Supplemental Table 1: Pathologist affiliation, years of experience, and participation in various aspects of the descriptor-based scoring evaluation. Glomerular descriptors were tested three times (Tests I, II, and III) with repeated tests on the same 131 glomeruli; Test II also included 184 additional glomeruli (total 315). Interstitial fibrosis and tubular atrophy and Podocyte descriptors were scored only once. Estimation of intra-pathologist agreement required participation in Tests I, II and II (131 glomeruli); estimation of inter-pathologist agreement was performed across pathologists for each of the tests (each column).

Pathologist	NEPTUNE affiliation	Years of experience	Descriptor reference manual	Glomerular Descriptors (51)			Interstitial fibrosis & tubular atrophy (2)	Podocytes (4)
				Test I 131 glomeruli	Test II 131+184 = 315 glomeruli	Test III 131 glomeruli	244 cases	178 cases
P0	NEPTUNE	>10years	x					
P1	NEPTUNE	>10years	x	x	x	x	x	x
P2	NEPTUNE	>10years	x	x	x	x		x
P3	NEPTUNE	<3 years						x
P4	NEPTUNE	>10years	x	x	x	x	x	x
P5	NEPTUNE	>10years	x	x	x	x		x
P6	NEPTUNE	<3 years	x	x	x	x	x	
P7	NEPTUNE	trainee	x	x	x	x	x	
P8	NEPTUNE	<10 years	x	x	x	x	x	
P9	Non-NEPTUNE	trainee					x	
P10	Non-NEPTUNE	<10 years			x			
P11	Non-NEPTUNE	>10years			x			
P12	Non-NEPTUNE	<3 years			x			

Supplemental Table 2: Intra-reader agreement for each NEPTUNE pathologist participating to Tests I, II & III (131 glomeruli) is estimated using Cohen's kappa for each evaluable descriptor* (max 51). Kappa statistics are categorized as Fair/Poor, Moderate, good and Excellent. For each category, the number of descriptors with a given intra-reader concordance measured comparing Test I to II and test II to III per participating pathologist (P) is shown.

		# Evaluable Descriptors*		Excellent (kappa>0.8)		Good (0.6<kappa≤0.8)		Moderate (0.4<kappa≤0.6)		Poor or Fair (kappa≤0.4)	
		Test I vs. II	Test II vs. III	Test I vs. II	Test II vs. III	Test I vs. II	Test II vs. III	Test I vs. II	Test II vs. III	Test I vs. II	Test II vs. III
Average		35.7	35.7	6.6	10.4	9.4	11.7	8.7	6.6	11.0	7.0
Pathologist	P1	34	34	12	10	12	14	6	5	4	5
	P2	36	36	8	27	6	3	8	1	14	5
	P4	36	37	2	6	9	15	10	6	15	10
	P5	36	34	5	6	10	14	7	7	14	7
	P6	39	39	8	9	15	12	7	12	9	6
	P7	33	35	9	8	4	10	10	8	10	9
	P8	36	35	2	7	10	14	13	7	11	7

***Descriptors not selected as present in either test by a given pathologist were excluded from the kappa calculation.**

Supplemental Table 3: Intra-reader Cohen's kappa coefficients for 8 NEPTUNE pathologists (P1-P8) rating 131 glomeruli at 3 test times (I, II, III) with intervening consensus webinars. Kappas were calculated for comparisons Test I vs. Test II and Test II vs. Test III.

Glomerular Descriptors	Test I vs. Test II (Kappa)							Test II vs. Test III (Kappa)						
	P1	P2	P4	P5	P6	P7	P8	P1	P2	P4	P5	P6	P7	P8
No/minimal changes	1.00	1.00	1.00	0.56	0.66	0.49	0.66	1.00	1.00	1.00	0.32	1.00	0.49	0.66
Global sclerosis with hyalinosis	0.49	0.00	0.39	0.65	1.00	0.56	0.48	0.80	1.00	0.39	0.69	1.00	0.66	0.66
Global sclerosis without hyalinosis	0.49	0.00	0.64	0.23	0.65	1.00	0.00	0.00	0.00	0.84	0.72	0.42	1.00	0.00
Global deflation	0.39	1.00	0.72	0.85	0.89	1.00	0.74	0.56	1.00	0.66	0.85	1.00	0.85	0.85
Global collapse	0.89	0.89	0.79	0.79	0.91	0.84	1.00	0.84	1.00	0.79	0.94	0.80	0.72	1.00
Obsolescent	0.95	0.33	0.00	0.84	0.66	0.95	0.76	0.95	0.95	NS*	0.94	0.79	0.95	0.76
Segmental perihylar sclerosis	NS*	NS*	NS*	0.00	1.00	NS*	0.00	NS*	NS*	0.00	0.49	0.00	0.00	0.00
Segmental extended perihylar sclerosis	0.43	0.22	0.51	0.38	0.89	0.38	0.52	0.53	0.69	0.67	0.27	0.51	0.17	0.67
Segmental sclerosis away from vascular and tubular pole	0.69	0.34	0.59	0.13	0.91	0.40	0.59	0.56	0.70	0.59	0.55	0.43	0.20	0.65
Segmental sclerosis cannot determine location	0.60	0.47	0.01	0.51	0.43	0.58	0.47	0.60	0.87	0.00	0.67	0.52	0.40	0.61
Global mesangial sclerosis*	0.85	0.48	0.36	0.63	0.72	0.45	0.49	0.82	0.91	0.48	0.74	0.50	0.70	0.58
Cellular tip lesion	0.73	0.81	0.60	0.72	0.60	0.89	0.76	0.73	0.93	0.65	0.78	0.70	0.78	0.83
Sclerosing tip lesion	0.79	0.85	0.40	0.65	0.59	1.00	0.53	0.79	1.00	0.68	0.65	0.43	0.66	0.65
Extended cellular tip lesion	NS*	NS*	NS*	NS*	0.00	NS*	NS*	NS*	0.00	NS*	NS*	0.00	NS*	NS*
Extended sclerosing tip lesion	NS*	0.00	0.00	0.00	0.80	NS*	NS*	NS*	0.00	0.00	0.00	0.66	NS*	NS*
Mid-glomerular sclerosis	0.66	0.49	0.72	1.00	0.66	0.66	0.49	0.66	1.00	0.89	0.85	1.00	0.49	0.80
Cellular non-tip	0.79	0.80	NS*	0.48	0.36	0.73	0.58	0.83	0.85	NS*	0.76	0.44	0.43	0.65
Segmental collapse	0.60	0.00	0.49	0.53	0.48	0.40	0.48	0.79	NS*	0.60	0.85	0.43	0.56	0.70
Segmental deflation	0.39	0.00	0.00	0.00	NS*	0.01	0.01	0.02	1.00	0.00	NS*	0.00	0.00	0.01
Periglomerular fibrosis	0.74	0.79	0.74	0.60	0.00	0.25	0.37	0.76	0.82	0.77	0.52	0.80	0.47	0.52
Foam cells	0.86	0.83	0.76	0.83	0.77	0.81	0.64	0.78	0.81	0.67	0.70	0.68	0.86	0.64
Hyaline droplets in epithelial cells (podocytes)	0.87	0.38	0.76	0.66	0.70	0.57	0.64	0.92	0.91	0.70	0.52	0.61	0.65	0.74
Hyalinosis at the vascular pole	0.82	0.68	0.78	0.43	0.93	0.49	0.66	0.91	0.61	0.57	0.51	0.55	0.70	0.76
Hyalinosis at the tubular pole	NS*	NS*	0.38	0.00	0.66	NS*	0.00	NS*	NS*	0.65	NS*	0.66	NS*	0.00
Hyalinosis away from vascular and tubular pole	0.76	0.60	0.38	0.12	0.56	0.31	0.22	0.51	0.81	0.23	0.60	0.74	0.13	0.32
Hyalinosis cannot determine location	0.80	0.64	0.47	0.50	0.73	0.29	0.36	0.75	0.93	0.60	0.73	0.58	0.57	0.46
Adhesion (sinechiae)	0.66	0.71	0.44	0.37	0.59	0.47	0.49	0.72	0.89	0.55	0.32	0.74	0.64	0.60
Segmental epithelial cell (podocyte) hypertrophy	0.65	0.55	0.35	0.70	0.69	0.67	0.36	0.60	0.90	0.45	0.61	0.84	0.59	0.44
Global epithelial cell (podocyte) hypertrophy	0.63	0.86	0.53	0.78	0.79	0.88	0.49	0.70	0.95	0.64	0.74	0.79	0.76	0.47

Segmental epithelial cell (podocyte) hyperplasia	0.48	0.19	0.51	0.33	0.29	0.59	0.46	0.68	1.00	0.56	0.48	0.64	0.39	0.54
Global epithelial cell (podocyte) hyperplasia	0.91	0.79	0.58	0.27	0.87	0.00	0.43	0.83	1.00	0.65	0.70	0.60	0.00	0.60
Halo (detachment of podocytes)	0.92	0.57	0.33	0.60	0.64	0.74	0.78	0.84	0.84	0.70	0.31	0.82	0.82	0.82
Segmental mesangial hypercellularity	0.55	0.46	0.37	0.39	0.53	0.35	0.20	0.55	0.94	0.76	0.24	0.50	0.71	0.15
Global mesangial hypercellularity	0.91	0.56	0.49	0.72	0.74	0.49	0.65	0.79	1.00	0.80	0.52	0.61	1.00	0.44
Segmental spikes*	NS*	NS*	NS*	0.00	NS*	NS*	NS*	NS*	NS*	0.00	0.66	NS*	0.00	NS*
Global spikes	1.00	1.00	1.00	1.00	0.80	1.00	0.80	1.00	1.00	1.00	1.00	0.80	1.00	0.80
Intracapillary inflammatory cells*	NS*	0.00	NS*	NS*	0.00	NS*	NS*	NS*	0.00	NS*	NS*	0.40	NS*	NS*
Segmental endocapillary hypercellularity*	NS*	0.00	0.00	0.00	NS*	NS*	NS*	NS*	0.49	1.00	0.00	0.00	NS*	NS*
Global endocapillary hypercellularity*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*
Segmental duplication of GBM*	0.00	0.00	0.00	NS*	0.00	0.00	0.00	0.00	0.00	0.32	NS*	0.00	1.00	NS*
Global duplication of GBM*	NS*	NS*	0.00	NS*	NS*	NS*	NS*	NS*	NS*	0.00	NS*	NS*	NS*	NS*
Segmental increased mesangial matrix*	0.00	0.00	0.00	NS*	0.00	NS*	0.00	0.00	0.00	0.17	NS*	NS*	NS*	0.00
Global increased mesangial matrix	NS*	NS*	NS*	NS*	0.32	NS*	NS*	NS*	NS*	NS*	NS*	0.00	NS*	NS*
Karyorrhexis*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*
Necrosis*	NS*	NS*	NS*	NS*	NS*	0.00	NS*	NS*	NS*	NS*	NS*	NS*	0.00	NS*
Very segmental cellular crescent*	NS*	NS*	NS*	NS*	0.00	NS*	NS*	NS*	NS*	NS*	NS*	NS*	0.00	NS*
Very segmental fibrocellular crescent	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*
Very segmental fibrous crescent*	NS*	NS*	NS*	NS*	NS*	NS*	1.00	0.00	NS*	NS*	NS*	NS*	NS*	NS*
Extensive cellular crescent*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*
Extensive fibrocellular crescent*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*
Extensive Fibrous crescent	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*	NS*

* NS=Not Seen (descriptors that were *not* observed by the pathologist at either test for all glomeruli)

Supplemental Table 4: Inter-reader concordance of percent of renal cortex involved in chronic tubulointerstitial damage using Pearson's correlation coefficie for 244 cases rated by 6 pathologists (five NEPTUNE pathologists: P1,P4,P6,P7,P8; and one non-NEPTUNE pathologist: P9)

	Overall: all stains and levels available	
	Interstitial fibrosis	Tubular atrophy
Average	0.82	0.82
P1 vs P4	0.83	0.80
P1 vs P6	0.81	0.76
P1 vs P7	0.83	0.75
P1 vs P8	0.78	0.74
P1 vs P9	0.78	0.75
P4 vs P6	0.88	0.87
P4 vs P7	0.93	0.92
P4 vs P8	0.88	0.90
P4 vs P9	0.88	0.90
P6 vs P7	0.91	0.90
P6 vs P8	0.86	0.86
P6 vs P9	0.84	0.85
P7 vs P8	0.90	0.89
P7 vs P9	0.89	0.88
P8 vs P9	0.84	0.85

Supplemental Table 5: Inter-reader concordance of podocyte descriptors using Kendall's coefficient of concordance for 178 cases rated by five NEPTUNE pathologists (P1-P5)

	Foot process effacement (0-4+)	Microvillous transformation (0-2+)	Condensation of actin cytoskeleton (0-2+)	Loss of primary processes (0-1+)
Average	**0.83**	**0.61**	**0.49**	**0.26**
P1 vs P2	**0.96**	**0.83**	**0.73**	**0.61**
P1 vs P3	**0.93**	**0.78**	**0.71**	**0.61**
P1 vs P4	**0.92**	**0.79**	**0.71**	**0.58**
P1 vs P5	**0.85**	**0.63**	**0.62**	**0.52**
P2 vs P3	**0.92**	**0.79**	**0.74**	**0.52**
P2 vs P4	**0.93**	**0.83**	**0.74**	**0.53**
P2 vs P5	**0.86**	**0.67**	**0.62**	**0.51**
P3 vs P4	**0.91**	**0.78**	**0.70**	**0.48**
P3 vs P5	**0.81**	**0.69**	**0.64**	**0.55**
P4 vs P5	**0.84**	**0.74**	**0.62**	**0.51**

Foot process effacement: semiquantitative analysis with 0 = 1-10%, 1+ = 11-25%, 2+ = 26-50%, 3+ = 51-75%, and 4+ = >75%.
Condensation of actin-based cytoskeleton and microvillous transformation: semiquantitative analysis with 0 = not observed, 1+ = segmental (≤50%), 2+ = global (>50%)
Loss of primary processes was scored as absent (0) or present (1+)

Supplement table 6:
Complete and revised descriptors reference manual as currently implemented by other international consortia (INTEGRATE)[§] (post study revision is in red):

WSI HISTOLOGY

Glomerular damage

Glomerular descriptors listed below are scored as present (1) or absent (0).

No (minimal) changes: None of the lesions below are present.

Global Sclerosis With Hyalinosis: Sclerosis involves 100% of the glomerular tuft Glomerular size is preserved, or, compared to the glomeruli obtained in the same biopsy, increased or decreased by not more than 50%.

Global Sclerosis Without Hyalinosis: Sclerosis involves 100% of the glomerular tuft, with no accompanying hyalinosis. Glomerular size is preserved or, compared to the glomeruli obtained in the same biopsy, increased or decreased by not more than 50%.

Global Deflation: Global wrinkling and folding of the GBM (≥80% of the tuft) without epithelial cell (podocyte) hypertrophy and hyperplasia (formerly known an ischemic type of collapse). The urinary space is patent. The wrinkling is generally made by small regular folds of the GBM.

Global Capillary Collapse: Wrinkling and folding of the GBM involving ≥80% of the tuft with occlusion or subocclusion of capillary lumina. Collapse is generally accompanied by hypertrophy and hyperplasia of overlying epithelial cells (pseudo-crescents). Epithelial cell hypertrophy and hyperplasia if present are marked separately as individual descriptors. The wrinkling is generally made by small and/or big irregular folds of the GBM.

Obsolescent glomeruli: Glomeruli are small and globally sclerotic without hyalinosis. Bowman's capsule is completely or partially absent and there is no periglomerular fibrosis. Obsolescent glomeruli are defined when glomerular size is decreased >50% compared to all other glomeruli in the same biopsy.

Global Mesangial Sclerosis: A generalized global increase (100%) of mesangial matrix is present with or without mesangial cell hypercellularity and hypertrophy of overlying epithelial cells.

Segmental Perihilar Sclerosis (vascular pole): Segmental solidification of the glomerular tuft is present with increased extracellular matrix in continuity with the vascular pole. If hyalinosis, foam cells, hypertrophy of overlying epithelial cells, halo and adhesion of the tuft to the Bowman's capsule is present, they should be marked as separate descriptors.

Extended Segmental Perihilar Sclerosis (vascular pole) Segmental solidification of the glomerular tuft with increased extracellular matrix in continuity with the vascular pole and extends beyond the middle line of the tuft, with or without involving the tip. If hyalinosis, foam cells, hypertrophy of overlying epithelial cells, halo and sinechia/adhesion of the tuft to the Bowman's capsule is present, they should be marked as separate descriptors. (This lesion includes segmental solidification known as "approaching" global sclerosis).

Segmental sclerosis Away from Vascular and Tubular Poles: Segmental solidification of the tuft with increased extracellular matrix. If hyalinosis, foam cells, hypertrophy of overlying epithelial cells, halo and adhesion of the tuft to the Bowman's capsule is present, these features should be marked as separate descriptors.

Segmental sclerosis Cannot Determine Location: None of the above. Vascular or tubular pole cannot be seen in section. If hyalinosis, foam cells, hypertrophy of overlying epithelial cells (podocytes), halo and adhesion of the tuft to the Bowman's capsule is present, they should be marked as separate descriptors.

Cellular Tip lesion: Foam cells with or without other intracapillary cells within the glomerular tuft at the tubular pole, accompanied by hypertrophy of glomerular epithelial cells exclusive of tubular epithelium, and/or bridging to the Bowman's capsule/proximal tubule take off area. The presence of foam cells or inflammatory cells needs to be marked separately as individual descriptors when present.

Sclerosing Tip lesion: Solidification of the tuft at the tubular pole with increased extracellular matrix with or without adhesion to Bowman's capsule. Glomerular epithelial cells (podocytes) may be hypertrophic and attached to the epithelium at the tubular pole.

Extended Cellular Tip lesion: Foam cells with or without other intracapillary cells within the glomerular tuft at the tubular pole. The process extends through a large portion of the glomerulus (>1/2 of the tuft) but does not involve the vascular pole, accompanied by hypertrophy of epithelial cells (podocytes) and/or bridging to the Bowman's capsule/proximal tubule take off area. The presence of foam cells or inflammatory cells needs to be marked separately as individual descriptors when present. (This lesion includes segmental solidification not involving the vascular pole but "approaching" global sclerosis).

Extended Sclerosing Tip lesion: Solidification of the tuft at the tubular pole with increased extracellular matrix and adhesion to Bowman's Capsule which extends through a large portion of the glomerulus but does not involve the vascular pole. No foam cells are present. Glomerular epithelial cells (podocytes) are hypertrophic and attached to epithelial cells at the tubular pole. (This lesion includes segmental solidification not involving the vascular pole but "approaching" global sclerosis).

Mid-Tuft/Central location of segmental sclerosis: Located neither at the tip, the perihilum, or the periphery of the tuft (no adhesion to the Bowman's capsule).

Cellular lesions – Non-Tip: Endocapillary hypercellularity with epithelial cell hypertrophy. Hypercellularity may be due to foam cells and/or endocapillary cells with or without karyhorrexis and is not at the tip of the glomerulus. The presence of foam cells, karyhorrexis or inflammatory cells needs to be marked separately as individual descriptors when present.

Segmental Capillary Collapse: Wrinkling and folding of the GBM involving at least one glomerular lobule and <80% of the tuft, with occlusion or subocclusion of capillary lumina. Collapse is generally accompanied by hypertrophy and hyperplasia of overlying epithelial cells (podocytes); epithelial cell (podocytes) hypertrophy and hyperplasia if present need to be marked separately as individual descriptors. The wrinkling is generally made by small and/or big irregular folds of the GBM.

Segmental Deflation: Wrinkling and folding of the capillaries without epithelial cell hyperplasia (formerly called ischemic type of collapse) involving <80% of the glomerular tuft. The wrinkling is generally made by small regular folds of the GBM.

Periglomerular Fibrosis: Circumferential fibrosis in the interstitium surrounding the Bowman's capsule.

Glomerular foam cells: Intracapillary foam cells in the presence or absence of segmental or global sclerosis.

Hyaline Droplets in Epithelial Cell (Podocyte): Protein droplets are present in glomerular epithelial cells (podocytes). These cells usually are also hypertrophic (if so, both descriptors apply).

Hyalinosis at the Vascular Pole: Hyalinosis is defined as glassy acidophilic, PAS positive, silver negative material

Hyalinosis at the Tubular Pole: Hyalinosis is defined as glassy acidophilic, PAS positive, silver negative material. Solidification of the tuft and/or foam cells may be present.

Hyalinosis Away from the Vascular and Tubular Poles: Hyalinosis is defined as glassy acidophilic, PAS positive, silver negative material. Both the vascular and the tubular pole are present in the glomerular cross section.

Hyalinosis Cannot Determine Location: Hyalinosis is defined as glassy acidophilic, PAS positive, silver negative material and can occur with or without adhesion to the Bowman's capsule in a location that is not the vascular pole of the tip of the glomerulus. The vascular and/or the tubular poles cannot be identified.

Synechiae: Continuity of glomerular tuft basement membrane to the Bowman's capsule with continuity of epithelial cell lining. Note: a sinechia generally includes 1-2 capillaries at the most and it may or may not be associated with segmental sclerosis, hyalinosis or foam cells. Larger adhering section of the glomerular tuft to the Bowman's capsule in the presence of significant hyalinosis and/or sclerosis is not considered a sinechia but an adhesion part of the segmental sclerosis.

Segmental Epithelial Cell (Podocyte) Hypertrophy: Hypertrophy is defined as enlarged cytoplasm or enlarged nuclei with prominent nucleoli or both. Segmental hypertrophy is defined by one layer of enlarged epithelial cells overlying the glomerular basement membranes and involving <50% of the glomerular tuft.

Global Epithelial Cell (Podocyte) Hypertrophy: Hypertrophy is defined as enlarged cytoplasm or enlarged nuclei with prominent nucleoli or both. Segmental hypertrophy is defined by one layer of enlarged epithelial cells overlying the glomerular basement membranes and involving ≥50% of the glomerular tuft.

Segmental Epithelial Cell (Podocyte) Hyperplasia: ≥ 2 layers of epithelial cells (podocytes) overlying the glomerular basement membranes are present, involving <50% of the glomerulus. Hyperplasia may occur with or without hypertrophy.

Global Epithelial Cell (Podocyte) Hyperplasia: ≥2 layers of epithelial cells (podocytes) overlying the glomerular basement membranes are present, involving ≥50% of the glomerulus. Hyperplasia may occur with or without hypertrophy.

Halo (detachment of overlaying podocytes): Detachment of epithelial cells (podocytes) from original underlying GBM is present with intervening new loose basement membrane material (pale on HE, PAS, trichrome or silver stain).

Segmental Mesangial Hypercellularity: > 3 mesangial cells per mesangial lobule involving <50% of the visible mesangial regions in a glomerulus

Global Mesangial Hypercellularity: > 3 mesangial cells per mesangial lobule involving ≥50% of the visible mesangial regions in a glomerulus

Segmental Presence of Spikes on Silver Stain: Spikes are defined as silver positive stain with an irregular profile on the outer side of the glomerular basement membranes and involving <50% of the glomeruli.

Global Presence of Spikes on Silver Stain: Spikes are defined as silver positive stains with an irregular profile on the outer side of the glomerular basement membranes involving ≥50% of the glomerulus.

Infiltrating Leukocytes: The presence of leukocytes in glomerular capillaries is recorded when ≥1 inflammatory cell is present in capillary lumina. (Note: the presence of infiltrating leukocystes although initially classified on a semiquantitative scale from 0-3 for each glomerulus with 0= none 1 = 1-7, 2=8-15, 3=>15 leukocytes per glomerulus, was revised and scored as a dichotomous value for this study).

Segmental endocapillary hypercellularity: hypercellularity due to increased number of cells within glomerular capillary lumina causing narrowing of the lumina" involving <50% of the glomerulus.

Global endocapillary hypercellularity: hypercellularity due to increased number of cells within glomerular capillary lumina causing narrowing of the lumina" involving >50% of the glomerulus.

Segmental GBM Duplication: is defined as a double contour of the GBM involving <50% of the glomerular tuft, with or without endocapillary hypercellularity (endocapillary hypercellularity is independent variable).

Global GBM Duplication: is defined as a double contour of the GBM involving >50% of the glomerular tuft, with or without endocapillary hypercellularity (endocapillary hypercellularity is independent variable).

Segmental Increased Mesangial Matrix: Defined as an increase in the extracellular material in the mesangium such that the width of the interspace exceeds two mesangial cell nuclei in at least one glomerular lobule but <50% of the glomerular tuft.

Global Increased Mesangial Matrix: Defined as an increase in the extracellular material in the mesangium such that the width of the interspace exceeds two mesangial cell nuclei in ≥50% of the glomerular tuft.

Karyorrhexis: presence of apoptotic, pyknotic and/or fragmented nuclei.

Necrosis: is defined as disruption of the glomerular basement membrane with fibrin exudation and karyorrhexis.

Very Segmental Extracapillary Cellular Proliferation (Cellular Crescent): extracapillary cell proliferation of more than two cell layers with >50% of the lesion occupied by cells, involving <25% of the Bowman's space.

Very Segmental Extracapillary Fibrocellular Proliferation (Fibrocellular Crescent): is defined as part of the circumference of Bowman's capsule covered by *a combination of cells and* extracellular matrix*, with <50% cells and <90% matrix* involving <25% of the Bowman's space. This lesion is often associated with disruption of Bowman's capsule. Ischemic, obsolescent glomeruli should be excluded.

Very Segmental Extracapillary Fibrosis (Fibrous crescent): is defined as more than 10% of the circumference of Bowman's capsule covered by a lesion composed of >90% extracellular matrix involving <25% of the Bowman's space.

Extensive Extracapillary Cellular Proliferation (Cellular Crescent): extracapillary cell proliferation of more than two cell layers with >50% of the lesion occupied by cells, involving >25% of the Bowman's space.

Extensive Extracapillary Fibrocellular Proliferation (Fibrocellular Crescent):: is defined as part of the circumference of Bowman's capsule covered by *a combination of cells and* extracellular matrix*, with <50% cells and <90% matrix* involving >25% of the Bowman's space. This lesion is often associated with disruption of Bowman's capsule. Ischemic, obsolescent glomeruli should be excluded.

Extensive Extracapillary Fibrosis (Fibrous crescent): is defined as more than 10% of the circumference of Bowman's capsule covered by a lesion composed of >90% extracellular matrix involving >25% of the Bowman's space.

Tubulo-interstitial damage

The following parameters will be quantitated as present of absent, on a semi-quantitative scale (0-3+) or quantitative scale (% of cortex involved).

a) present or absent (0 = absent, 1 = present): interstitial edema, microcysts and inflammation with eosinophils or neutrophils >10%
b) semi-quantitative scale (0-3+; 0 = absent,1 + = mild, <25% of cortex, 2 + = moderate, 25-50% of cortex; 3 + = severe, >50% of cortex): acute tubular injury
c) quantitative (% cortex involved): tubular atrophy, interstitial fibrosis, interstitial inflammation and interstitial foam cells

****Acute Tubular Damage*** Defined by the presence of tubular degenerative changes (such as flattening of the tubular epithelium, loss of proximal cell brush borders, pyknotic cells) and/or tubular regenerative changes (hypertrophic epithelial cells with large nuclei and prominent nucleoli, mitotic activity).

Tubular Atrophy: Small tubules with thick tubular basement membranes lined by small cuboidal or flat cells. Generally accompanied by fibrosis. Includes "thyroidization" of the parenchyma.

****Microcysts:*** Presence of dilated tubules (> twice the diameter of a normal proximal tubule) containing eosinophilic amorphous material, and is generally accompanied by scalloping of the cast profile. The epithelium lining the microcyst is generally flattened and does not reveal brush border.

Interstitial Fibrosis. The interstitium is expanded by the presence of collagen that stain blue on trichrome. Tubular are not back to back, but rather separated by fibrosis and can be atrophic.

****Interstitial Edema***: The interstitium is occupied by pale acellular material.

Interstitial Inflammation – mononuclear WBC: Inflammation involving fibrotic as well as non-fibrotic renal cortex, composed of lymphocytes, monocytes, plasma cells.

Interstitial Inflammation – eosinophils: If eosinophils are noted in >10% of the cortex and representing >10% of the inflammatory cells.

Interstitial Inflammation – neutrophils: If neutrophils are noted in >10% of the cortex and representing >10% of the inflammatory cells.

Interstitial Foam Cells: Presence of interstitial foam cells containing optically clear vacuoles.

Vascular damage

The following will be scored semiquantitatively on a scale from 0-3+ using the vessel with the most severe lesion. If arteries or arterioles are not present in the sections it will be scored as n/a (999).
0 absent
1 + = mild, thickness of intima of <25% of media width in any number of vessels
2 + = moderate, 25-50% of media width in any number of vessels
3 + = severe, >50% of media width in any number of vessels

Arterial sclerosis: Defined as thickening of the intima with fibrosis and/or duplication of the elastic lamina in interlobular and arcuate arteries.

Arteriolar hyalinosis: Defined as accumulation of hyaline material in the wall and/or arteriolar sclerosis

ELECTRON MICROSCOPY

A minimum of 5 electron micrographs are reviewed.
Podocytes: Foot process effacement, microvillous transformation and condensation of the actin-based cytoskeleton are scored semiquantitatively and loss of primary processes and present or absent.
Endothelial cells: endothelial cells loss of fenestration is recorded on a semiquantitative scale based on % of peripheral cytoplasm involved tubuloreticular inclusions and honeycombing-like appearance as present or absent.
Glomerular basement membranes (GBM): Abnormalities in texture are recorded as present or absence.
Electron dense deposits: The percentage of glomerular basement membrane involved by subepithelial deposits in each stage (I-IV) is recorded. The predominance of stages are indicated, e.g., II>III, or II, or II>I>III, etc. Mesangial deposits (including mesangial and paramesangial) and subendothelial deposits are recorded as present or absent. The presence of transmembrane deposits and deposits with nuclear pore appearance is recorded as present or absente.

Foot process effacement*:* Loss of foot processes. % of glomerular capillary surface area affected by effacement will be recorded as semi-quantitative value. (0 = 0-10%; 1 = 11-25%; 2 = 26-50%; 3 = 51-75%; 4 = 76-100% of the outer GBM surface)

Condensation of the actin-based cytoskeleton: Electron dense cytoskeleton is reorganized and condensed at the GBM aspect of epithelial cell foot processes. % of glomerular capillary surface area affected by effacement will be recorded as semi-quantitative value. (0 = 0-5%; 1 = ≤ 50%; 2 = >50% of the outer GBM surface)

Microvillous transformation: Cytoplasmic projections into the urinary space that emanate from the luminal side of epithelial cell membrane are present. % of glomerular capillary surface area affected by effacement will be recorded as semi-quantitative value (0 = 0-5%; 1 = ≤ 50%; 2 = >50% of the outer GBM surface)

Loss of primary processes: Epithelial cell (podocyte) body sits directly on underlying GBM. This is generally accompanied by complete effacement (loss of foot processes).It will be recorded as present or absent (0 = present - normal; 1 = absent – loss).

****Epithelial cell (podocyte) detachment***: Detachment of epithelial cells from underlying GBM is present with intervening new loose basement membrane material (halo). Recorded as present or absent (0 = absent, 1 = present).

****Thickening of the GBM***: GBM thickness will be assessed on 10 cross sections of capillary loops at foci where there are no capillary wall deposits.

- Decreased thickness is scored as such when at least 25% of the GBM appear thinner than normal. (0 = absent, 1 = present).
- Increased thickness is scored as such when at least 25% of the GBM appear thicker than normal. (0 = absent, 1 = present).
- Mix pattern when thin and thick areas are present within the same biopsy. (0 = absent, 1 = present).

****GBM abnormal texture:*** Presence of basket-wave appearance, electron lucent areas alternating with granular or curvilinear electron dense areas, the presence of microspherule, microparticles different from organized deposits or rests of invaginating cells within the lamina densa of the GBM. Scored as absent or present (0 = absent, 1 = present).

****Tubuloreticular inclusions:*** Presence of at least one subcellular organized inclusion (TRI) in endothelial cell cytoplasm is recorded (0 = absent, 1 = present).

****Glomerular endothelial cell fenestration:*** Absence of typical fenestration resulting in a solid rim of endothelial cell cytoplasm away from the perinuclear region (0 = 0-5%; 1 = ≤ 50%; 2 = >50% of the inner GBM surface)

****Endothelium honeycombing-like appearance:*** Presence of cribriform or reticular organization of the endothelial cell cytoplasm, most often, but not exclusively, present at the mesangial side of the capillary lumen. Scored as present or absent, assuming that the absence of it is the pathologic event (0 = present - normal; 1 = absent – loss).

****Subepithelial deposits Stage I:*** Electron dense deposits are present on the outer surface of the GBM with little or no lateral accumulation of basement membrane material.

****Subepithelial deposits Stage II:*** Electron dense deposits are present on the outer surface of the GBM and partially surrounded by extracellular matrix (spikes)

****Subepithelial deposits Stage III:*** Electron dense deposits are embedded in the extracellular matrix (intramembranous)

****Subepithelial deposits Stage IV:*** Electron dense deposits are partially reabsorbed and formed by irregular electron lucent areas and more electron dense areas.

Predominant stage: I=1; II=2; III=3; IV=4

Transmembranous deposits: Deposits present throughout the entire thickness of the GBM.

Nuclear pore configuration: Deposits with a concentric circular (nuclear pore) configuration.

Subendothelial deposits: Electron dense deposits located in between the GBM and the endothelial cell cytoplasm.

Mesangial deposits: Electron dense deposits involving the mesangium and paramesangium.

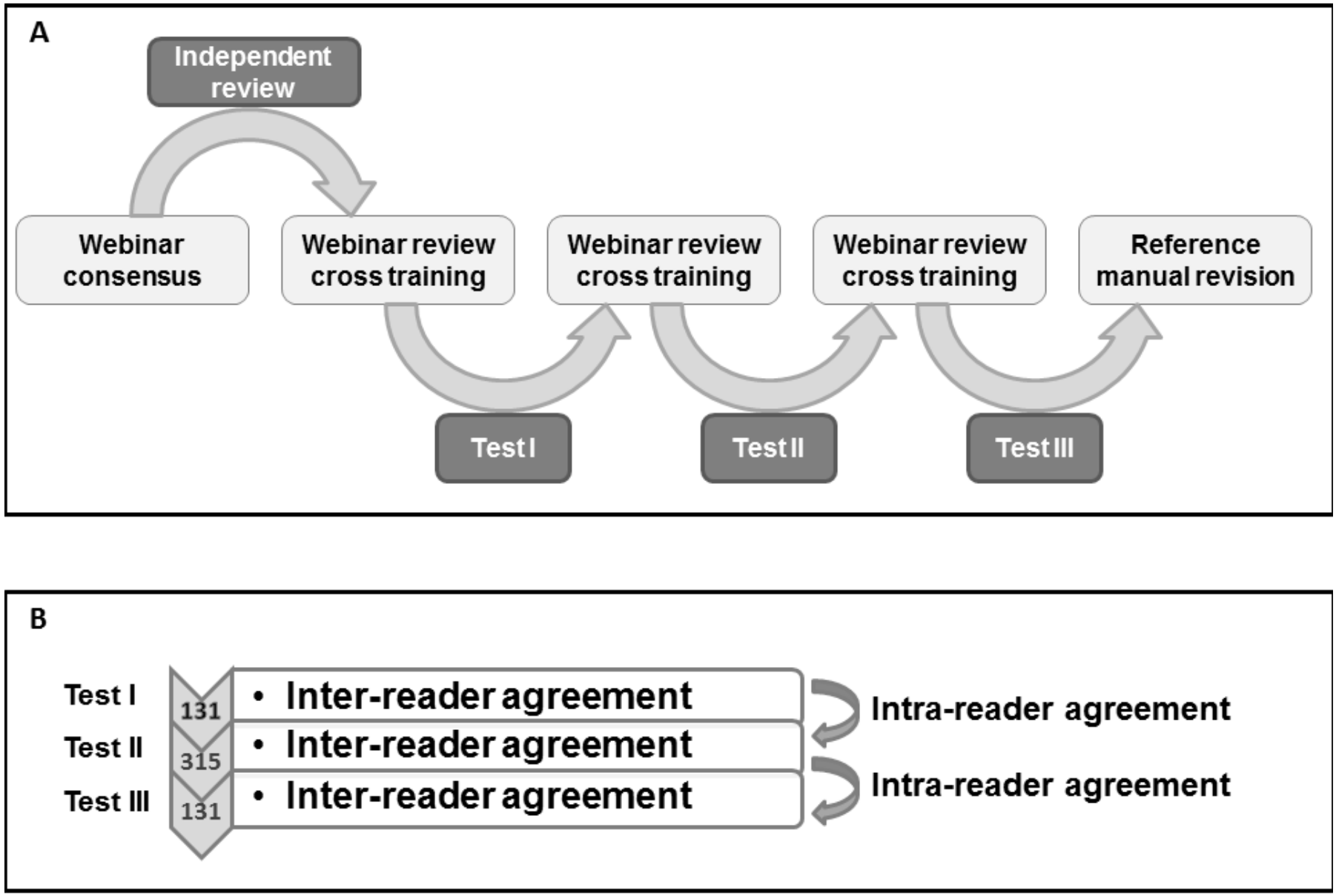
Note: descriptors marked with "**" were not tested in this study but they are part of the proposed NDPSS and in the process of being tested. Descriptors in red and with "**", were added to the NDPSS after the current reproducibility study was terminated and are in the process of being tested. Descriptors marked with "*" had an insufficient number of observations on the 131 images tests, although were more represented in the 315 image test and/or were consistently marked as absent by all participating pathologists. In red are sections that were reviewed after the reproducibility study was completed to add clarity to the descriptor definitions.
[§]Refinement of descriptors was also accomplished thanks to the contribution of INTEGRATE members participating to international webinar sections. All INTEGRATE affiliated consortia (EURenOmics, NEPTUNE and CHINA-DiKiP) are currently using this reference manual.

Supplemental Figure legends:

Supplemental Figure 1: Study design. A) Webinar based reviews were implemented at the outset of the study and between scoring tests for NEPTUNE pathologists. **B)** Inter-reader concordance was tested on 131 glomeruli in Tests I and III and 315 (the same 131 plus 184 additional glomeruli) in Test II for NEPTUNE pathologists. Intra-reader concordance was tested comparing individual pathologist results from Test I vs. II and Test II vs. III for the 131 glomeruli only. Non-NEPTUNE pathologists had a single webinar training and scored 315 glomeruli only once.

Supplemental Figure 2: The NEPTUNE electronic scoring sheet used for documenting glomerular descriptors: The electronic scoring spread sheet is pre-populated by “0” = “absent” as indicated in the blue cells. When a descriptor is selected the cell is automatically changes color to red (“1” = present). Glomeruli with specific features are profiled by the selection of one or more descriptors applicable to that glomerulus.

Supplemental Figure 1. Study design to test intra- and inter-reader concordance for glomerular descriptors



Supplemental Figure 2. Electronic scoring sheet

Biopsy ID	glom #1	glom #2	glom #3	glom #4	glom #5	glom #6	glom #7	glom #8	glom #9
no/minimal changes	1	0	0	0	0	0	0	1	0
global sclerosis with hyalinosis	0	0	0	1	0	0	0	0	0
global sclerosis without hyalinosis	0	0	0	0	0	0	1	0	0
global deflation (ischemic type of wrinkling- 100%)	0	0	0	0	0	0	0	0	0
global collapse (>80%)	0	0	0	0	1	0	1	0	0
obsolescent	0	1	0	0	0	0	0	0	0
global mesangial sclerosis	0	0	0	0	0	0	0	0	0
segmental perihilar sclerosis	0	0	0	0	0	0	0	0	1
segmental extended perihilar sclerosis	0	0	0	0	0	0	0	0	0
segmental sclerosis away from vascular and tubular pole	0	0	0	0	0	0	0	0	1
segmental sclerosis cannot determine location	0	0	0	0	0	0	0	0	0
cellular tip lesion	0	0	1	0	0	0	0	0	0
sclerosing tip lesion	0	0	0	0	0	0	0	0	0
extended cellular tip lesion	0	0	0	0	0	0	0	0	0
extended sclerosing tip lesion	0	0	0	0	0	0	0	0	0
mid-glomerular sclerosis	0	0	0	0	0	0	0	0	0
Cellular non-tip	0	0	0	0	0	0	0	0	0
segmental collapse (<80%)	0	0	0	0	0	0	0	0	0
segmental deflation (<80%)	0	0	0	0	0	0	0	0	0
foam cells	0	0	1	0	0	1	0	0	0
hyalin droplets in epithelial cells	0	0	0	0	1	0	0	0	0
hyalinosis at the vascular pole	0	0	0	0	0	0	0	0	1
hyalinosis at the tubular pole	0	0	0	0	0	0	0	0	0
hyalinosis away from vascular and tubular pole	0	0	0	0	0	0	0	0	0
hyalinosis cannot determine location	0	0	0	0	0	0	0	0	0
adhesion	0	0	1	0	0	0	0	0	0
segmental epithelial cell hypertrophy (<50%)	0	0	1	0	0	1	0	0	1
global epithelial cell hypertrophy (>50%)	0	0	0	0	1	1	0	0	0
segmental epithelial cell hyperplasia (<50%)	0	0	0	0	0	0	0	0	0
global epithelial cell hyperplasia (>50%)	0	0	0	0	1	0	0	0	0
halo	0	0	1	0	0	0	0	0	0
segmental mesangial hypercellularity	0	0	1	0	0	0	1	0	0
global mesangial hypercellularity	0	0	0	0	0	0	0	0	0
segmental spikes	0	0	0	0	0	0	0	0	0
global spikes	0	0	0	0	0	0	0	0	0
marginating leukocytes	0	0	0	0	0	0	0	0	0
segmental endocapillary hypercellularity	0	0	0	0	0	0	0	0	0
global endocapillary hypercellularity	0	0	0	0	0	0	0	0	0
segmental duplication of GBM	0	0	0	0	0	0	0	0	0
global duplication of GBM	0	0	0	0	0	0	0	0	0
segmental increased mesangial matrix without hypercellularity	0	0	0	0	0	0	0	0	0
global increased mesangial matrix without hypercellularity	0	0	0	0	0	0	0	0	0
karyorrhexis	0	0	0	0	0	0	0	0	0
necrosis	0	0	0	0	0	0	0	0	0
very segmental cellular crescent	0	0	0	0	0	0	0	0	0
very segmental fibrocellular crescent	0	0	0	0	0	0	0	0	0
very segmental fibrous crescent	0	0	0	0	0	0	0	0	0
extensive cellular crescent	0	0	0	0	0	0	0	0	0
extensive fibrocellular crescent	0	0	0	0	0	0	0	0	0
extensive fibrous crescent	0	0	0	0	0	0	0	0	0