Supplemental Table S1. Biomarker Measurement Details

Biomarker	Biomarker Name	Assay
KIM-1	Kidney injury molecule-1	Duoset DY1750, R & D Systems Inc., Minneapolis, MN
IL-18	Interleukin-18	Medical & Biological Laboratories Co., Nagoya, Japan
MCP-1	Monocyte chemoattractant protein-1	Meso Scale Diagnostics, Gaithersberg, MD
UMOD	Uromodulin	Meso Scale Diagnostics, Gaithersberg, MD
NGAL	Neutrophil gelatinase-associated lipocalin	NGAL ELISA Kit 036; Bioporto, Grusbakken, Denmark
YKL-40	Chitinase 3-like 1	Meso Scale Diagnostics, Gaithersberg, MD
Albumin	Albumin	Siemens ProSpec analyzer (Siemens GMBH)
Creatinine	Creatinine	Roche ModP Chemistry Analyzer (Roche Diagnostics) before January 2014 Cobas 6000 Chemistry Analyzer after January 2014
Osmolarity	Osmolarity	Advanced Instruments Micro-Osmometer Model 3320

Supplemental Table S2. Kidney Function at Different Study Timepoints in Participants Stratified by AKI and Baseline CKD Status

	AKI		No AKI	
	No CKD (n=463)	**CKD (n=306)**	**No CKD (n=463)**	**CKD (n=306)**
Baseline eGFR	83.8 (17.8)	42 (12.1)	86.1 (16.1)	46 (10.2)
eGFR at 3 months	79.8 (22.5)	44.3 (17.3)	86.9 (17.9)	51.2 (14.7)
Number (%) of CKD incidence or progression	137 (30%)	70 (23%)	66 (14%)	27 (9%)
eGFR decline from baseline to events for participants with the outcome	-16.3 (10.3)	-32 (15.1)	-29.1 (10.7)	-20 (12.4)
eGFR decline from baseline to censoring for participants without the outcome	-3.9 (14.5)	-0.7 (13.8)	-3.1 (11.7)	1.7 (12.9)

eGFR values and changes are presented as mean (SD).
AKI and CKD are defined at hospitalization and as baseline, respectively.

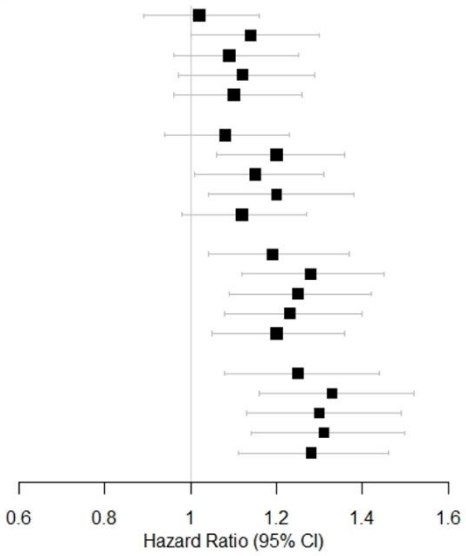
Supplemental Table S3. Predictive performance of biomarkers for 3-year composite CKD outcomes using different approaches to account for urine concentration.

		Hospitalization				3 Months after Discharge			
		AKI		No AKI		AKI		No AKI	
Biomarker	**model**	**C-statistics**	**p value**	**C-statistics**	**p value**	**C-statistics**	**p value**	**C-statistics**	**p value**
KIM-1	Biomarker Alone	0.51	Reference	0.54	Reference	0.61	Reference	0.52	Reference
	Biomarker-Cr Ratio	0.57	<0.001	0.51	0.73	0.65	0.029	0.57	0.18
	Biomarker-Osm Ratio	0.55	<0.001	0.51	0.79	0.66	<0.001	0.57	0.019
	Biomarker Adjusted for Cr	0.6	0.016	0.61	0.095	0.65	0.065	0.57	0.45
	Biomarker Adjusted for Osm	0.63	<0.001	0.64	0.033	0.68	0.008	0.61	0.13
IL-18	Biomarker Alone	0.52	Reference	0.55	Reference	0.59	Reference	0.51	Reference
	Biomarker-Cr Ratio	0.55	0.015	0.52	0.82	0.61	0.43	0.54	0.74
	Biomarker-Osm Ratio	0.54	0.001	0.5	0.68	0.63	0.001	0.52	0.9
	Biomarker Adjusted for Cr	0.59	0.047	0.59	0.32	0.61	0.51	0.54	0.6
	Biomarker Adjusted for Osm	0.62	0.002	0.63	0.083	0.65	0.013	0.6	0.29
MCP-1	Biomarker Alone	0.55	Reference	0.57	Reference	0.62	Reference	0.54	Reference
	Biomarker-Cr Ratio	0.6	0.001	0.47	0.26	0.64	0.13	0.57	0.35
	Biomarker-Osm Ratio	0.58	<0.001	0.48	0.33	0.65	0	0.58	0.051
	Biomarker Adjusted for Cr	0.61	0.039	0.59	0.46	0.65	0.16	0.58	0.54
	Biomarker Adjusted for Osm	0.63	0.007	0.63	0.12	0.68	0.006	0.63	0.15
Albumin	Biomarker Alone	0.61	Reference	0.5	Reference	0.67	Reference	0.56	Reference
	Biomarker-Cr Ratio	0.63	0.091	0.46	0.7	0.68	0.79	0.54	0.5
	Biomarker-Osm Ratio	0.62	0.1	0.53	0.066	0.69	0.046	0.56	0.98
	Biomarker Adjusted for Cr	0.64	0.1	0.59	0.14	0.68	0.8	0.53	0.62
	Biomarker Adjusted for Osm	0.64	0.071	0.63	0.041	0.7	0.18	0.57	0.74
NGAL	Biomarker Alone	0.57	Reference	0.54	Reference	0.64	Reference	0.58	Reference
	Biomarker-Cr Ratio	0.59	0.086	0.53	0.6	0.63	0.76	0.59	0.87
	Biomarker-Osm Ratio	0.59	0.004	0.51	0.12	0.66	0.03	0.6	0.22
	Biomarker Adjusted for Cr	0.61	0.081	0.58	0.3	0.64	0.9	0.59	0.8
	Biomarker Adjusted for Osm	0.63	0.008	0.63	0.13	0.66	0.17	0.62	0.44
YKL-40	Biomarker Alone	0.59	Reference	0.54	Reference	0.65	Reference	0.62	Reference

	Biomarker-Cr Ratio	0.6	0.042	0.53	0.79	0.66	0.7	0.63	0.72
	Biomarker-Osm Ratio	0.6	0.008	0.53	0.27	0.67	0.025	0.65	0.2
	Biomarker Adjusted for Cr	0.62	0.12	0.59	0.49	0.66	0.66	0.63	0.87
	Biomarker Adjusted for Osm	0.63	0.021	0.63	0.18	0.67	0.2	0.64	0.64
UMOD	Biomarker Alone	0.58	Reference	0.57	Reference	0.63	Reference	0.57	Reference
	Biomarker-Cr Ratio	0.45	0.011	0.51	0.48	0.59	0.048	0.53	0.45
	Biomarker-Osm Ratio	0.45	0.017	0.51	0.009	0.57	0	0.53	0.18
	Biomarker Adjusted for Cr	0.59	0.32	0.6	0.51	0.63	0.86	0.57	0.76
	Biomarker Adjusted for Osm	0.63	0.004	0.65	0.14	0.65	0.1	0.6	0.43

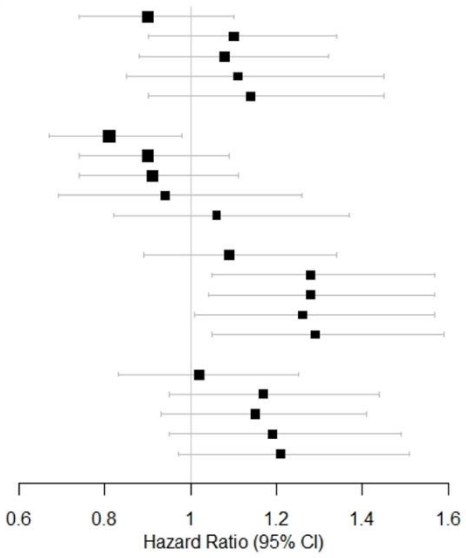
Supplemental Figure S1A. Hazard ratio of urine IL-18, MCP-1, NGAL and YKL-40 collected during hospitalization in AKI patients with composite CKD outcome using different approaches to account for urine concentration.

Biomarker	Model	HR for biomarker	HR for UCr or UOsm
IL-18	Biomarker Alone	1.02 (0.89- 1.16)	
	Biomarker-Cr Ratio*	1.14 (1- 1.3)	
	Biomarker-Osm Ratio*	1.09 (0.96- 1.25)	
	Biomarker Adjusted for Cr*	1.12 (0.97- 1.29)	0.8 (0.7- 0.93)
	Biomarker Adjusted for Osm*	1.1 (0.96- 1.26)	0.8 (0.71- 0.92)
MCP-1	Biomarker Alone	1.08 (0.94- 1.23)	
	Biomarker-Cr Ratio *	1.2 (1.06- 1.36)	
	Biomarker-Osm Ratio *	1.15 (1.01- 1.31)	
	Biomarker Adjusted for Cr *#	1.2 (1.04- 1.38)	0.78 (0.68- 0.9)
	Biomarker Adjusted for Osm *	1.12 (0.98- 1.27)	0.81 (0.72- 0.92)
NGAL	Biomarker Alone	1.19 (1.04- 1.37)	
	Biomarker-Cr Ratio	1.28 (1.12- 1.45)	
	Biomarker-Osm Ratio *	1.25 (1.09- 1.42)	
	Biomarker Adjusted for Cr *#	1.23 (1.08- 1.4)	0.81 (0.72- 0.93)
	Biomarker Adjusted for Osm	1.2 (1.05- 1.36)	0.82 (0.73- 0.93)
YKL-40	Biomarker Alone	1.25 (1.08- 1.44)	
	Biomarker-Cr Ratio *	1.33 (1.16- 1.52)	
	Biomarker-Osm Ratio *	1.3 (1.13- 1.49)	
	Biomarker Adjusted for Cr	1.31 (1.14- 1.5)	0.8 (0.71- 0.91)
	Biomarker Adjusted for Osm	1.28 (1.11- 1.46)	0.81 (0.71- 0.91)



Supplemental Figure S1B. Hazard ratio of urine IL-18, MCP-1, NGAL and YKL-40 collected during hospitalization in non- AKI patients with composite CKD outcome using different approaches to account for urine concentration.

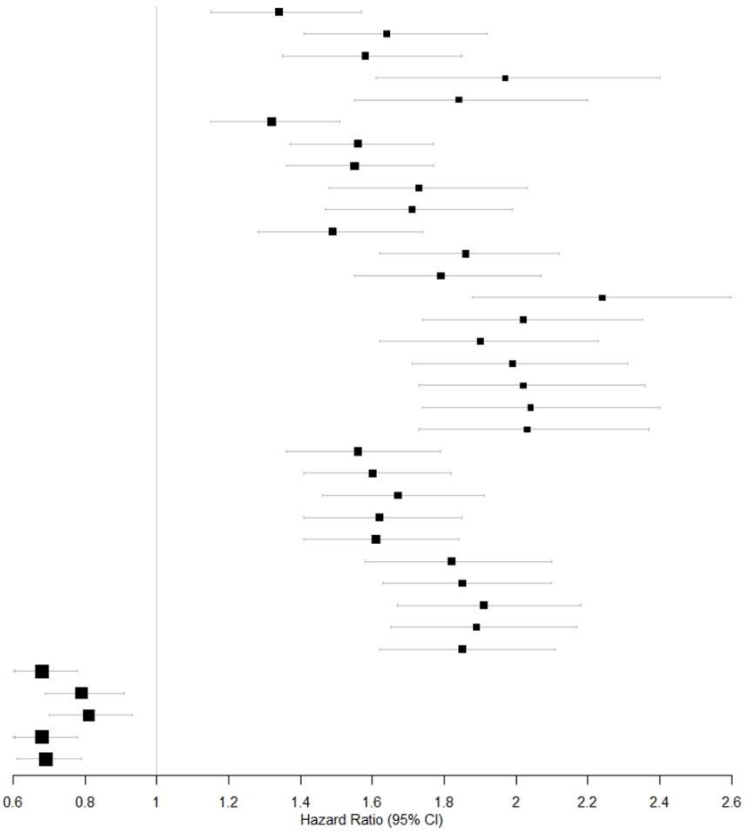
Biomarker	Model	HR for biomarker	HR for UCr or UOsm
IL-18	Biomarker Alone	0.9 (0.74- 1.1)	
	Biomarker-Cr Ratio*	1.1 (0.9- 1.34)	
	Biomarker-Osm Ratio*	1.08 (0.88- 1.32)	
	Biomarker Adjusted for Cr	1.11 (0.85- 1.45)	0.72 (0.55- 0.94)
	Biomarker Adjusted for Osm*	1.14 (0.9- 1.45)	0.65 (0.52- 0.81)
MCP-1	Biomarker Alone	0.81 (0.67- 0.98)	
	Biomarker-Cr Ratio	0.9 (0.74- 1.09)	
	Biomarker-Osm Ratio *	0.91 (0.74- 1.11)	
	Biomarker Adjusted for Cr	0.94 (0.69- 1.26)	0.81 (0.6- 1.11)
	Biomarker Adjusted for Osm *	1.06 (0.82- 1.37)	0.67 (0.52- 0.86)
NGAL	Biomarker Alone	1.09 (0.89- 1.34)	
	Biomarker-Cr Ratio *	1.28 (1.05- 1.57)	
	Biomarker-Osm Ratio *	1.28 (1.04- 1.57)	
	Biomarker Adjusted for Cr *	1.26 (1.01- 1.57)	0.69 (0.56- 0.87)
	Biomarker Adjusted for Osm *	1.29 (1.05- 1.59)	0.63 (0.52- 0.77)
YKL-40	Biomarker Alone	1.02 (0.83- 1.25)	
	Biomarker-Cr Ratio*	1.17 (0.95- 1.44)	
	Biomarker-Osm Ratio*	1.15 (0.93- 1.41)	
	Biomarker Adjusted for Cr*	1.19 (0.95- 1.49)	0.71 (0.57- 0.89)
	Biomarker Adjusted for Osm*	1.21 (0.97- 1.51)	0.65 (0.53- 0.79)



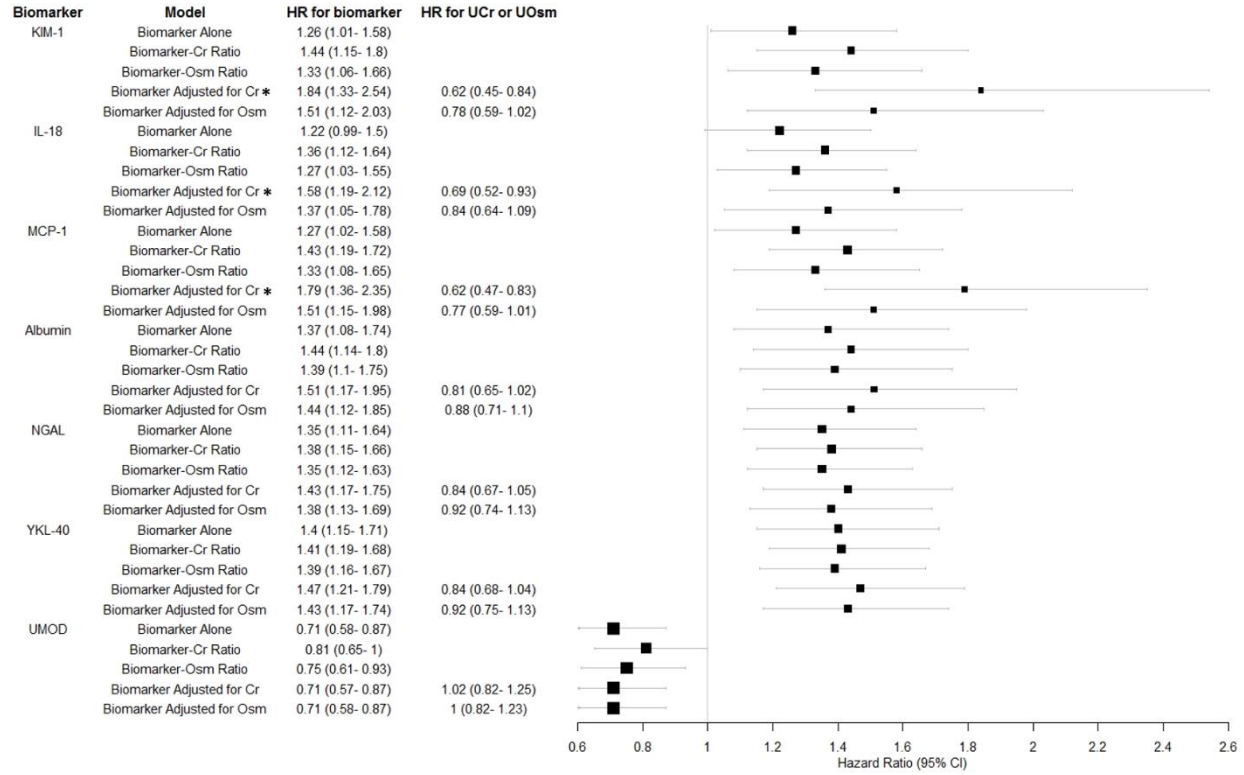
* p value less than 0.01 comparing biomarker's association with composite CKD outcome when urine creatinine or osmolarity is accounted for versus biomarker alone.
# p value less than 0.01 comparing biomarker's association with composite CKD outcome when using urine creatinine versus urine osmolarity
All urine measurements were converted to log-2 base normally distributed Z score. HR therefore represents change per 1 standard deviation (SD) increase of each biomarker on its log-2 scale.
IL-18: interleukin-18; MCP-1: monocyte chemoattractant protein-1; NGAL: neutrophil gelatinase-associated lipocalin (NGAL); YKL-40: chitinase 3-like 1

Supplemental Figure S2A. Hazard ratio of urine biomarkers collected 3 months after discharge in AKI patients with composite CKD outcome using different approaches to control for urine concentration.

Biomarker	Model	HR for biomarker	HR for UCr or UOsm
KIM-1	Biomarker Alone	1.34 (1.15- 1.57)	
	Biomarker-Cr Ratio *	1.64 (1.41- 1.92)	
	Biomarker-Osm Ratio *	1.58 (1.35- 1.85)	
	Biomarker Adjusted for Cr *	1.97 (1.61- 2.4)	0.59 (0.49- 0.71)
	Biomarker Adjusted for Osm *	1.84 (1.55- 2.2)	0.58 (0.49- 0.68)
IL-18	Biomarker Alone	1.32 (1.15- 1.51)	
	Biomarker-Cr Ratio *	1.56 (1.37- 1.77)	
	Biomarker-Osm Ratio *	1.55 (1.36- 1.77)	
	Biomarker Adjusted for Cr *	1.73 (1.48- 2.03)	0.64 (0.54- 0.75)
	Biomarker Adjusted for Osm *	1.71 (1.47- 1.99)	0.6 (0.52- 0.7)
MCP-1	Biomarker Alone	1.49 (1.28- 1.74)	
	Biomarker-Cr Ratio *	1.86 (1.62- 2.12)	
	Biomarker-Osm Ratio *	1.79 (1.55- 2.07)	
	Biomarker Adjusted for Cr *	2.24 (1.88- 2.67)	0.55 (0.46- 0.64)
	Biomarker Adjusted for Osm *	2.02 (1.74- 2.35)	0.55 (0.47- 0.64)
Albumin	Biomarker Alone	1.9 (1.62- 2.23)	
	Biomarker-Cr Ratio	1.99 (1.71- 2.31)	
	Biomarker-Osm Ratio *	2.02 (1.73- 2.36)	
	Biomarker Adjusted for Cr *	2.04 (1.74- 2.4)	0.75 (0.65- 0.86)
	Biomarker Adjusted for Osm *	2.03 (1.73- 2.37)	0.68 (0.59- 0.78)
NGAL	Biomarker Alone	1.56 (1.36- 1.79)	
	Biomarker-Cr Ratio	1.6 (1.41- 1.82)	
	Biomarker-Osm Ratio *	1.67 (1.46- 1.91)	
	Biomarker Adjusted for Cr *	1.62 (1.41- 1.85)	0.81 (0.71- 0.93)
	Biomarker Adjusted for Osm *	1.61 (1.41- 1.84)	0.74 (0.65- 0.84)
YKL-40	Biomarker Alone	1.82 (1.58- 2.1)	
	Biomarker-Cr Ratio	1.85 (1.63- 2.1)	
	Biomarker-Osm Ratio	1.91 (1.67- 2.18)	
	Biomarker Adjusted for Cr	1.89 (1.65- 2.17)	0.77 (0.68- 0.89)
	Biomarker Adjusted for Osm	1.85 (1.62- 2.11)	0.73 (0.64- 0.83)
UMOD	Biomarker Alone	0.68 (0.59- 0.78)	
	Biomarker-Cr Ratio *	0.79 (0.69- 0.91)	
	Biomarker-Osm Ratio *	0.81 (0.7- 0.93)	
	Biomarker Adjusted for Cr	0.68 (0.59- 0.78)	1 (0.87- 1.15)
	Biomarker Adjusted for Osm	0.69 (0.61- 0.79)	0.81 (0.71- 0.92)

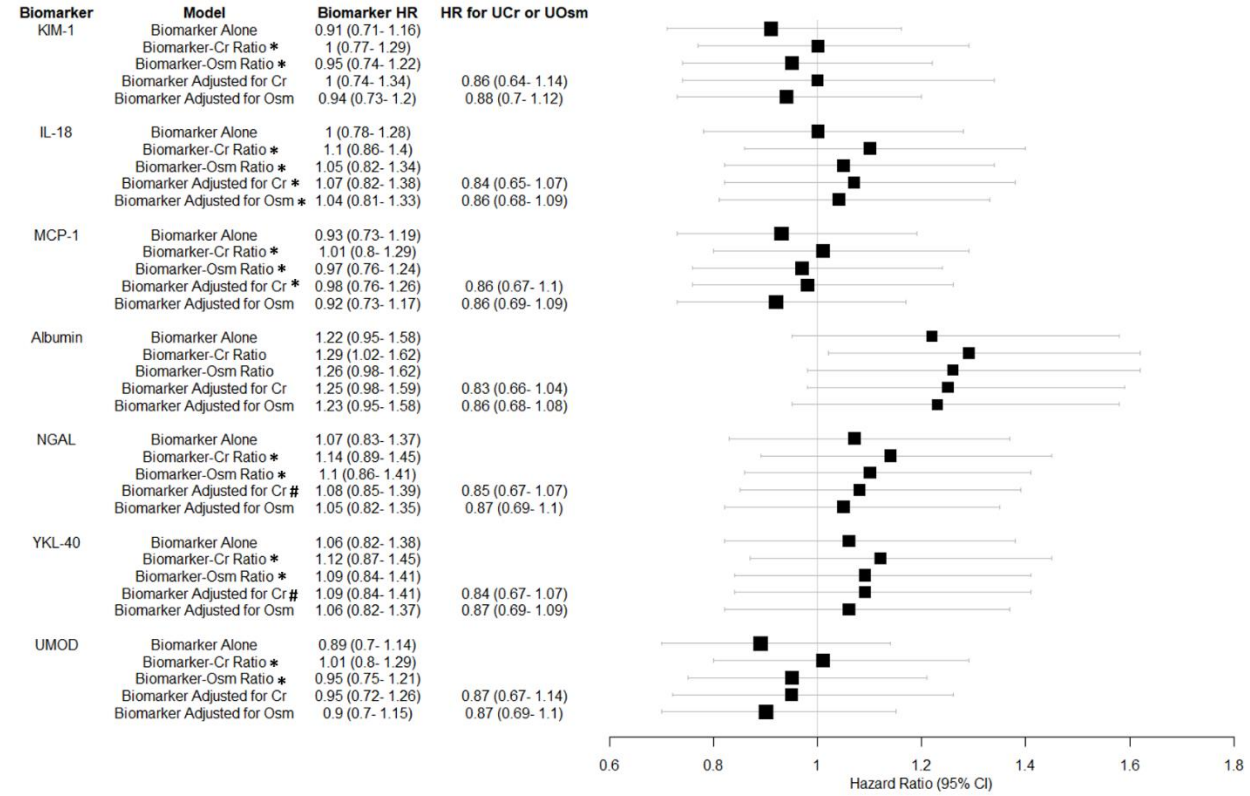


Supplemental Figure S2B. Hazard ratio of urine biomarkers collected 3 months after discharge in non-AKI patients with composite CKD outcome using different approaches to control for urine concentration.



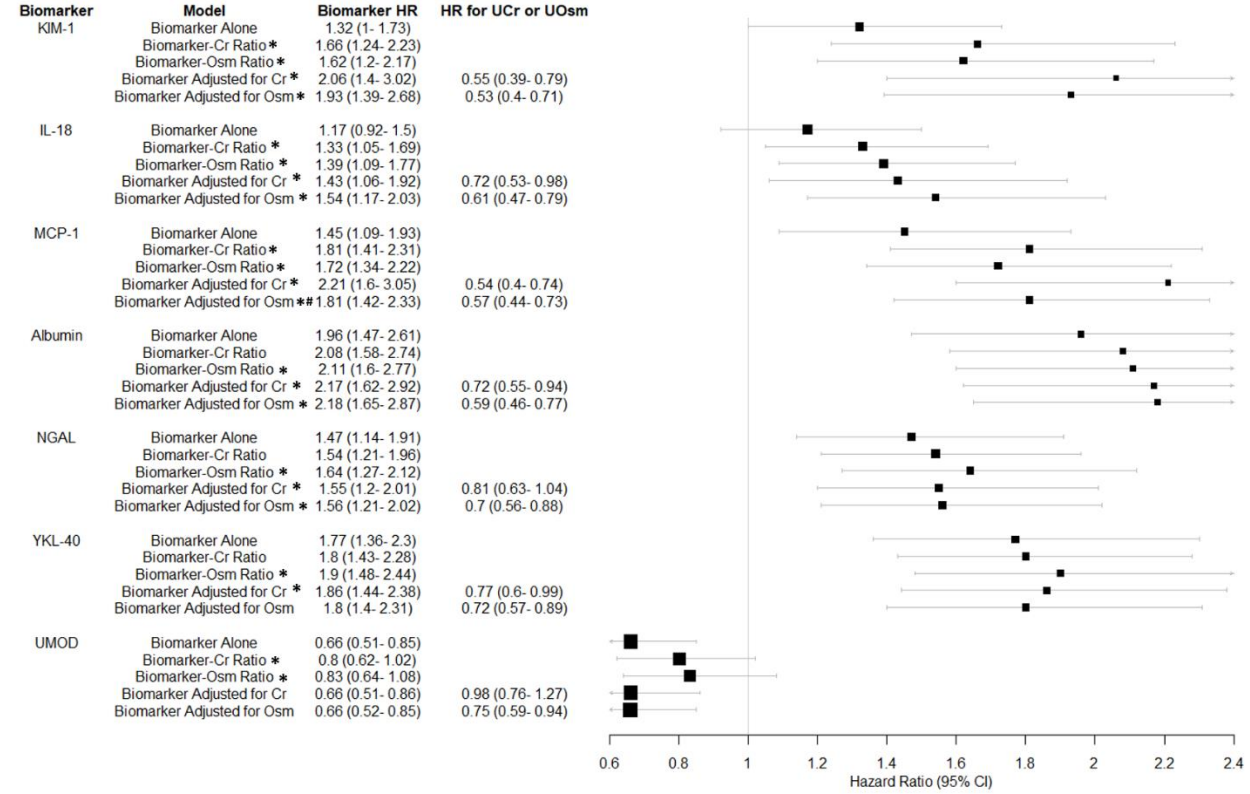
* p value less than 0.01 comparing biomarker's association with composite CKD outcome when urine creatinine or osmolarity is accounted for versus biomarker alone.
# The different between biomarker's association with composite CKD outcome when using urine creatinine versus urine osmolarity were insignificant in any models (p value greater than 0.01 for all comparisons)
All urine measurements were converted to log-2 base normally distributed Z score. HR therefore represents change per 1 standard deviation (SD) increase of UCr or UOsm on their log-2 scale.
IL-18: interleukin-18; KIM-1: kidney injury molecule-1; MCP-1: monocyte chemoattractant protein-1; NGAL: neutrophil gelatinase-associated lipocalin (NGAL); UMOD: uromodulin; YKL-40: chitinase 3-like 1

Supplemental Figure S3A. Hazard ratio of urine biomarkers collected during in subgroup of stage 2-3 AKI patients with composite CKD outcome using different approaches to control for urine concentration



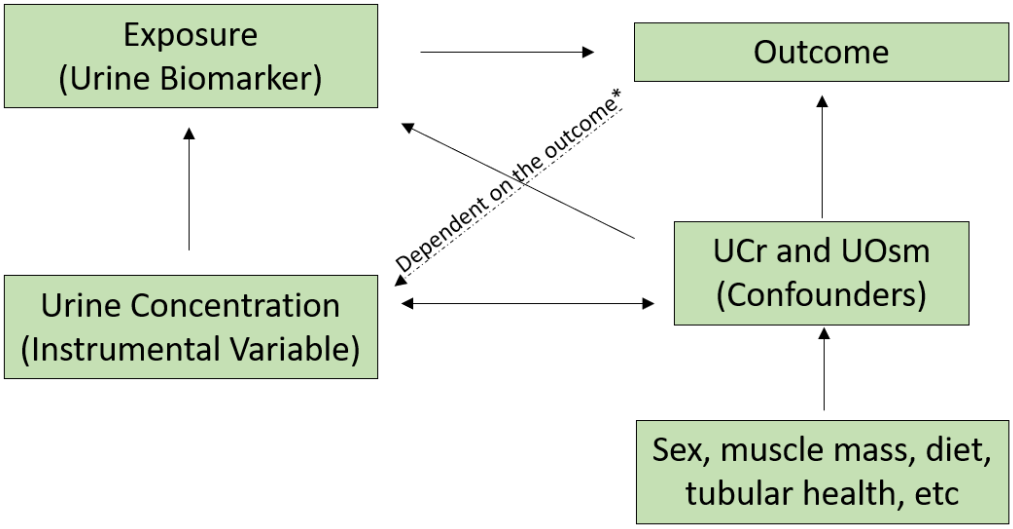
* p value less than 0.01 comparing biomarker's association with composite CKD outcome when urine creatinine or osmolarity is accounted for versus biomarker alone.
# p value less than 0.01 comparing biomarker's association with composite CKD outcome when using urine creatinine versus urine osmolarity
All urine measurements were converted to log-2 base normally distributed Z score. HR therefore represents change per 1 standard deviation (SD) increase of UCr or UOsm on their log-2 scale.
IL-18: interleukin-18; KIM-1: kidney injury molecule-1; MCP-1: monocyte chemoattractant protein-1; NGAL: neutrophil gelatinase-associated lipocalin (NGAL); UMOD: uromodulin; YKL-40: chitinase 3-like 1

Supplemental Figure S3B. Hazard ratio of urine biomarkers collected three months after discharge in subgroup of stage 2-3 AKI patients with composite CKD outcome using different approaches to control for urine concentration



* p value less than 0.01 comparing biomarker's association with composite CKD outcome when urine creatinine or osmolarity is accounted for versus biomarker alone.
# p value less than 0.01 comparing biomarker's association with composite CKD outcome when using urine creatinine versus urine osmolarity
All urine measurements were converted to log-2 base normally distributed Z score. HR therefore represents change per 1 standard deviation (SD) increase of UCr or UOsm on their log-2 scale.
IL-18: interleukin-18; KIM-1: kidney injury molecule-1; MCP-1: monocyte chemoattractant protein-1; NGAL: neutrophil gelatinase-associated lipocalin (NGAL); UMOD: uromodulin; YKL-40: chitinase 3-like 1

Supplemental Figure S4. Direct Acyclic Graph Depicting the Conceptual Framework of Urine Creatinine and Urine Osmolarity as Confounders rather than Surrogates for Urine Concentration in Investigating Etiological Relationship between Urine Biomarkers and Outcomes.



*Urine concentration may be affected by the outcome (such as chronic kidney disease progression)

Abbreviations**:** UCr: urine creatinine; UOsm: urine osmolarity

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	8-10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	10
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-14
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	19-20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21-22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.