	20	4	0

The Correlation of Serum Phosphorus level and all-cause mortality in PD patients

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Continuous P ^d	1.264 (1.185-1.348)	<0.001	1.223 (1.127-1.326)	<0.001	1.253 (1.155-1.359)	<0.001
P Quartile 1	1.0		1.0		1.0	
P Quartile 2	1.547 (0.947-2.527)	0.082	1.755 (1.029-2.993)	0.039	1.835 (1.073-3.139)	0.027
P Quartile 3	2.096 (1.304-3.366)	0.002	1.934 (1.144-3.269)	0.014	1.964 (1.160-3.324)	0.012
P Quartile 4	3.935 (2.535-6.108)	<0.001	3.432 (2.073-5.681)	<0.001	3.944 (2.383-6.525)	<0.001

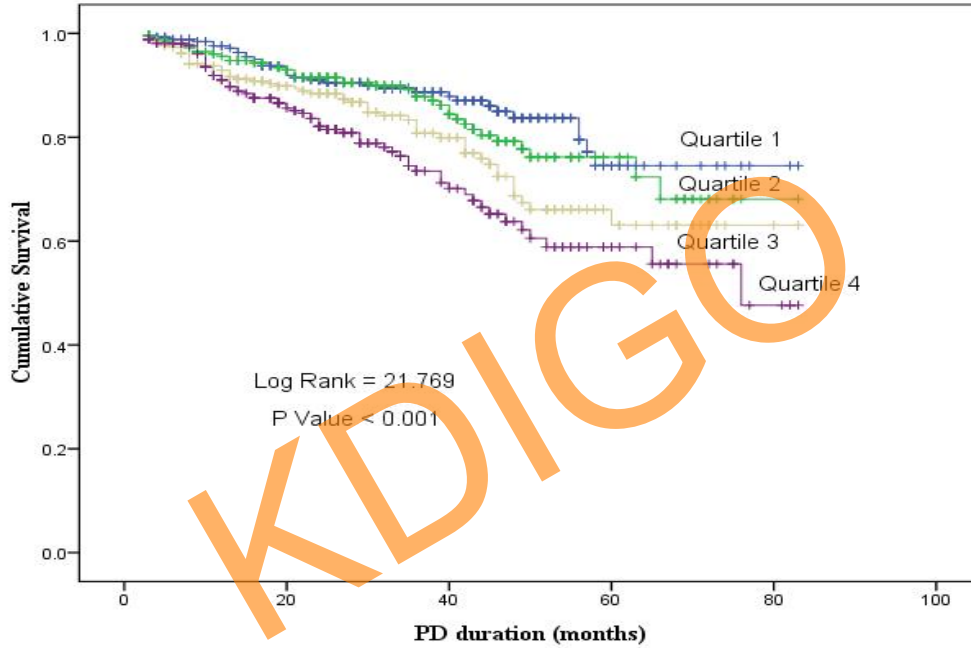
^aModel 1 : unadjusted.

^bModel 2 : adjusted gender , age , residual urine volume, complications score , Hb, Albumin, Serum calcium, iPTH

^cModel 3 : Phosphate binder concerned besides Model 2

^dper increases 1 mg/dl

The Correlation of Ca×P level and all-cause mortality in PD patients



Number at risk

Q1	262	208	107	19	2	0
Q2	263	202	98	23	1	0
Q3	263	190	86	22	3	0
Q4	261	177	63	21	5	0

The correlation between all-cause mortality and Ca×P value in PD patients (Cox proportional hazards models)

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Continuous Ca*P ^d	1.164 (1.085-1.249)	<0.001	1.209 (1.114-1.313)	<0.001	1.186 (1.096-1.284)	<0.001
Ca*P Quartile 1	1.0		1.0		1.0	
Ca*P Quartile 2	1.199 (0.757-1.900)	0.439	1.190 (0.715-1.981)	0.504	1.008 (0.600-1.694)	0.977
Ca*P Quartile 3	1.723 (1.120-2.651)	0.013	1.992 (1.237-3.206)	0.005	2.147 (1.324-3.481)	0.002
Ca*P Quartile 4	2.365 (1.560-3.585)	<0.001	2.631 (1.650-4.196)	<0.001	2.608 (1.621-4.196)	<0.001

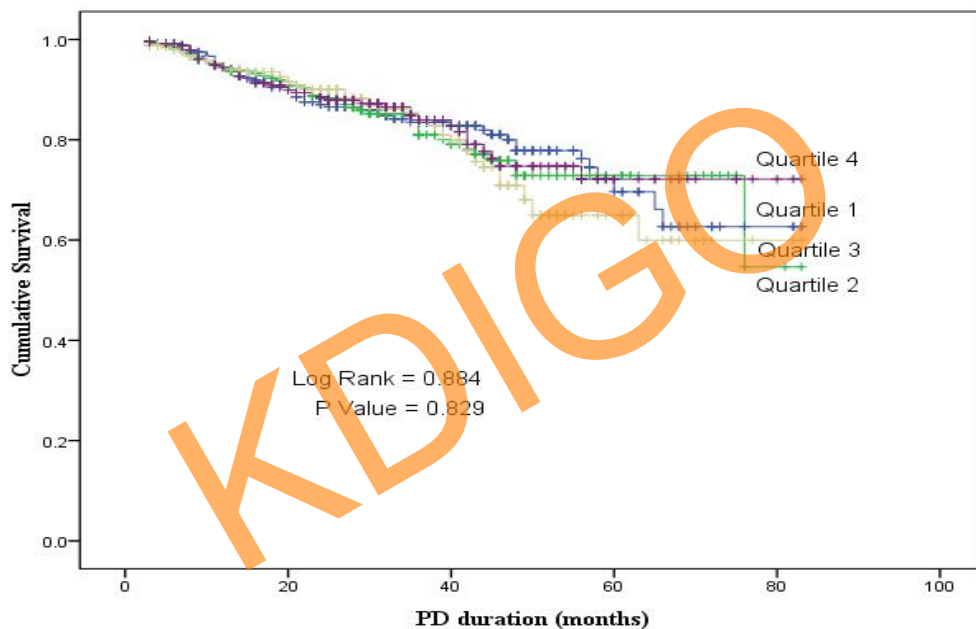
^aModel 1 : unadjusted

^bModel 2 : adjusted gender , age , residual urine volume , complications score , Hb , iPTH

^cModel 3 : Rocaltrol ,calcium agents, phosphate binders and low calcium dialysate are adjusted besides on Model 2

^dper increases10 (mg/dl)²

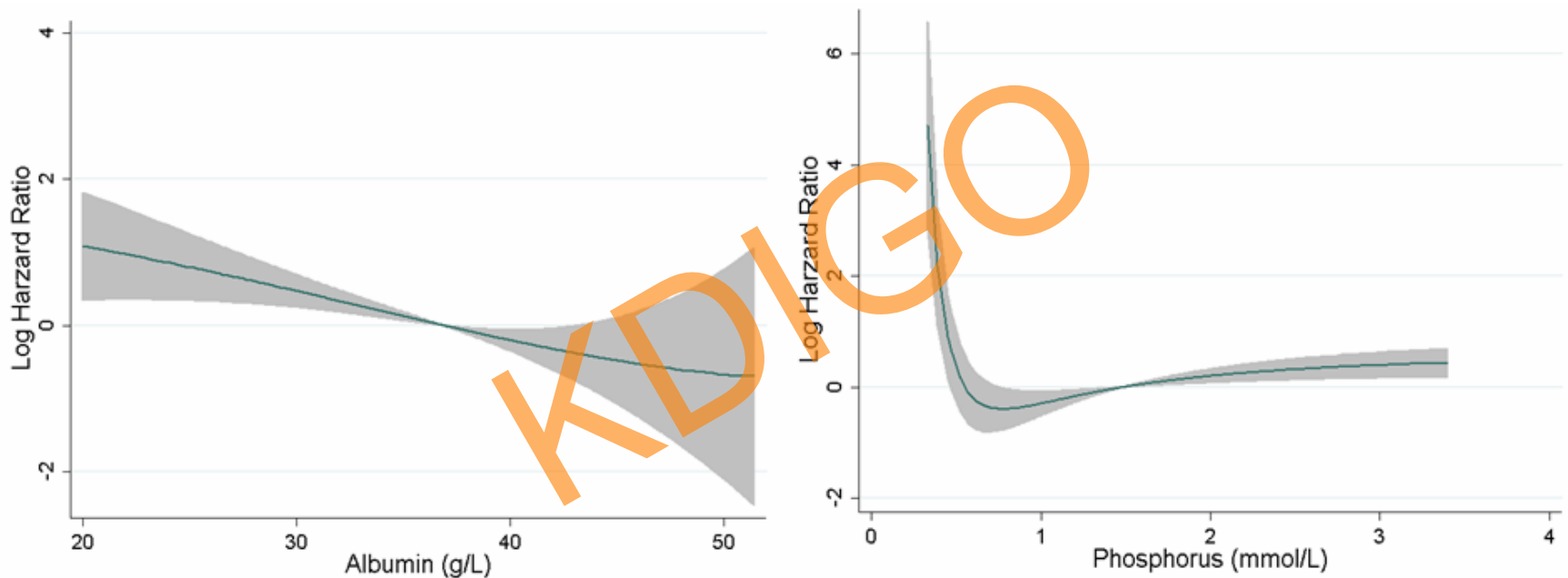
The correlation of iPTH and all-cause mortality in PD patients



Number at risk

Q1	250	189	114	27	4	0
Q2	251	184	84	24	2	0
Q3	251	186	82	17	2	0
Q4	247	187	71	17	3	0

Interaction Between Phosphate and Serum Albumin

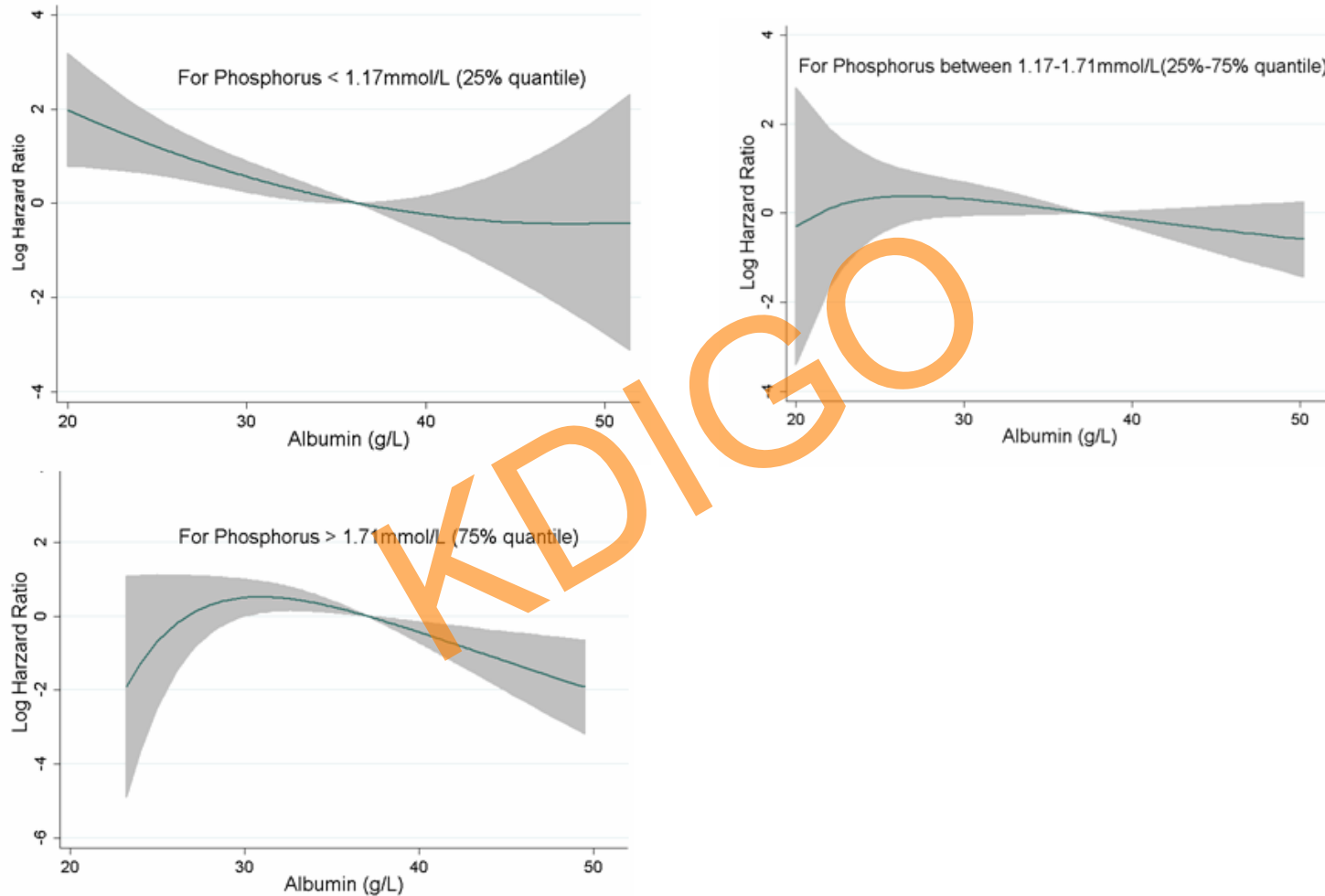


HR was adjusted by age, gender, diabetes, CVD, calcium, iPTH, hsCRP, RRF and hyperphosphoremia treatment drug.

Data from Sun Yat-sen University PD registration database



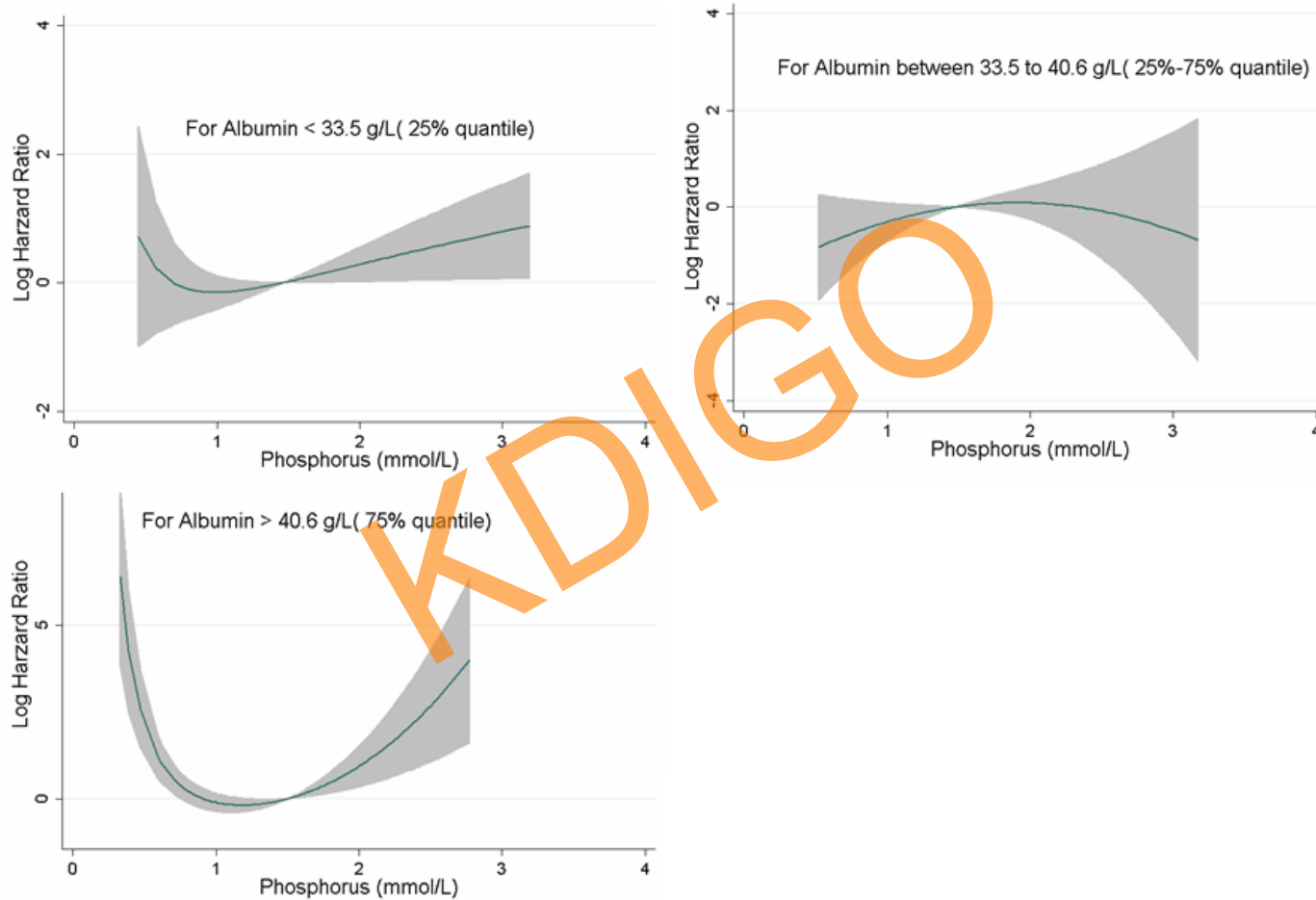
HR of albumin with fixed phosphorus



HR was adjusted by age, gender, diabetes, CVD, calcium, iPTH, hsCRP, RRF and lowering hyperphosphoremia agents.



HR of phosphorus with fixed albumin



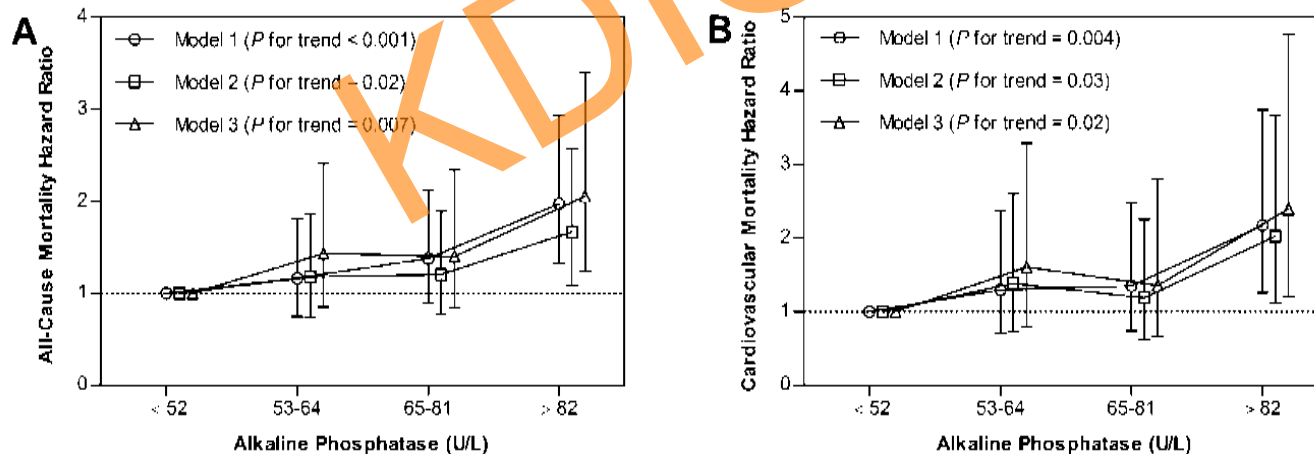
HR was adjusted by age, gender, diabetes, CVD, calcium, iPTH, hsCRP, RRF and hyperphosphoremia treatment drug.

Alkaline Phosphatase and Mortality in Patients on Peritoneal Dialysis

Xinhui Liu, Qunying Guo, Xiaoran Feng, Juan Wang, Juan Wu, Haiping Mao, Fengxian Huang, Xueqing Yu, and Xiao Yang

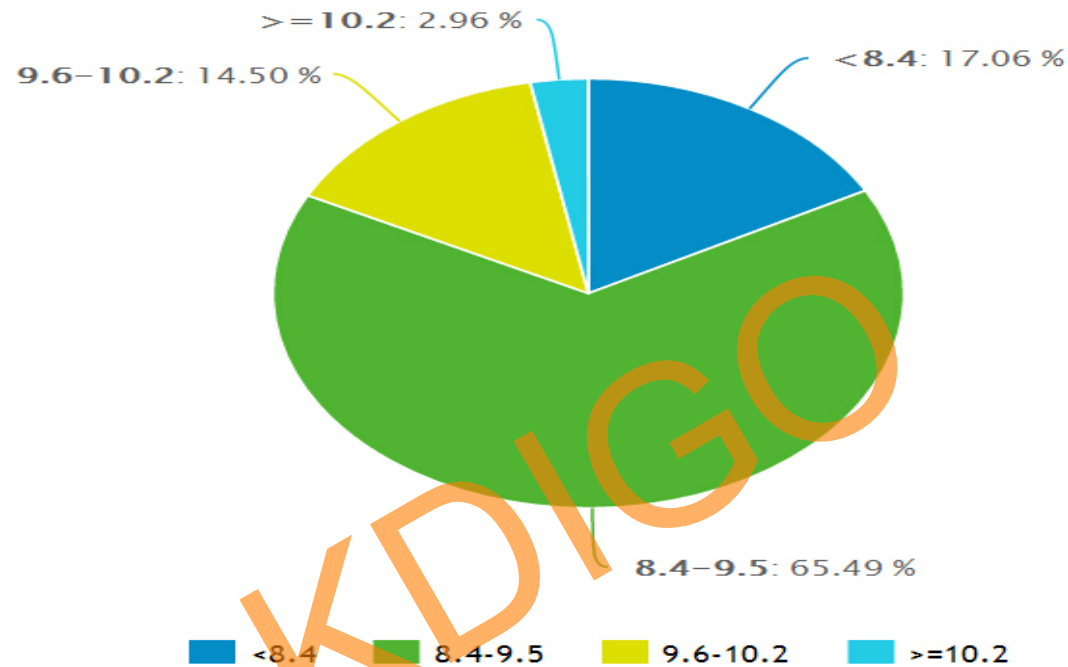
Higher level of Alkaline phosphatase is independently related to the CVD mortality in PD patients

- A total of 1021 incident PD patients were enrolled.
- mean age was 47.5 (\pm 5.5) yrs and 22.8% were diabetic.
- median follow-up period was 31 months (IQR19 – 45 months)



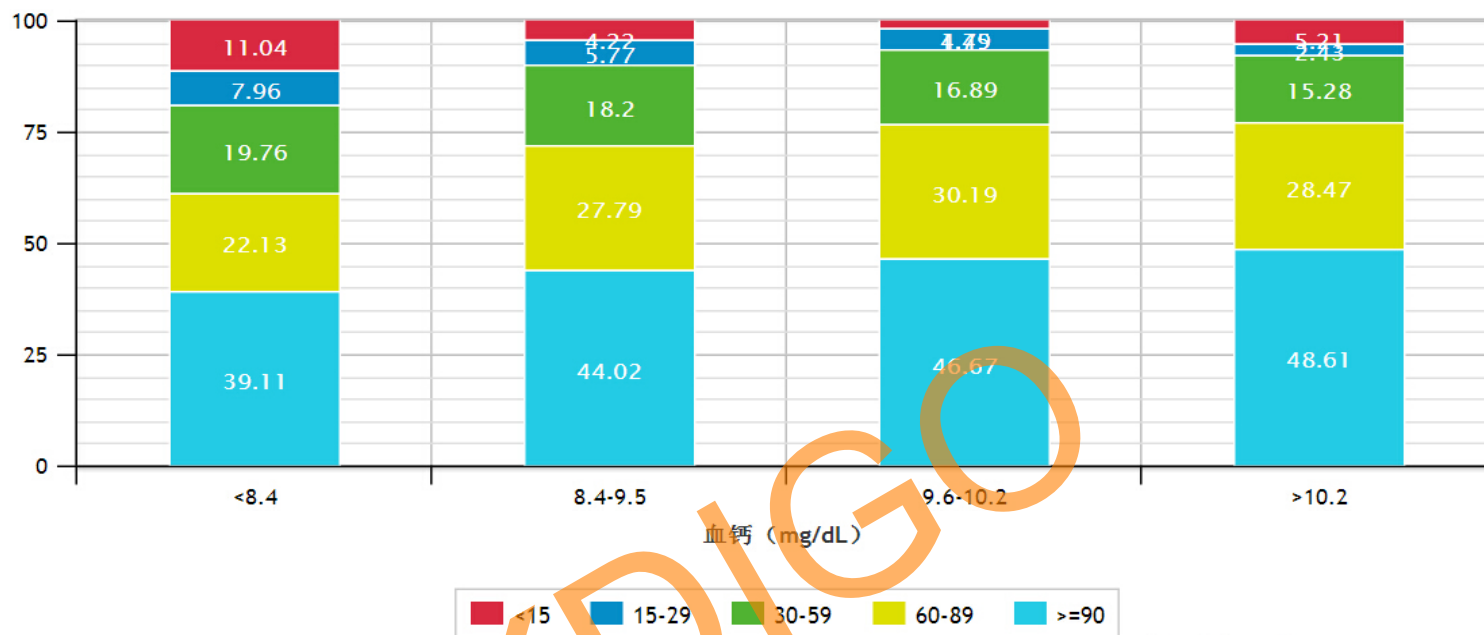
Model 1: Unadjusted. Model 2: Adjusted for age, gender, 24h urine output, blood pressure, comorbidity score, hemoglobin, albumin, serum ALT, AST, neutrophil to lymphocyte ratio and phosphate binders use. Model 3: Model 2 + adjusted for corrected calcium, phosphorus and iPTH

Serum Calcium Distribution of IgAN Patients



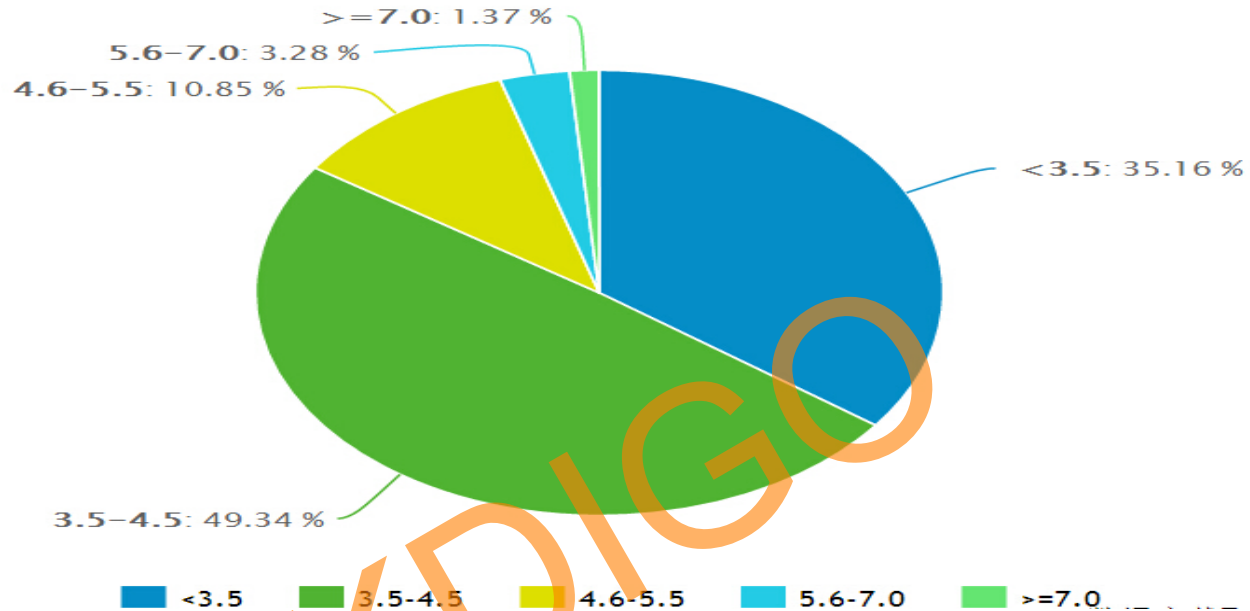
Calcium (mg/dl)	Cases	Proportion (%)
<8.4	2061	17.06
8.4-9.5	7910	65.49
9.6-10.2	1751	14.50
>10.2	357	2.96
Total	12079	100

Serum Ca Distribution of different CKD Stages



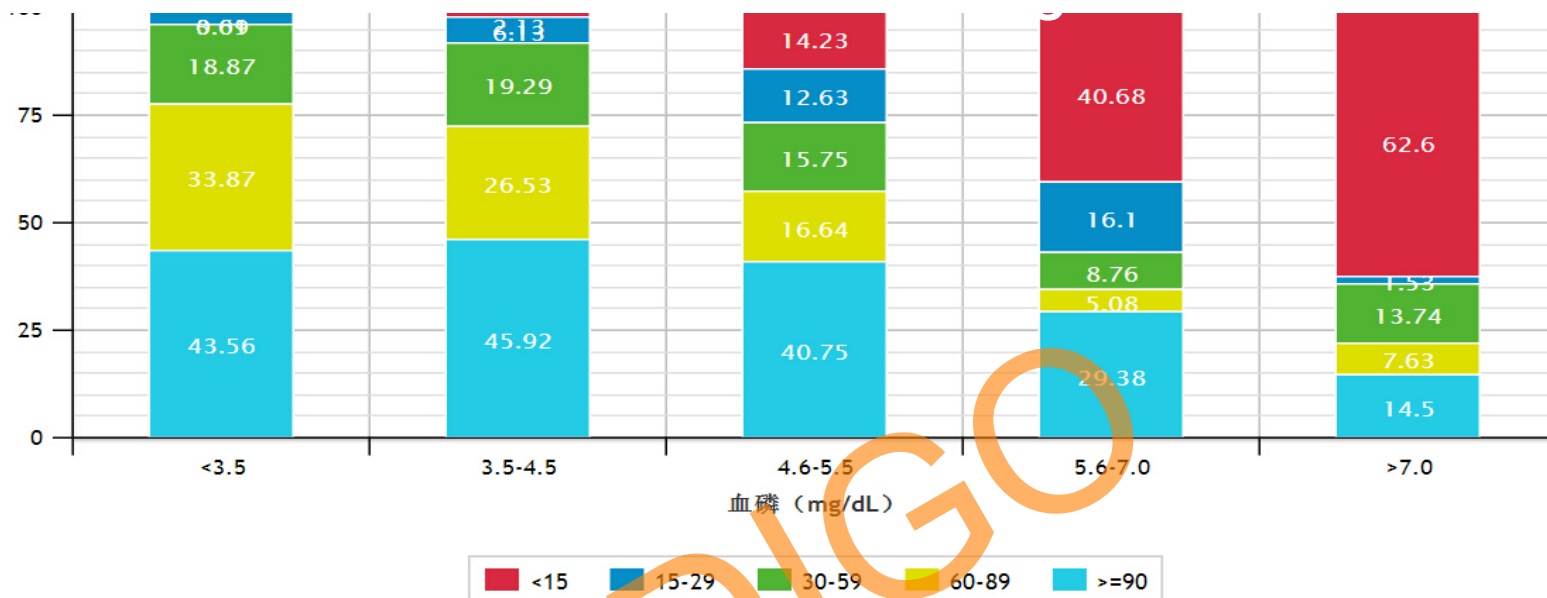
Calcium (mg/dl)	< 15 (n, %)	15-29 (n, %)	30-59 (n, %)	60-89 (n, %)	≥90 (n, %)
<8.4	219 (37.4)	158 (23.2)	392 (18.6)	439 (13.9)	776 (15.3)
8.4-9.5	321 (54.8)	439 (64.5)	1384 (65.5)	2114 (67.0)	3348 (66.0)
9.6-10.2	31 (1.8)	77 (11.3)	292 (13.8)	522 (16.5)	807 (15.9)
>10.2	15 (5.3)	7 (1.02)	44 (2.1)	82 (2.6)	140 (2.8)
Total	586 (100%)	681(100%)	2112(100%)	3157(100%)	5071(100%)

Serum P Distribution of IgAN Patients



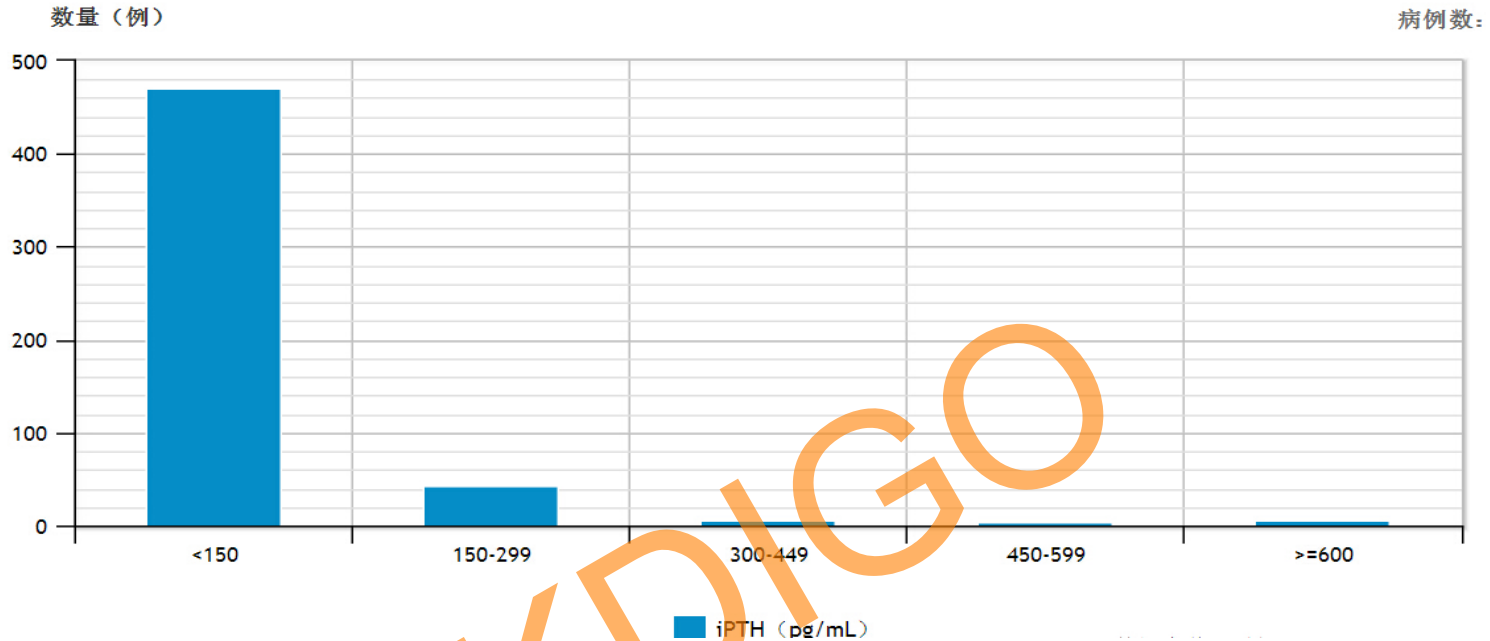
P (mg/dl)	Patients	Proportion (%)
<3.5	3802	35.16
3.5-4.5	5335	49.34
4.6-5.5	1173	10.85
5.6-7.0	355	3.28
>7.0	148	1.37
Total	10813	100

Serum P Distribution in Different CKD stages



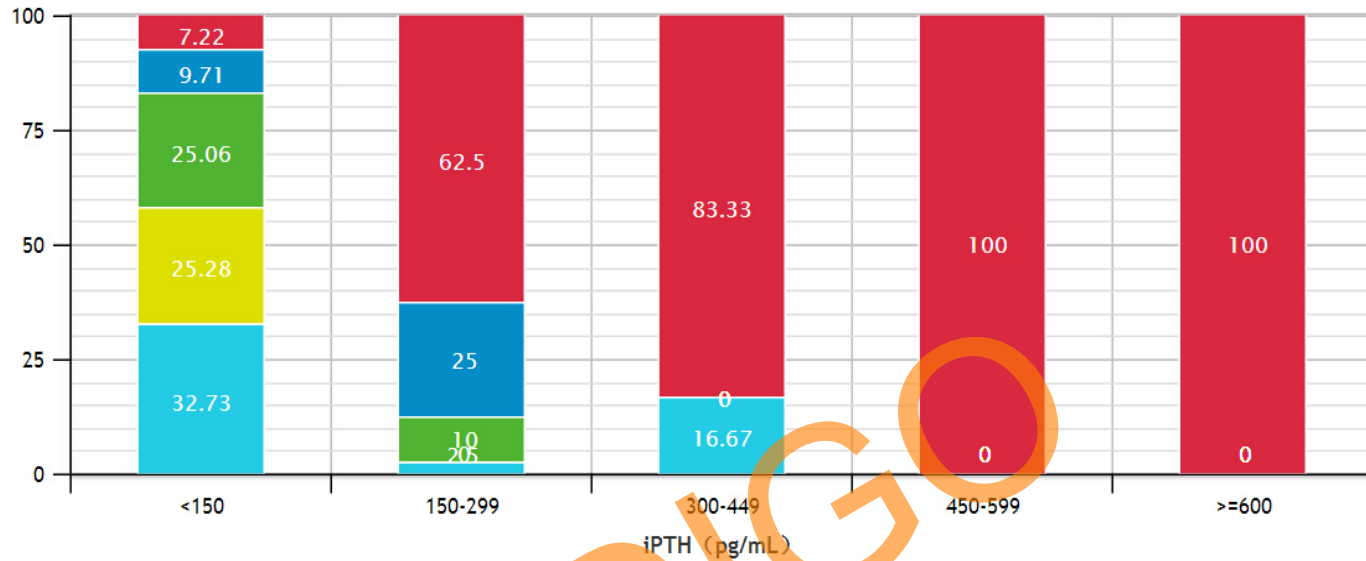
P (mg/dl)	< 15 (n, %)	15-29 (n, %)	30-59 (n, %)	60-89 (n, %)	≥90 (n, %)
<3.5	25 (4.8)	109 (17.6)	683 (36.2)	1226(44.0)	1577(35.3)
3.5-4.5	108 (20.8)	311 (50.1)	979 (51.9)	1346(48.3)	2330(52.2)
4.6-5.5	160 (30.8)	142 (22.9)	177 (9.4)	187(6.7)	458(10.3)
5.6-7.0	144 (27.7)	57 (9.2)	31 (1.6)	18(0.65)	104(2.3)
>7.0	82 (15.8)	2 (0.3)	18 (0.95)	10(0.36)	19(0.4)
Total	519 (100%)	621(100%)	1,888(100%)	2,787(100%)	4,468(100%)

Serum PTH Distribution of IgAN Patients



iPTH (pg/ml)	Cases	Proportion (%)
<150	471	89.04
150~299	42	7.94
300~449	6	1.13
450~599	4	0.76
≥600	6	1.13
Total	529	100

iPTH Distribution in Different CKD Stages



iPTH (pg/mL)	< 15 (Case, %)	15-29 (Case, %)	30-59 (Case, %)	60-89 (Case, %)	≥90 (Case, %)
<150	32(44.4)	43(81.1)	111(96.5)	112(100)	145(98.6)
150-299	25(34.7)	10(18.9)	4(3.5)	0(0)	1(0.7)
300-449	5(6.9)	0(0)	0(0)	0(0)	1(0.7)
450-599	4(5.6)	0(0)	0(0)	0(0)	0(0)
≥ 600	6 (8.3)	0(0)	0(0)	0(0)	0(0)
Total	72 (100)	53(100)	115(100)	112(100)	147(100)

Serum Ca Distribution of LN Patients

Ca (mg/dl)	Cases	Proportion (%)
<8.4	2104	59.2
8.4-9.5	1241	34.9
9.6-10.2	153	4.3
> 10.2	55	1.6
Total	3553	100

High incidence of hypocalcemia in LN patients

Serum Calcium Distribution of LN Patients in different CKD Stages

Ca(mg/dl)	CKD 5 (n,%)	CKD 4 (n,%)	CKD 3 (n,%)	CKD 2 (n,%)	CKD 1 (n,%)
<8.4	203(61.1)	219(74.0)	455(69.5)	419(60.3)	703(50.6)
8.4-9.5	106(31.9)	62(20.9)	165(25.2)	229(32.9)	606(43.6)
9.6-10.2	14(4.2)	9(3.0)	26(4.0)	37(5.3)	65(4.7)
>10.2	9(2.7)	6(2.0)	9(1.4)	10(1.4)	16(1.2)
Total	332 (100)	296(100)	655(100)	695(100)	1,390(100))

Serum P Distribution of LN Patients

P (mg/dl)	Cases	Proportion (%)
<3.5	691	23.7
3.5-4.5	1215	41.7
4.6-5.5	592	20.3
5.6-7.0	264	9.1
> 7.0	154	5.3
Total	2916	100

Higher prevalence of hyperphosphatemia in LN Patients



Serum Phosphorus Distribution Varies different CKD Stages

P(mg/dl)	CKD 5 (n,%)	CKD 4 (n,%)	CKD 3 (n,%)	CKD 2 (n,%)	CKD 1 (n,%)
<3.5	15(5.4)	24(9.8)	110(20.7)	154(27.3)	355(30.7)
3.5-4.5	42(15.1)	62(25.2)	220(41.4)	255(45.1)	573(49.5)
4.6-5.5	57(20.4)	75(30.5)	133(25.0)	117(20.7)	189(16.3)
5.5-7.0	83(29.7)	61(24.8)	58(10.9)	29(5.1)	32(2.8)
>7.0	82(29.4)	24(9.8)	11(2.1)	10(1.8)	9(0.8)
Total	279 (100)	246(100)	532(100)	565(100)	1,158(100)



Summary

- CKD-MBD is prevalent in Chinese CKD patients and existed in early stages of CKD and poor attention
- There are big gap of CKD-MBD management in China compared to that of developed countries by DOPPS
- CKD-MBD is of unsatisfying treatment efficiency and targets achieving.
- Reduction of serum phosphorus and employment of phosphate binders effectively improve the prognosis of CKD patients
- New phosphate binders offers Chinese patients more alternatives



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Thank you !

KDIGO