### Supplementary Table 1: Detailed Study Description for Replicated Studies and Extent of Replication.

| First Author, Year | Outcome Definition | Timing of Biomarker Measurements | Exclusion Criteria | Sample Size in TRIBE* |
|--------------------|--------------------|-----------------------------------|--------------------|-----------------------|
| de Geus, 2011      | ≥ 50% increase in SCr occurring and persisting for >24h after admission (followed for 72h) | uNGAL, pNGAL at admission | Age < 18 years, readmission during study period, nephrectomy, CKD | Preoperative eGFR < 60 mL/min per 1.73 m² | 56 701 |
| Kokkoris, 2012     | Any AKI by RIFLE in 7 days | pNGAL, sCr, uNGAL at admission | ESRD, known CKD, nephrectomy, renal transplantation, expected ICU stay or death < 48h, transfer, brain death, age < 18 years, inability to draw blood or urine | Preoperative eGFR < 15 mL/min per 1.73 m² (based on Figure 1 footnote) | 189 1030 |
| Cho, 2013          | ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL in 5 days | uNGAL, uLFABP at admission | ESRD, kidney transplantation, life expectancy < 48h | 407 812 |
| Liu, 2013          | ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL or ≥ 0.3 mg/dL in 72h | CuNGAL, CuLFABP at 0h & 2h | Age < 18 years, ESRD needing renal replacement therapy, emergency surgery, died during or within 24h of surgery | 369 850 |
| Luo, 2013          | ≥ 0.5 mg/dL or ≥ 0.5 mg/dL or ≥ 0.5 mg/dL or ≥ 0.5 mg/dL or ≥ 0.5 mg/dL or ≥ 0.5 mg/dL | uKIM1, uNGAL, uNGAL, uKIM1, uNGAL, uKIM1, uNGAL | Age < 18 years, CKD, established AKI, Preoperative serum | 196 887 |
| Siew, 2013 | ≥ 0.3 mg/dL or ≥ 50% increase of sCr within 48h after surgery | CuNGAL, CuLFABP at 0h and 48h | CuNGAL, CuLFABP at 0-6h after surgery | Chronic lung disease, pulmonary fibrosis, cardiac arrest before enrollment, transfer orders within 4 h, died or discharged < 48 h after ICU admission, admitted for uncomplicated overdose, in the ICU > 3 days before enrollment, renal transplant, history of chronic dialysis, enrollment eGFR ≤ 60 ml/min per 1.73 m², did not experience a 0.3 mg/dL or 50% increase in sCr between admission and study enrollment | Preoperative eGFR ≤ 60 mL/min per 1.73 m² | 154 | 641 |
| Zeng, 2014 | ≥ 0.3 mg/dL or ≥ 50% increase of SCr within 48h | CuNGAL at 12h, CuLFABP at 4h | (1) CuNGAL at 6-12h, CuLFABP at 0-6h after surgery | Age <18 years, preoperative AKI, CKD, prior kidney transplantation | Preoperative eGFR < 60 mL/min per 1.73 m² | 154 | 641 |
|-------------|-----------------------------------------------|-----------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|------|-----|
|             | ≥ 0.3 mg/dL or ≥ 50% increase of SCr within 48h | CuNGAL at 12h, CuLFABP at 12h | (2) CuNGAL at 12-18h, CuLFABP at 0-6h after surgery |                                                |                                                |      |     |

Information regarding the exclusion criteria for each replicated study, as well as the number of cases and controls in TRIBE when AKI was defined according to each study’s criteria. Abbreviations: CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; sCr – serum creatinine; ESRD – end-stage renal disease; ICU – intensive care unit; AKI – acute kidney injury.

*When an article excluded individuals with CKD but a definition for CKD was not explicitly given, we excluded individuals with baseline eGFR < 60 mL/min per 1.73 m². Exclusion criteria applied are in addition to TRIBE-AKI exclusion criteria (age < 18 years, evidence of AKI prior to surgery, pre-operative serum creatinine above 4.5 mg/dL or end-stage renal disease (ESRD)).

Includes individuals with missing biomarker measurements.

Paper considered sustained and transient AKI; here we report analyses related only to sustained vs. no AKI.
## Supplementary Table 2: Assays Used.

| Study      | Analyte                                           |     |     |     |     |     |     |     |     |     |
|------------|--------------------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|            | Study                                            |     |     |     |     |     |     |     |     |     |
|            | Urine NGAL                                      |     |     |     |     |     |     |     |     |     |
|            | Urine IL-18                                      |     |     |     |     |     |     |     |     |     |
|            | Urine KIM-1                                      |     |     |     |     |     |     |     |     |     |
|            | Urine L-FABP                                     |     |     |     |     |     |     |     |     |     |
|            | Urine Creatinine                                 |     |     |     |     |     |     |     |     |     |
|            | Plasma NGAL                                      |     |     |     |     |     |     |     |     |     |
|            | Serum Creatinine                                 |     |     |     |     |     |     |     |     |     |
| TRIBE-AKI  | ARCHITECT (Abbott Diagnostics, Abbott Park, IL)  |     |     |     |     |     |     |     |     |     |
|            | ARCHITECT (Sekisui Diagnostics, Sekisui ELISA)   |     |     |     |     |     |     |     |     |     |
|            | Modified Jaffe reaction                          |     |     |     |     |     |     |     |     |     |
|            | Triage assay with Triage Meter                   |     |     |     |     |     |     |     |     |     |
|            | Hospital lab                                     |     |     |     |     |     |     |     |     |     |
| de Geus,   | Biosite Triage N/A                               | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 2011       |                                                   |     |     |     |     |     |     |     |     |     |
| Kokkoris,  | ARCHITECT assay N/A                             | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 2012       |                                                   |     |     |     |     |     |     |     |     |     |
| Cho, 2013  | BioPorto ELISA, Gentofte, Denmark N/A            | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Liu, 2013  | R&D Systems, Minneapolis, MN, USA N/A            | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Luo, 2013  | BioPorto R&D Systems Medical and Biological ELISA| N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |

Note: The table represents the assays used in different studies for various analytes. The assays include ARCHITECT (Abbott Diagnostics), ARCHITECT (Sekisui Diagnostics), Modified Jaffe reaction, and Triage assay with Triage Meter (Biosite, Inc., San Diego, CA).
| Siew, 2013 | Enzo Life Sciences ELISA (Plymouth Meeting, PA) | N/A | Hycult Biotech ELISA | Jaffe enzymatic method | N/A | Hospital lab |
|------------|-----------------------------------------------|-----|----------------------|-----------------------|-----|-------------|
| Zeng, 2014 | R&D System ELISA                              | N/A | Hycult Biotech ELISA | Cobas 6000 analyzer (Roche Diagnostics, Mannheim, Germany) | N/A | Cobas 6000 analyzer |

*High correlation with ELISA methods previously used.*
### Supplementary Table 3: Sources of Bias in Biomarker Combination Studies.

| Study Design | Selection bias may result from eligibility criteria and/or selective sampling (17, 37, 39, 41-43, 46, 47, 49, 50, 56). |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              | Retrospective studies susceptible to lower data quality and biased patient populations (42, 48-50, 57).                                                                                                                                                           |
|              | Registries and archival samples may be susceptible to selection bias and unrecognized biases (39, 45).                                                                                                                                                             |
|              | Batch effects can lead to bias (17).                                                                                                                                                                                                                             |
|              | Matching can lead to bias (17, 52).                                                                                                                                                                                                                             |
|              | Treatment received (37, 43, 46, 49, 50).                                                                                                                                                                |
|              | Center differences in multi-center studies (37).                                                                                                                                                     |
|              | Verification bias due to non-blind assessments of outcome (37, 43, 45, 48, 55).                                                                                                                                                                                 |
|              | Bias due to non-blind assessment of predictors (37, 42, 43, 45, 50, 55).                                                                                                                                                                                          |
|              | Misclassification of outcome due to suboptimal reference standard (41, 43).                                                                                                                                                                                          |
|              | Small sample size can lead to optimistic bias due to overfitting (43).                                                                                                                               |
|              | Inaccurate and/or non-reproducible methods used to measure predictors and/or outcomes (17, 41, 45, 48-50, 54).                                                                                             |
|              | Analysis plan not prespecified (45, 57).                                                                                                                                                               |
| Model Development | Stepwise methods and univariate screening lead to multiple comparisons and unstable models which can result in predictor selection bias (large but spurious associations) (16, 37, 43, 46, 48, 60). |
|               | Categorizing continuous variables can lead to optimism and predictor selection bias, particularly if data-driven approaches are used (37, 40-43, 50).                                                                 |
|               | Other methods to handle predictors (non-linearity, transformations, etc)                                                                                                                                |
could lead to predictor selection bias (43).

“Overanalysis” (including examining many endpoints and/or performing subset analyses) leads to increased chances of spurious findings (39, 42, 50, 57).

Missing data can lead to selection bias if a complete case analysis is used (17, 37, 39, 40, 43, 48, 50, 60, 61).

Loss to follow-up can bias the results of logistic regression (37).

Need special approaches if data are clustered (e.g. multi-center studies) (37).

| Evaluation |
|------------|
| Resubstitution bias is a source of optimism resulting from developing and evaluating the model in the same data (16, 37, 43, 48, 63). |
| Model selection bias is a source of optimism due to model (variable) selection (16, 37, 48). |
| Can have bias due to center differences in multi-center studies (17, 37). |
| Sample splitting with small datasets leads to replication instability and increases the chances of being misled (43, 48). |
| Simplifying the risk prediction model affects accuracy (43, 61). |
| When comparing risk prediction tools developed to predict different but related outcomes, could have outcome selection bias (66). |
| Validation studies conducted by the authors who developed a prediction model could be biased in support of the model (44, 61, 66). |
| Other sources of optimism exist, including optimization of the evaluation criterion, optimization of the dataset (where investigators attempt to find a dataset where the model performs well), and optimization of competing methods (choose “strawman” competitors) (58). |

| Reporting |
|-----------|
| Publication bias (39, 49, 57, 66). |
| Selective reporting bias (only a subset of results are reported) (39). |