

1 **Surveillance of CKD epidemiology in the US – a joint analysis of NHANES and KEEP**

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6

7 **Abstract**

8 Chronic Kidney Disease (CKD), is highly prevalent in the United States. Epidemiological
9 systems for surveillance of CKD rely on data that are based solely on the NHANES survey,
10 which does not include many patients with the most severe and less frequent forms of CKD. We
11 investigated the feasibility of estimating CKD prevalence from the large-scale community
12 disease detection Kidney Early Evaluation and Program (KEEP, $n = 127,149$).

13 We adopted methodologies from the field of web surveys to address the self-selection bias
14 inherent in KEEP. Primary outcomes studied were CKD Stage 3-5 (estimated glomerular
15 filtration rate [eGFR] <60 mL/min/1.73m², and CKD Stage 4-5 (eGFR <30 mL/min/1.73m²).

16 The unweighted prevalence of Stage 4-5 CKD was higher in KEEP (1.00%, 95% CI: 0.94-1.05%)
17 than in NHANES (0.51%, 95% CI: 0.43-0.59%). Application of a selection model with IPW of
18 variables related to demographics, recruitment and socio-economic factors resulted in estimates
19 similar to NHANES (0.55%, 95% CI: 0.50-0.60%). Weighted prevalence of Stages 3-5 CKD in
20 KEEP was 6.45% (95% CI: 5.70-7.28%) compared to 6.73% (95% CI: 6.30-7.19%) for
21 NHANES. Application of methodologies that address the self-selection bias in the KEEP
22 program may allow the use of this large, geographically diverse dataset for CKD surveillance.

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33 INTRODUCTION

34 Chronic Kidney Disease (CKD) is a growing public health concern in the United States
35 due to its high prevalence (~13% of the adult US population), association with increased
36 morbidity, mortality and progression to End Stage Renal Disease (ESRD). Treating CKD and
37 ESRD and their complications is extremely costly, accounting for more than 20% of fee-for-
38 service Medicare spending and over 80 billion dollars in the US for 2013 alone (1).
39 Epidemiological systems for geo-temporal CKD surveillance could both fulfil public health
40 objectives (2,3), and direct research efforts towards a better understanding of localized “hotspots”
41 of CKD similar to what has been reported in other contexts (4).

42 Efforts to develop such a project (2,3) culminated in the establishment of the Center for
43 Diseases Control surveillance project (5), which provides data on CKD incidence, prevalence,
44 disease awareness and other disease indicators. Despite the wealth of data incorporated in the
45 CDC project, prevalence estimates in the general population are based solely on the NHANES
46 survey(5–9). An important limitation of this feature is that individuals with the most severe and
47 costly, but less frequent stages of CKD (4-5) are not well represented in NHANES (7).
48 Incorporating additional, larger data sources that are more likely to ascertain persons with more
49 severe forms of CKD has the potential to enhance our existing CKD surveillance infrastructure.
50 In this report, we examine the feasibility of estimating CKD prevalence using data from the large
51 community disease detection program of the National Kidney Foundation’s Kidney Early
52 Evaluation and Program (KEEP)(10) in juxtaposition to the population-based data from
53 NHANES.

54 As a voluntary detection program, KEEP is likely to suffer from a substantial degree of
55 self-selection bias. If it is possible to address this bias, KEEP would provide a population-level

56 data source on all aspects of CKD, including the less common but costly advanced stages of the
57 disease. Use of a national reference population to standardize a sample is used routinely in public
58 health surveillance(11,12). Fueled by the expansion of internet based data collection strategies,
59 there has been a growing literature regarding the handling of self-selection effects in voluntary
60 surveys (13,14) by matching against a reference, representative, probability sample. To our
61 knowledge, similar techniques have not been applied to kidney disease research. In this report,
62 we address the self-selection bias in the KEEP dataset by developing selection models based on
63 subject level factors related to recruitment (selection) probabilities in KEEP. We accomplish this
64 by estimating propensities for KEEP participation relative to NHANES, and using them to form
65 inverse-probability weights (IPW), the application of which adjust the observed percentages of
66 CKD prevalence from this self-selected sample. We demonstrate that this approach can make the
67 estimated CKD prevalence rate from KEEP directly comparable to those of NHANES, opening
68 up the possibility of using this large, geographically diverse dataset for the purpose of CKD
69 surveillance.

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72 **RESULTS**

73 **Baseline characteristics and selection effects in KEEP**

74 The KEEP study made more than 185,000 assessments from August 2000 to June 2013.
75 We analyzed the initial encounter for program eligible KEEP participants assessed by 48
76 regional affiliates from 2001 to the end of 2012 using data provided by NKF. Participants were
77 excluded if <20 years of age, on dialysis, were pregnant, had a previous kidney transplant, were
78 lacking a valid state of residence or had other invalid demographic variable values (32,026
79 records excluded, Figure 1). Another 6,317 records that lacked a valid eGFR stage determination
80 were excluded to obtain 127,876 participants (147,168 records) with CKD stage. We then
81 removed follow up visits (19,292 records) and participants seen before 2001 ($n = 727$) to obtain a
82 sample of 127,149 KEEP participants for propensity score estimation. Our original NHANES
83 sample from 2001 – 2012 had 59,423 participants attending an MEC. We excluded NHANES
84 participants <20 years old ($n = 27,796$), pregnant women ($n = 963$), hemodialysis patients ($n =$
85 114) and participants without a valid eGFR determination ($n = 2,033$) to obtain a sample with
86 28,517 NHANES participants for propensity score estimation.

87 KEEP participant characteristics are compared to NHANES general population estimates
88 in Table 1. KEEP participants were older, more likely to be female, less likely to be non-
89 Hispanic White but more likely to be Black than NHANES. KEEP recruitment resulted in an
90 oversampling relative to NHANES of participants with self-reported diabetes, hypertension,
91 CKD, CHF/CAD/Stroke, a family history of diabetes and of heart attack. KEEP participants
92 were also more likely to have reported being obese, to be uninsured and to have at least a high
93 school education. KEEP participants were less likely to be current smokers than the general
94 population. The boosted CART model that produced the best agreement between expected and

95 predicted KEEP frequencies was the model with four-way interactions. Prevalence of CKD
96 within the KEEP sample by IPW decile shows the success of KEEP affiliates recruiting
97 participants at a higher risk of CKD. Smaller deciles (higher probability of selection into KEEP)
98 have significantly higher prevalence of CKD Stages 3-5 than large deciles ($P < 0.001$,
99 Supplemental Figure 2). After KEEP summaries were estimated using weights from this model,
100 frequencies were much closer to NHANES (Table 1). Before weighting the youngest and oldest
101 age categories were under and over represented in KEEP by -19% and 16.6%, but after weighted
102 estimations all categories were within 1.1% of NHANES. Females were 51.1% of NHANES and
103 52.2% in weighted KEEP compared to 67.7% of the unweighted KEEP sample. Weighted KEEP
104 estimates were also much closer to NHANES for race/ethnicity categories so that all groups were
105 within 2% of expected. Differences between weighted KEEP percentages and NHANES that
106 were more than $\pm 1\%$ included fewer self-reported diabetes (-1.1%), more hypertension (1.9%),
107 family history of diabetes (3.2%), overweight (2.7%), obese (2.9%) and insured (1.4%).

108 **Prevalence of CKD stages in NHANES and KEEP**

109 Prevalence of CKD stage 3 in the general population age 20 and older for 2001-2012 was
110 6.23% (95% CI: 5.82-6.66) from NHANES ($n = 2,453$ cases) compared to 13.14% (95% CI
111 12.95-13.33) in the KEEP sample during the same period (Table 2, $n = 16,706$ cases). Simple
112 reweighting the KEEP data reduced the prevalence estimate by more than one third to 8.57% and
113 accounting for clustering of KEEP samples within regional affiliates reduced the estimate to
114 6.45% (5.70-7.28%, Table 2 Weighted-GEE). The average prevalence of CKD Stage 4-5 among
115 all participants was 0.51% in the NHANES general population (95% CI 0.43-0.59%, $n = 239$
116 cases) and was 1.00% in the KEEP sample (95% CI 0.94-1.05%, Table 2, $n = 1,267$ cases). IPW

117 adjustment accounting for affiliate clusters removed almost all bias so the weighted KEEP
118 prevalence was 0.52% (95% CI 0.42-0.64%, Weighted-GEE).

119 Age and sex stratified results in Figure 2 show that both age and sex have substantial
120 impacts on CKD endpoints. Both NHANES and KEEP showed low CKD Stage 3 prevalence at
121 younger ages that increased with age for females more than males (KEEP age x sex interaction P
122 = 0.037). Stage 4-5 prevalence also increased with age with female versus male differences not
123 uniform over ages (KEEP age x sex interaction P = 0.026).

124 **Temporal Trends in the prevalence of CKD Stage**

125 Prevalence of Stages 3-5 and Stages 4-5 by KEEP year are shown in Figure 4-3 with and
126 without IPW. NHANES estimates are plotted in the middle of each two-year survey period so
127 that the KEEP estimates falling immediately before and after NHANES estimates are most
128 relevant for comparisons. Tests for non-linear time trends were not significant for CKD Stage 3
129 (P = 0.13), Stages 3-5 (P = 0.08) or Stages 4-5 (P = 0.07), and no CKD Stage showed a
130 significant positive or negative trend (Supplemental Table 2, all P -values > 0.63). Weighted
131 prevalence of CKD Both Stage 3 and Stage 4-5 weighted estimates are close to NHANES in all
132 years with 95% confidence intervals for KEEP trend lines overlapping NHANES point
133 estimates. Weighted KEEP CKD prevalence was slightly higher in early and late years of the
134 series compared to middle years. We used graphical methods to explore whether covariate
135 imbalance in age, sex and race/ethnicity by year may be associated with this extra variation
136 (Supplemental Figures 3 – 5). All three covariates had variation in balance over years, and the
137 pattern for sex most closely matched that seen in weighted KEEP prevalence.

138

139

140 **DISCUSSION**

141 In this paper we explored the use of data from a voluntary, self-selected community
142 disease detection program to model point prevalence and temporal trends for epidemiologic
143 surveillance of CKD in the US over a period of 10 years. By using a national representative
144 survey as a reference, we demonstrate the potential of IPW based adjustments to address the self-
145 selection bias inherent in community based disease detection programs. To our knowledge, this
146 is the first application of this approach in the setting of chronic (kidney) disease and opens up the
147 possibility of using large, readily available samples of convenience in epidemiologic surveillance
148 programs.

149 The use of self-selected samples for the purpose of tabulating official statistics has been
150 receiving increasing attention in the era of administered surveys distributed over the
151 internet(15,16). Similar to community based disease detection programs, the practical use of these
152 designs suffer from self-selection bias. In recent years, there has been a growing literature
153 regarding the modeling of self-selection effects in such surveys. This literature suggests that a
154 number of approaches, including post-stratification weighting of the observations of participants
155 in the self-selected samples(17) or the direct modeling of the probability of self-selection
156 (“propensity score adjustment”)(13,18,19) against a referent population may allow the valid use
157 of these convenience samples in place of random probability samples. To our knowledge, similar
158 techniques have not been applied to CKD prevalence data. Therefore, we explored both IPW and
159 post-stratification as a novel means to address the self-selection bias in KEEP. Our analyses
160 indicate that even though both methods may substantially decrease this bias, the greater
161 flexibility afforded by the logistic regression model in IPW leads to greater comparability with
162 the sample estimates from NHANES. We postulate that this performance of the IPW is likely to
163 hold true in other health domains outside the field of CKD research.

164 A major strength of our proposed approach to the surveillance of the CKD epidemiology is the
165 use of co-temporal, national, representative cohort of NHANES to calculate the self-selection
166 probabilities in KEEP. The use of such a reference, random probability sample is an integral
167 component of existing approaches for handling selection bias(13,17,20,21). Even if such a
168 reference sample is available though, in order for sample weighting to reduce bias, the covariates
169 used should be strongly correlated with the target population(15) and the mechanism underlying
170 the self-selection process should be one of Missing-At-Random (MAR). In such a case, IPW will
171 allow the unbiased estimation of quantities of interest e.g. point prevalence for impaired eGFR or
172 microalbuminuria (15). In our approach, the rich data collected during KEEP and the in-depth
173 knowledge of the KEEP data collection, the community advertisement and engagement
174 processes led us to consider a-priori plausible subsets of covariates to use for the weighting
175 process, and suggested the need to employ a GEE model to allow for variation among the NKF
176 affiliates where screenings were performed. These factors are likely responsible for the enhanced
177 comparability of the weighted estimates of KEEP to NHANES over the entire period 2001-2012
178 and at specific points in time during the same time interval.

179 In terms of practical applications, successfully addressing the bias in KEEP offers the
180 possibility of using this readily available sample of convenience for the purpose of CKD
181 surveillance. In particular, the existing CKD surveillance project about the general US
182 population is based on a limited number of NHANES participants with an eGFR <60 ($n = 2,700$)
183 and eGFR<30 ($n = 239$). Our analyses indicate the potential to expand this dataset almost six-
184 fold by appropriate weighting of the nearly 18,000 KEEP participants with decreased renal
185 function. Notwithstanding the increase in sample size, the ability to combine these datasets
186 affords the opportunity to overcome the pitfalls of each of these two studies when considered in

187 isolation (7,10,22,23). Whereas KEEP suffers from self-selection bias(10,22), NHANES does not
188 represent well the advanced, but also less common stages 3-4 of CKD (7). Such patients are
189 “oversampled” in KEEP so that these studies directly complement each other. Our report
190 illustrates the feasibility of using relatively simple weighting adjustments to make the estimates
191 of the studies directly comparable. Hence, it represents a significant advance over the existing,
192 semi-qualitative use of the two data sources by the nephrology research community. In
193 particular, it was previously stated that the results of KEEP are best understood in “the context of
194 the US population” and in comparison against results from a representative sample
195 (NHANES)(22,24). By applying methodologies to address the self-selection bias in KEEP we
196 took this approach to its logical conclusion and derived a common analytic file that is available
197 for the epidemiologic surveillance of CKD in the general population.

198 Despite the ability of our methodology to bring about a quantitative agreement between
199 NHANES and weighted versions of KEEP, our analyses have certain limitations. First,
200 recruitment efforts for the KEEP survey was rather heterogeneous over the continental US and
201 may have not reached some population segments. This potential source of bias may not be
202 accounted for in our approach and is a topic under investigation using recruitment information
203 like screening event location, and measures of advertising ‘effort’ as potential covariates. In our
204 analyses we handled these factors indirectly by including the regional affiliates as clusters in the
205 GEE estimation procedure. It is likely that more detailed modeling may have led to more precise
206 estimation of the prevalence of the different stages of CKD. Another limitation concerns the
207 handling of race and ethnicity, which are clinically significant correlates of CKD risk in the
208 source datasets. Whereas NHANES collects detailed race and ethnicity information, the
209 coarseness of classification in public use files likely combines groups with unequal risk. These

210 categories were not entirely congruent with the ones adopted in the KEEP program, thus raising
211 the possibility of residual confounding in our weighting schemes. Finally, adjustment by post-
212 stratification typically relies on a known reference distribution such as from official census
213 statistics.

214 In summary, we present the first to our knowledge application of self-selection bias
215 correction methodologies for the analysis of data related to the prevalence of CKD in the general
216 US population. We found that two methodologies, i.e. IPW and to a lesser degree post-
217 stratification weighting may be used to render estimates from a self-selected cohort (KEEP)
218 directly comparable to those from a national representative sample (NHANES). Future studies
219 should build on this effort and utilize this novel analytic set to expand the existing national CKD
220 surveillance system. Such efforts may be directed towards understanding the epidemiology of
221 CKD by utilizing the geographic information collected during KEEP so as to build prevalence
222 maps of this challenging, costly chronic disease over both space and time.

223 **MATERIALS AND METHODS**

224 **Study Populations**

225 We used individual level data from participants in the National Kidney Foundation's
226 (NKF) Kidney Early Evaluation Program (KEEP) and from participants in the National Health
227 and Nutrition Examination Survey (NHANES). Both KEEP and NHANES are national samples:
228 KEEP is a self-selected sample of adults with elevated risk of kidney disease coordinated by
229 local NKF organizations, and NHANES is a nationally representative sample designed to study
230 health and nutritional status of adults and children in the United States. KEEP used advertising
231 campaigns to attract participants to examinations coordinated by regional affiliates. Advertising
232 targeted participants that were at least 18 years old with risk factors for CKD: high blood
233 pressure, diabetes, or a family history of diabetes or hypertension or kidney disease. We obtained
234 data from NKF for KEEP participants assessed by 48 regional affiliates from 2001 to the end of
235 2012 (185,511 records, SAS file name keep_saf_2013). Participants were excluded if <20 years
236 of age, on dialysis, were pregnant, had a previous kidney transplant, if eGFR could not be
237 determined, were lacking a valid state of residence or had other invalid demographic variable
238 values. NHANES employs cross-sectional, multi-stage, stratified, cluster probability samples
239 with several subgroups oversampled to improve precision. The subgroups vary by two-year
240 survey period with respect to status race, ethnicity and poverty level. We studied participants
241 attending mobile examination centers (MEC) during six survey periods covering 2001 – 2012.

242

243 **Selection Model Variables**

244 Covariates for selection models were chosen if they were related to messages used for
245 KEEP recruitment, if they could be identified in both datasets, and if they received or could be

246 re-encoded similarly in both datasets over the 2001 – 2012 study. Demographic covariates
247 included continuous age, sex, and race/ethnicity (non-Hispanic White, non-Hispanic Black,
248 Mexican/Other Hispanic, Other). Factors related to KEEP recruitment advertising included
249 patient reported diabetes, hypertension, CKD, and family history of CKD, diabetes or
250 hypertension. Other self-reported factors potentially associated with KEEP participation were
251 obesity status, smoking, family history of heart attack, and participant cardiovascular disease
252 (self-report of stroke, congestive heart failure, angina or heart attack). We also included variables
253 for participant socioeconomic status, education and type of insurance.

254

255 **CKD Endpoints**

256 Our CKD end points to be estimated from KEEP data after adjusting for self-selection were the
257 single sample ('point') prevalence of impaired renal function: CKD Stages 3, eGFR 30 - <60
258 ml/min/1.73 m², Stages 3-5, eGFR <60 ml/min/1.73 m², and Stage 4-5 CKD, eGFR <30
259 ml/min/1.73 m². eGFR was estimated using the Chronic Kidney Disease Epidemiology
260 Collaboration (CKD-EPI) equation based on race, sex and serum creatinine(25,26). KEEP serum
261 creatinine values were standardized to the Cleveland Clinic(27) prior to calculation eGFR. Urine
262 creatinine concentrations before 2007 in the NHANES data were standardized to later years
263 using a piece-wise regression adjustment described for NHANES results (28).

264

265 **Statistical Analyses**

266 The analyses had two phases: 1) estimation of propensity scores using NHANES and
267 KEEP, and 2) estimation of CKD prevalence. Sampling weights for NHANES were the two-year
268 MEC weights. We conducted analyses to determine whether individual propensity scores for

269 KEEP were sensitive to the approach used in developing the reference population (Supplemental
270 Methods). We created an NHANES summary file composed of weighted reference population
271 frequencies for all cross-tabulations of our selection model covariates. These weighted
272 frequencies considered the complex sampling design and used NHANES PSU, strata, and MEC
273 in calculations. We appended these weighted subgroup frequencies to KEEP data to also estimate
274 propensity scores. Analyses using the two approaches confirmed that propensity scores for
275 KEEP participants were not sensitive how we created a reference population. Using the
276 individual NHANES records and MEC without upscaling to subgroup frequencies for the total
277 reference population avoids the problem of some subgroup cells estimated from very few
278 NHANES observations. Our approach also enables use of continuous variables like age and BMI
279 in estimating propensity scores.

280 Descriptive summaries of NHANES participants by subgroups (e.g., age, sex,
281 race/ethnicity) were estimated using methods that accounted for the complex sampling design
282 when summarizing the reference population (SURVEYFREQ, SAS v9.4). The population
283 distribution of KEEP for these subgroups were estimated without and with weighting for self-
284 selection.

285 For propensity score analyses we used boosted the classification and regression tree
286 (CART) methods implemented in the *twang* R-package(29), as this method outperforms logistic
287 regression(30) and can utilize sampling weights. We entered NHANES observations using the
288 MEC weights, and KEEP observations using sampling weights equal to 1.0. The shrinkage
289 parameter was set at 0.001 and number of random trees equaled 20,000. We varied interaction
290 depths from four to six levels and assessed the balance achieved by comparing KEEP weighted
291 frequencies to the expected frequencies based on the NHANES reference population and selected

292 as our propensity score estimation model the one with best agreement between KEEP
293 frequencies expected for the reference population and the weighted frequencies from the boosted
294 CART models. Separate propensity score analyses by two-year NHANES sampling periods
295 estimated weights that tracked changes in KEEP sampling distribution and intensity by regional
296 KEEP affiliates. Achieved covariate balance by NHANES survey period was assessed using
297 unstandardized and standardized differences in proportions(31), and logistic regression was used
298 to assess whether CKD Stage 3-5 prevalence in the unweighted KEEP sample was constant over
299 IPW deciles(32).

300 We conducted analyses to determine whether individual propensity scores for KEEP
301 were sensitive to the approach used in developing the reference population (Supplemental
302 Methods). We created an NHANES summary file composed of weighted reference population
303 frequencies for all cross-tabulations of our selection model covariates. These weighted
304 frequencies considered the complex sampling design and used NHANES PSU, strata, and MEC
305 in calculations. We appended these weighted subgroup frequencies to KEEP data to also estimate
306 propensity scores. Analyses using the two approaches confirmed that propensity scores for
307 KEEP participants were not sensitive how we created a reference population. Using the
308 individual NHANES records and MEC without upscaling to subgroup frequencies for the total
309 reference population avoids the problem of some subgroup cells estimated from very few
310 NHANES observations. Our approach also enables use of continuous variables like age and BMI
311 in estimating propensity scores.

312 The second analysis stage had the goal of estimating CKD prevalence by Stage using the
313 KEEP sample but adjusted for self-selection. Unweighted and weighted prevalence and 95%
314 confidence interval are reported (SURVEYFREQ, SAS v9.4) along with population average

315 estimates that account for participants clustered within regional affiliate recruitment and
316 examination programs (GEE, GENMOD, SAS v9.4). Confidence intervals based on robust
317 standard errors are reported. Intercept-only models estimated overall prevalence during 2001-
318 2012 by CKD Stage and during 2003-2012 for albuminuria. Models with fixed effects for age
319 and sex and for KEEP screening year estimated prevalence grouped by these factors. Linear time
320 models and models with restricted cubic splines ($k = 3$ knots) were used to estimate trends in
321 prevalence. Prevalence estimates from NHANES for comparison with weighted KEEP
322 accounted for the complex sampling design but did not use a GEE approach
323 (SURVEYLOGISTIC, SAS v9.4).

324

325 **Data availability**

326 NHANES data are available from the survey website at the Center for Disease Control
327 (<https://www.cdc.gov/nchs/nhanes/index.htm>). The KEEP data that support the findings of this
328 study are available from the National Kidney Foundation (NKF) but restrictions apply to the
329 availability of these data, which were used under license for the current study, and so are not
330 publicly available. Data are however available from the authors upon reasonable request and
331 with permission of NKF.

332 This secondary analysis of the KEEP and NHANES was approved by the Human Research
333 Protection Office (HRPO) of the University of New Mexico Health Sciences Center (Decision
334 Number HRCC #14-264 on 9/12/2014).

335 **REFERENCES**

- 336 1. 2015 USRDS Annual Data Report [Internet]. Available from:
337 <https://www.usrds.org/2015/view/Default.aspx> [cited 2016 Jul 14]
- 338 2. Powe NR, Plantinga L, Saran R: Public health surveillance of CKD: principles, steps, and
339 challenges. *Am. J. Kidney Dis.* 53: S37-45, 2009
- 340 3. Saran R, Hedgeman E, Plantinga L, Burrows NR, Gillespie BW, Young EW, Coresh J,
341 Pavkov M, Williams D, Powe NR, CKD Surveillance Team: Establishing a national
342 chronic kidney disease surveillance system for the United States. *Clin J Am Soc Nephrol* 5:
343 152–161, 2010
- 344 4. Sherman RL, Henry KA, Tannenbaum SL, Feaster DJ, Kobetz E, Lee DJ: Applying Spatial
345 Analysis Tools in Public Health: An Example Using SaTScan to Detect Geographic Targets
346 for Colorectal Cancer Screening Interventions. *Preventing Chronic Disease* [Internet] 11:
347 2014 Available from: http://www.cdc.gov/pcd/issues/2014/13_0264.htm [cited 2014 Aug
348 18]
- 349 5. Chronic Kidney Disease (CKD) Surveillance Project [Internet]. Available from:
350 <https://nccd.cdc.gov/ckd/> [cited 2016 Jun 16]
- 351 6. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS:
352 Prevalence of chronic kidney disease in the United States. *JAMA* 298: 2038–2047, 2007
- 353 7. Castro AF, Coresh J: CKD surveillance using laboratory data from the population-based
354 National Health and Nutrition Examination Survey (NHANES). *Am. J. Kidney Dis.* 53:
355 S46-55, 2009
- 356 8. Stauffer ME, Fan T: Prevalence of Anemia in Chronic Kidney Disease in the United States.
357 *PLOS ONE* 9: e84943, 2014
- 358 9. Wu B, Bell K, Stanford A, Kern DM, Tunceli O, Vupputuri S, Kalsekar I, Willey V:
359 Understanding CKD among patients with T2DM: prevalence, temporal trends, and
360 treatment patterns—NHANES 2007–2012. *BMJ Open Diab Res Care* [Internet] 4: 2016
361 Available from: <http://drc.bmj.com/content/4/1/e000154.abstract>
- 362 10. Vassalotti JA, Li S, Chen S-C, Collins AJ: Screening populations at increased risk of CKD:
363 the Kidney Early Evaluation Program (KEEP) and the public health problem. *Am. J. Kidney*
364 *Dis.* 53: S107-114, 2009
- 365 11. Shryock HS, Siegel JS: *The Methods and Materials of Demography*. Academic Press;
- 366 12. Klein RJ, Schoenborn CA: Age adjustment using the 2000 projected U.S. population.
367 *Healthy People 2010 Stat Notes* 1–10, 2001

- 368 13. Bethlehem J: Selection Bias in Web Surveys. *International Statistical Review* 78: 161–188,
369 2010
- 370 14. Bethlehem J: Can We Make Official Statistics with Self-Selection Web Surveys? [Internet].
371 In: *Proceedings of Statistics Canada Symposium 2008*, 2009 Available from:
372 <http://www.statcan.gc.ca/pub/11-522-x/2008000/article/10989-eng.pdf>
- 373 15. Bethlehem J: Selection Bias in Web Surveys. *International Statistical Review* 78: 161–188,
374 2010
- 375 16. Bethlehem J: Can We Make Official Statistics with Self-Selection Web Surveys? [Internet].
376 In: *Proceedings of Statistics Canada Symposium 2008*, 2009 Available from:
377 <http://www.statcan.gc.ca/pub/11-522-x/2008000/article/10989-eng.pdf>
- 378 17. Steinmetz S, Tijdens K, de Pedraza P: Comparing different weighting procedures for
379 volunteer web surveys. Amsterdam Institute for Advanced Labour Studies, University of
380 Amsterdam;
- 381 18. Schonlau M, van Soest A, Kapteyn A: Beyond demographics: are “Webographic” questions
382 useful for reducing the selection bias in web surveys? [Internet]. In: *Proceedings of the*
383 *Survey Research Methods Section, American Statistical Association*, 2007 Available from:
384 <http://www.amstat.org/sections/srms/Proceedings/y2007/Files/JSM2007-000026.pdf>
- 385 19. Lee S, Valliant R: Estimation for Volunteer Panel Web Surveys Using Propensity Score
386 Adjustment and Calibration Adjustment. *Sociological Methods & Research* 37: 319–343,
387 2009
- 388 20. Bethlehem J: Solving the Nonresponse Problem With Sample Matching? *Social Science*
389 *Computer Review* 34: 59–77, 2016
- 390 21. Loosveldt G, Sonck N: An evaluation of the weighting procedures for an online access
391 panel survey. *Survey Research Methods* 2: 93–105, 2008
- 392 22. Jurkowitz CT, Qiu Y, Wang C, Gilbertson DT, Brown WW: The Kidney Early Evaluation
393 Program (KEEP): program design and demographic characteristics of the population. *Am. J.*
394 *Kidney Dis.* 51: S3-12, 2008
- 395 23. McCullough PA, Brown WW, Gannon MR, Vassalotti JA, Collins AJ, Chen S-C, Bakris
396 GL, Whaley-Connell AT: Sustainable community-based CKD screening methods employed
397 by the National Kidney Foundation’s Kidney Early Evaluation Program (KEEP). *Am. J.*
398 *Kidney Dis.* 57: S4-8, 2011
- 399 24. Whaley-Connell AT, Kurella Tamura M, Jurkowitz CT, Kosiborod M, McCullough PA:
400 Advances in CKD Detection and Determination of Prognosis: Executive Summary of the
401 National Kidney Foundation–Kidney Early Evaluation Program (KEEP) 2012 Annual Data
402 Report. *American Journal of Kidney Diseases* 61: S1–S3, 2013

- 403 25. Levey AS, Stevens LA, Schmid CH, Zhang Y (Lucy), Castro AF, Feldman HI, Kusek JW,
404 Eggers P, Van Lente F, Greene T, Coresh J: A New Equation to Estimate Glomerular
405 Filtration Rate. *Ann Intern Med* 150: 604–612, 2009
- 406 26. Matsushita K, Mahmoodi BK, Woodward M, Emberson JR, Jafar TH, Jee SH,
407 Polkinghorne KR, Shankar A, Smith DH, Tonelli M, Warnock DG, Wen C-P, Coresh J,
408 Gansevoort RT, Hemmelgarn BR, Levey AS: Comparison of risk prediction using the
409 CKD-EPI equation and the MDRD Study equation for estimated glomerular filtration rate.
410 *JAMA* [Internet] 307: 2012 Available from:
411 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3837430/> [cited 2015 Oct 20]
- 412 27. Stevens LA, Stoycheff N: Standardization of serum creatinine and estimated GFR in the
413 Kidney Early Evaluation Program (KEEP). *Am. J. Kidney Dis.* 51: S77-82, 2008
- 414 28. NHANES 2007 - 2008: Albumin & Creatinine - Urine Data Documentation, Codebook, and
415 Frequencies [Internet]. Available from: [http://wwwn.cdc.gov/nchs/nhanes/2007-](http://wwwn.cdc.gov/nchs/nhanes/2007-2008/ALB_CR_E.htm)
416 [2008/ALB_CR_E.htm](http://wwwn.cdc.gov/nchs/nhanes/2007-2008/ALB_CR_E.htm) [cited 2016 Jun 21]
- 417 29. Ridgeway G, McCaffrey D, Morral A, Burgette L, Griffin BA: twang: Toolkit for
418 Weighting and Analysis of Nonequivalent Groups [Internet]. Available from: [https://cran.r-](https://cran.r-project.org/web/packages/twang/)
419 [project.org/web/packages/twang/](https://cran.r-project.org/web/packages/twang/)
- 420 30. McCaffrey DF, Ridgeway G, Morral AR: Propensity score estimation with boosted
421 regression for evaluating causal effects in observational studies. *Psychol Methods* 9: 403–
422 425, 2004
- 423 31. Austin PC, Grootendorst P, Anderson GM: A comparison of the ability of different
424 propensity score models to balance measured variables between treated and untreated
425 subjects: a Monte Carlo study. *Stat Med* 26: 734–753, 2007
- 426 32. Brookhart MA, Wyss R, Layton JB, Stürmer T: Propensity Score Methods for Confounding
427 Control in Nonexperimental Research. *Circulation: Cardiovascular Quality and Outcomes*
428 6: 604–611, 2013
- 429
- 430

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436 in 2017.

437

438 **Author Contributions**

439 All co-authors contributed in this collaborative work: Dr OM programmed the analyses in SAS,
440 created graphs and tables and drafted the Methods and Results of the manuscript. Dr VSP,
441 oversaw statistical analyses and contributed in the Methods section. Dr's KM, JV, AG
442 contributed their in-depth knowledge of the KEEP and NHANES datasets and contributed
443 sections in Introduction, Methods and Discussion. Dr MU contributed sections in the
444 Introduction and Discussion. Dr CA devised the overall analytic strategy and prepared the
445 Introduction and the Discussion sections of the first draft of the text. All authors, interpreted
446 results and modified the draft of the text over four iterations in order to produce the final version
447 of the manuscript.

448

449 **Additional Information**

450 *Competing Interests Statement:* The authors declare no competing interests

451

452 **Supplementary Information**

453 Supplementary Methods and Results are available from the journal website

454 Table 1. Self-reported characteristics of NHANES reference population and KEEP participants
 455 without and with inverse probability weighting, 2001-2012. CHF/CAD/stroke – congestive heart
 456 failure/coronary artery disease or stroke; CKD – chronic kidney disease; KEEP – Kidney Early
 457 Evaluation Program; NHANES - National Health and Nutrition Examination Survey
 458

	NHANES (n = 28,517)		KEEP (n = 127,149)		
	Weighted		Unweighted	Weighted	
	n	%	n	%	%
Age					
20-39	9,396	36.9	21,625	17.0	35.9
40-59	9,317	39.4	54,931	43.2	39.4
60-69	4,526	11.9	27,423	21.6	12.5
70+	5,278	11.8	23,170	18.2	12.2
Female	14,230	51.1	86,076	67.7	52.2
Race/Ethnicity					
Mexican American/Other Hispanic	7,116	12.8	16,275	12.8	14.9
non-Hispanic White	13,852	70.8	57,078	44.9	68.8
non-Hispanic Black	5,737	10.5	40,577	31.9	11.2
Other	1,812	5.9	13,219	10.4	5.2
Diabetes	3,736	9.6	36,309	28.6	8.5
Hypertension	9,777	29.7	69,813	54.9	31.6
Chronic kidney disease	731	2.0	5,562	4.4	1.7
CHF/CAD/Stroke	3,236	8.5	15,885	12.5	8.4
Diabetes family history	12,162	40.8	71,001	55.8	44.0

	NHANES		KEEP		
	<i>(n</i> = 28,517)		<i>(n</i> = 127,149)		
	Weighted		Unweighted	Weighted	
	<i>n</i>	%	<i>n</i>	%	%
Heart attack family history	3,599	13.8	43,885	34.5	13.3
Weight status					
Overweight	9,782	33.9	41,409	32.6	36.6
Obese	9,783	32.9	46,480	36.6	35.8
Smoking status					
Smoker	6,313	22.8	13,145	10.3	22.1
Former smoker	7,248	24.8	32,981	25.9	25.0
Insurance					
None reported	6,534	19.3	27,816	21.9	18.3
Insured	19,773	75.5	91,718	72.1	76.9
Medicaid	2,210	5.2	7,615	6.0	4.9
Education					
Less than high school or GED	8,080	18.4	19,642	15.4	18.9
High school or GED	6,684	24.1	32,702	25.7	22.9
Greater than school graduate	13,753	57.5	74,805	58.8	58.2

459

460

461 Table 2. CKD prevalence estimated from NHANES and from KEEP without and with inverse
 462 probability weighting, 2001 – 2012. Weighted estimates accounted for NHANES sampling
 463 design or self-selection by KEEP. KEEP GEE estimates accounted for participant clustering within
 464 regional affiliates. CKD – chronic kidney disease; KEEP – Kidney Early Evaluation Program;
 465 NHANES - National Health and Nutrition Examination Survey
 466

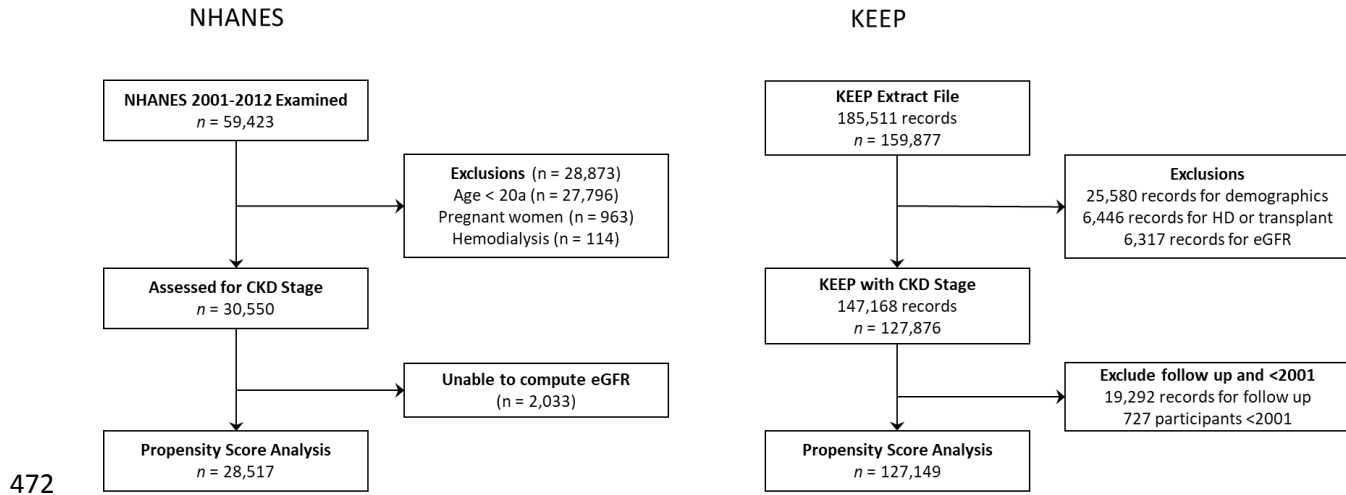
Measure	NHANES (<i>n</i> = 28,517)		KEEP (<i>n</i> = 127,149)				
	<i>n</i>	Weighted % (95% CI)	<i>n</i>	Unweighted % (95% CI)	Unweighted-GEE % (95% CI)	Weighted % (95% CI)	Weighted-GEE % (95% CI)
CKD Stage 3	2,453	6.23 (5.82-6.66)	16,706	13.14 (12.95-13.33)	12.83 (11.88-13.85)	8.57 (8.30-8.85)	6.45 (5.70-7.28)
CKD Stage 3-5	2,692	6.73 (6.30-7.19)	17,973	14.14 (13.94-14.33)	13.86 (12.88-14.90)	9.14 (8.86-9.43)	6.90 (6.12-7.78)
CKD Stage 4-5	239	0.51 (0.43-0.59)	1,267	1.00 (0.94-1.05)	1.01 (0.93-1.09)	0.55 (0.50-0.60)	0.52 (0.42-0.64)

467

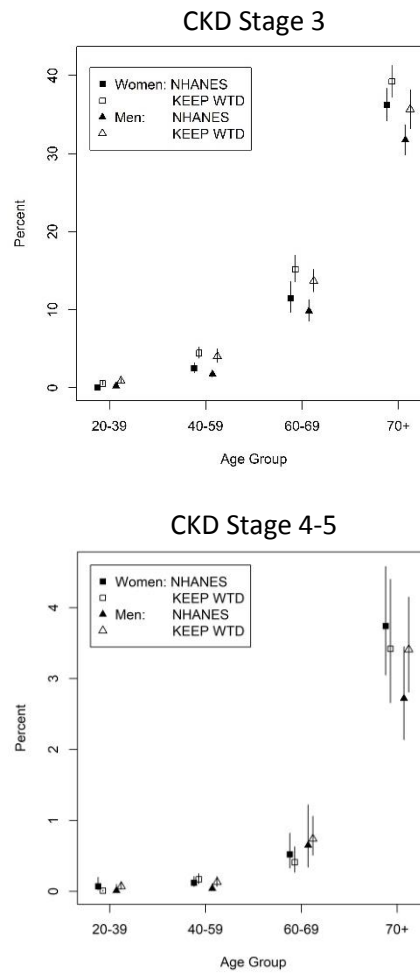
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470 Figure 1. National Health and Nutrition Examination Survey (NHANES) and Kidney Early
471 Evaluation Program (KEEP) participation in study.

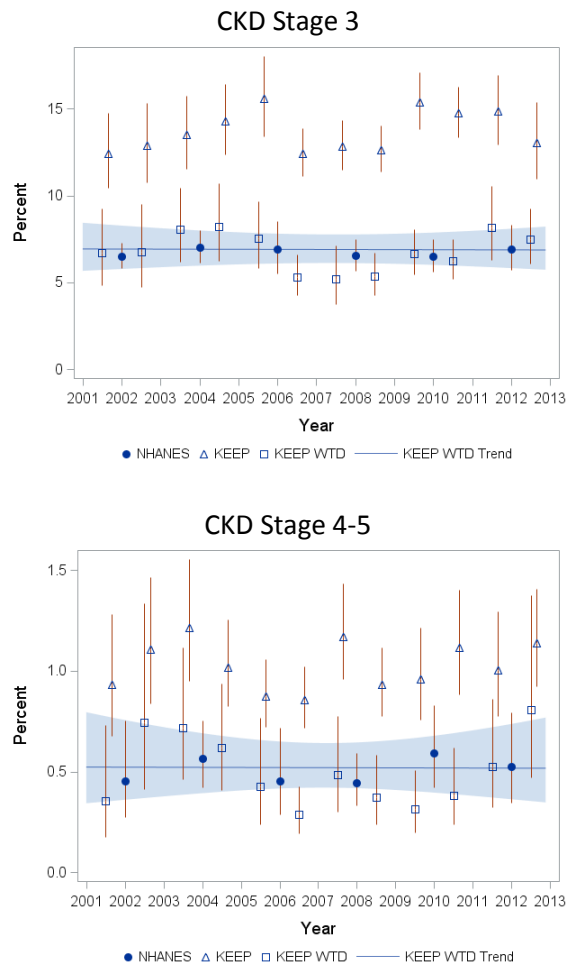


473 Figure 2. Prevalence of CKD Stage 3 and Stage 4-5 by year screened for KEEP and NHANES.
474 (KEEP – Kidney Early Evaluation Program; NHANES - National Health and Nutrition
475 Examination Survey)



476

477 Figure 3. Prevalence (%) of CKD Stage 3 and Stage 4-5 by year screened for KEEP and
478 NHANES. (KEEP – Kidney Early Evaluation Program; NHANES - National Health and
479 Nutrition Examination Survey)



480

481 **Figure Legends**

482 Figure 1. National Health and Nutrition Examination Survey (NHANES) and Kidney Early
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484

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