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Associations between Socio-Demographic Characteristics and 1 **Chemical Concentrations Contributing to Cumulative Exposures in** 2 the United States 3 Hongtai Huang^{1,2}, Ph.D., Rogelio Tornero-Velez², Ph.D., Timothy M. 4 Barzyk², Ph.D. 5 6 ¹Oak Ridge Institute for Science and Education (ORISE) and ²National Exposure Research Laboratory, U.S. Environmental Protection Agency, 7 Research Triangle Park, NC 27709 8 Address correspondence to H. Huang, U.S. Environmental Protection Agency, 9 National Exposure Research Laboratory, 109 T.W. Alexander Drive, Mail 10 Code E205-2, Room D-482, Research Triangle Park, NC 27711 USA. 11 12 Telephone: (919) 541- 5407. Fax: 919-541-9444. Email: 13 Huang.Hongtai@epa.gov. **Running Title:** Quantifying Combined Effects of Multiple Stressors 14 15 This research was supported in part by an appointment to the Post-doctoral Research Program at the U.S. Environmental Protection Agency's National 16 17 Exposure Research Laboratory (Research Triangle Park, NC) administered by the Oak Ridge Institute for Science and Education through an Interagency 18 19 Agreement between the U.S. Department of Energy and the U.S.

20 Environmental Protection Agency. The views expressed in this article are

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- 22 the U.S. Environmental Protection Agency.
- 23 All authors declare no actual or potential competing financial interests.

24 Abstract

Background: Association rule mining (ARM) has been widely used to identify
associations between various entities in many fields. Although some studies
have utilized it to analyze the relationship between chemicals and human
health effects, fewer have used this technique to identify and quantify
associations between environmental and social stressors.

30 Methods: Socio-demographic variables were generated based on U. S.

- 31 Census tract-level income, race/ethnicity population percentage, education
- level, and age information from 2010-2014, 5-year summary files in the
- 33 American Community Survey (ACS) database, and chemical variables were
- 34 generated by utilizing the 2011 National-Scale Air Toxics Assessment (NATA)
- 35 census tract-level air pollutant exposure concentration data. ARM was then
- applied to quantify and visualize the associations between the chemical and
- 37 socio-demographic variables.

38 Results: Census tracts with a high percentage of racial/ethnic minorities, and

39 populations with low income, tended to have higher estimated chemical

- 40 exposure concentrations (4th quartile), especially for diesel PM, 1, 3-
- 41 butadiene, and toluene. In contrast, census tracts with an average
- 42 population age of 40 to 50 years old, a low percentage of racial/ethnic
- 43 minorities, and moderate-income levels, were more likely to have lower
- 44 estimated chemical exposure concentrations (1st quartile).
- 45 Conclusion: Unsupervised data mining methods can be used to evaluate
- 46 potential associations between environmental inequalities and social
- 47 disparities, while providing support in public health decision-making
- 48 contexts.
- 49 Key words: Multiple Stressors, Rule Mining, Cumulative Risks, Combined
- 50 Effects, Environmental Justice
- 51

52 **INTRODUCTION**

53 Quantitatively evaluating the combined effects of multiple 54 chemical/non-chemical stressors has been simultaneously a crucial focus of 55 and a challenge for cumulative risk assessment (CRA)¹. CRA defines 56 cumulative risk as 'the combined risks from aggregate exposures to multiple 57 agents or stressors'². Environmental Justice (EJ) communities are often host to multiple chemical and non-chemical stressors, such as poverty or pre-58 59 existing health conditions, which could decrease individual or population 60 resilience, and increase the potential impacts from chemical exposures³. The 61 role of CRA in public health decision making related to EJ is vital⁴, and there have been a significant number of methodological approaches developed 62 63 which intend to capture the combined effects of multiple stressors in 64 addressing EJ issues⁵.

65 In general, most of the approaches used in CRA chemical/non-66 chemical studies can be divided into three categories: effect-based (topdown), stressor-based (bottom-up) and the hybrid of these two, 67 vulnerability-based^{5, 6}, which considers impacts from a number of chemical 68 and non-chemical stressors. In practice, vulnerability-based studies utilize 69 70 existing data and information, and can also effectively address the prioritized 71 stressors without exhaustively considering all the non-chemical or chemical variables. Several guantitative CRA studies belong to this category⁷⁻¹⁷. 72 73 Specifically, chemical or socio-demographic stressors of interest were

74 quantified and used as the basis to either compare exposure levels or health 75 effects among different groups in the population⁸⁻¹⁶, or serve as a screening 76 tool to address cumulative impacts in areas featured by social disadvantage^{7,} 77 ¹⁷. Other quantitative measures or indices such as Margin of Exposure (MOE), no observed adverse effect level (NOAEL), benchmark Dose (BMD) 78 79 and reference dose (RfD) were also used to assess the combined health risk of chemical mixtures for regulatory purposes¹⁸. Regression models have 80 81 proved useful in characterizing associations between exposure or health 82 effects and different stressors¹⁹⁻²¹, but this technique does require pre-83 defining the response variable and explanatory variables. Interpretation of 84 the interaction term in the model can also be challenging, especially when there are a large number of variables involved²². 85

Very few CRA studies adopt alternative data mining methods, such as
unsupervised association rule mining techniques, to quantify associations
between chemical/non-chemical stressors and health effects, especially
those related to exposure and dose-response assessments.

Association rule mining (ARM)^{23, 24} has been widely applied in many different scientific areas²⁵⁻²⁹. Recently, researchers used ARM to analyze the relationship between environmental stressors and adverse human health impacts^{30, 31}. There are three main advantages of using ARM. First, it can provide better characterization of the interactions between multiple stressors without having to pre-define them as response or explanatory variables. Second, outputs from this method are in general easily interpretable by
those without an advanced mathematical background ³¹. Finally, as a nonparametric method, ARM makes no assumptions about the probability
distributions of the variables being assessed.

In this study, ARM was applied to analyze the inter-relationships between different chemical/non-chemical stressors, in order to demonstrate the use of advanced data mining techniques to understand social disparities and disproportionate environmental burdens. The null hypothesis is that increased chemical exposures are not associated with combinations of EJrelated variables.

107 DATA AND METHODS

108 Data

Socio-demographic data and chemical exposure estimates were
collected for each census tract across the United States. In total, more than
73 000 census tracts were evaluated, representing more than 317 million
people living in the U.S.

113 Socio-demographic variables were selected based on their relevance to 114 EJ communities. These variables are individual income, race/ethnicity 115 population percentage, educational attainment, and age by sex information 116 at the census tract level from the 2010-2014, 5-Year Summary file in the 117 American Community Survey (ACS) database. Note that the Summary file is 118 not an average of the 5-year period but aggregated data collected 119 continuously on a daily basis for 5 years³². 120 Chemical variables were generated by utilizing the Environmental 121 Protection Agency (EPA) 2011 National-Scale Air Toxics Assessment (NATA), 122 census tract-level, modeled pollutant exposure estimates 123 (http://www.epa.gov/national-air-toxics-assessment/2011-nata-124 assessment-results). Six pollutants were chosen for analysis, including 125 acetaldehyde, benzene, cyanide, particulate matter components of diesel engine emissions (namely diesel PM), toluene, and 1,3-butadiene. These 126 chemicals were selected based on their potential for health impacts as well 127

as their relevance to mobile source (i.e., vehicular traffic) and industrial
emissions, both of which are highly concentrated in EJ areas^{33, 34}.

Socio-demographic variables were binned such that every census tract had a score for each variable, and chemical exposure estimates were divided into quartiles for each census tract. Although variables were selected based on their relevance to EJ communities, given the national scale and lack of pre-defined associations, there was no assumption that EJ relationships would necessarily manifest themselves in the results.

136 Method

Data analysis was performed using statistical software, R (version 3.2.1; R Core Team, Vienna, Austria). Execution of ARM and visualization of the resultant association rules were based on the R packages 'arules'³⁵ and 'arulesViz'³⁶ respectively.

141 Association Rule mining

ARM, a form of frequent item set mining³⁷, is a tool used to search for associations between different variables within a database without explicitly specifying the cause (the left-hand-side, LHS) or corresponding effect (the right-hand-side, RHS). As is the case for many situations, if the values of all variables of concern are binary, i.e., either 0 or 1, the association rule is categorically referred to as market basket analysis²³. Therefore, each observation or record constitutes a 'transaction' which, in our case, refers to a census tract. Each element within a record is an 'item' that corresponds to
a stressor in this study. Essentially, ARM is mining co-occurrence
relationships between two separate sets of items.

152 The proportion of transactions that contain the item set is defined as 153 the support (i.e., the proportion of tracts that contain the stressor) and 154 confidence is the estimated conditional probability of the co-occurrence of 155 both LHS and RHS, or support of the rule given the support of the LHS³⁵. 156 *Lift* is defined as the confidence normalized by the support of the RHS, 157 meaning the conditional probability of rule support given supports of the 158 LHS and RHS²³. High values of support, confidence, and lift are indicative of 159 a strong association rule, in that it involves a large number of observations 160 (i.e., tracts with those characteristics) and therefore can be generalized to a 161 wider scope. When the rule size is only 2, which means that only one item 162 showed up in both the LHS and RHS (such as an income score mapped to a 163 chemical exposure score), the rule can be interpreted in the context of an odds ratio³⁸ and relative risks³⁹. Mathematical relations/derivation between 164 165 these measures can be found in Supplementary Material, Equations (1)-(9).

166 Stressors

167 Census tract-level individual income, race/ethnicity population
168 percentage, and personal education attainment levels were obtained from
169 the ACS 2010-2014, 5-Year Summary file to define, quantify, and assign

170 scores for the demographic variables poverty, race, and education. Variable 171 'poverty' was defined as the percentage of people in each census tract 172 whose ratio of income to the poverty level (over the past 12 months)⁴⁰ is 173 below 1.5. Variable 'race' represents the non-white population percentage at 174 each census tract. The definition of variable 'education' is the percentage of 175 population who received a degree (Associate degree and above) at each 176 census tract. Note that variables were initially calculated as a percentage 177 value for each census tract. A score was then assigned to each census tract 178 given the percentages ranging from score 1 (lowest percentage range – 179 [0,10%] to 10 (highest percentage range – [90%, 100%)). Note that the 180 percentages are evenly divided into ten sub-ranges and therefore, 10 score 181 categories. The education score 8-10 was merged into one score category, 182 and poverty score 7-10 into another, due to the small sample size of these 183 score categories. The number of census tracts associated with each score 184 can be found in Supplementary Material, Table S-1.

The tract-level 'age by sex' variable in the ACS database was used, and the average weighted age calculated for each census tract by summing the products of the percentage of each age group and the median (or predefined value if there was no upper bound of the interval) of the corresponding age interval. This variable was then sub-divided into 7 variables, namely '0-20 years, '20-30 years, '30-35 years, '35-38 years, '38-40 years, '40-50 years and '50-100 years. These age intervals were chosen based on biological stages and sample size (see Supplementary Material,
Table S-1). We calculated the average of weighted age by sex assuming that
the ratio of male to female was 1:1.

Each of the six chemical variables was converted into four quartile 195 196 variables based on the chemical concentrations for each tract. Taking 197 benzene as an example, the original benzene exposure concentration value 198 for each census tract was converted into a label depending on which quartile 199 that particular concentration value resides. For instance, if the value was 200 within the first quartile of benzene exposure concentrations across all census 201 tracts, the numeric value was converted to a category label 'Q1'. As six 202 chemical variables were considered, these became 24 distinct quartile 203 variables.

In total, there were 56 variables: 10 race/ethnicity groups, 8 education groups, 7 poverty groups, 7 age groups, and 24 chemical quartile groups.

207 Data Analysis

Two separate experiments were conducted by applying the ARM method with different minimum support thresholds. In the first experiment, the LHS of the association rule was set to be only non-chemical stressors and the RHS to be only chemical variables for interpretation purposes. In order to understand the internal connections among non-chemical stressors, the second experiment was performed requiring both the LHS and RHS to be
socio-demographic variables. The rules were only analyzed when the lift was
greater than 1. In addition, the focus was on those rules with size equal to 2
(a 1-to-1 map of LHS and RHS) in order to better utilize the statistical
measures Odds Ratio (OR) and Relative Risk (RR).

218 The 95% confidence intervals (CI) were estimated for OR using 219 bootstrapping⁴¹ random sampling for 10 000 times, for particular rules of 220 interest. Specifically, a new data set was created each time using random 221 sample records with replacement, and ARM was applied on these newly 222 created data. The rule of interest was then obtained and the corresponding 223 OR calculated. For 10 000 bootstrapping runs, we eventually had 10 000 224 new data sets and corresponding OR values. The 2.5 and 97.5 percentiles 225 were identified among these 10 000 OR values, which was the estimated 95% CI. 226

The chemical exposure was also compared to the concentration levels associated with each of the three demographic variables (poverty, race/ethnicity & education attainment) using Student's t tests, in order to examine the statistical significance of the differences between score categories of these variables.

233 **RESULTS**

234 Association Rules

235 Because there were 56 total variables, the possible number of item set combinations was 2^{56} -1 ($\approx 7.2 \times 10^{16}$, or 72 quadrillion) as the basis for 236 237 generating association rules. With confidence set to be 0.1 and support 0.1, 238 212 rules were obtained. Without setting a lower bound on the confidence 239 value, there were 30 932 rules given a minimum support threshold of 0.1 240 (details in Supplementary Material, Table S-2). Imposed criteria regarding 241 the content of the LHS or RHS further restricted the number of rules. 242 -Rules with Larger Minimum Support Values 243 Table 1 lists the rules for support >0.1 and lift >1.0 and shows that

only two demographic variables, "Race Minority Score 1" (0-10% non-white)
and "Age= 40-50" resulted as the LHS of these rules while most of the
chemical variables represented first or second quartile concentrations,
except cyanide. Odds ratios for these rules ranged from 1.433 to 2.947.

The graph-based visualization of all the association rules with support >0.1 and lift >1 is shown in Figure 1. All associations are connected through blank circles. The size of a circle represents the co-occurrence support value, and color indicates the lift value of the rule. Larger circles mean higher support values, while deeper colors suggest greater lift. It can be observed that both variables 'Age = 40-50' (average population age of 40 to 50 years old) and Race score 1 (low non-white percentage) were associated with 1st
 quartile chemicals.

Table 2 shows all the association rules with criteria that both the LHS and RHS were socio-demographic variables, and with minimum support value greater than 0.1 and lift greater than 1. Only three variables appeared in these 6 rules, including "Race Minority Score 1", "Age=40-50" and "Poverty Score 2". Interestingly, all three of these variables were interacting with each other, forming three loops.

262 -Rules with Smaller Minimum Support Values

If a similar criterion was applied, but with the minimum support value 263 264 set to 0.01, more rules were found with size greater than 2 (see Supplementary Material, Table S-3). Not only did 1st and 2nd quartiles 265 266 chemical variables show up in the RHS, but also those in the fourth 267 quartiles. Corresponding LHS of the fourth quantile rules were high race 268 minority scores (high non-white percentage), high poverty scores (high low-269 income percentage), and low education scores (low percentage of degree 270 attainment).

Table 3 summarizes the total number of rules with particular LHS and RHS given a minimum support value of 0.01 and lift greater than 1. For the LHS, the focused was on low and high demographic scores. All the rules with race minority score 1 and race minority score 2 on the LHS were pooled together, since they both represent low percentages of non-white
population, and so were race minority scores 7, 8, 9 and 10. Similarly, all
the rules with poverty score 1, 2, and 3 were evaluated at the same time,
and those with education score 1, 2, and 3 examined together. For the RHS,
the total number of rules was counted that contained particular quartiles of
chemical exposure concentrations given the specific LHS.

281 In general, rules containing low race score (low non-white 282 percentage), low poverty score (less poor census tract), and average 283 population age of 38 to 50 years old were more likely to contain the first 284 quartile (i.e., Q1 or lower values) of chemical exposure concentrations, while 285 rules encompassing high race score (high non-white percentage), high 286 poverty score (poorer tracts), and high education score (high percentage of 287 residents with education) tended to include the fourth quartile of chemical 288 exposure concentration (or Q4, indicating high chemical exposure 289 concentration). Specifically, 20 out of 29 rules (69%) that contained race 290 score 7, 8, 9 or 10 had Q4 as their RHS, while only 16 out of 342 rules (5%) 291 that contained race score 1 or 2 included Q4. The number of rules with high 292 race score increased monotonically, as the chemical exposure concentration increased in the RHS (from 0 for Q1 to 20 for Q4). In contrast, the number 293 of rules with low race scores gradually decreased as the chemical 294 295 concentration became higher (from 144 for Q1 to 22 for Q4).

There were 9 out of 14 rules (64%) with poverty score 7-10 containing Q4, but there were only 27 out of 354 rules (8%) with poverty score 1, 2 or 3 containing Q4. A high poverty score was positively associated with chemical exposure concentrations in terms of rule number (from 1 rule for Q1, to 9 for Q4), while low poverty score had a negative association with chemical exposure concentration (144 for Q1, and only 28 for Q4).

Rules with average population age of 38-40 and 40-50 years old tended to have Q1 as their RHS (50% and 37% respectively). As the RHS of these rules changed from Q1 to Q4, the rule numbers decreased consistently (from 31 to 8, and 106 to 4 respectively).

Interestingly, rules with high education score (8-10) were associated with Q4 (46%), but those with low education score (1, 2, or 3) were more inclined to contain either Q1 (49%) or Q4 (22%). The number of rules with high education score increased gradually when RHS changed from Q1 to Q4. For rules with low education score, there was no monotonic change in rule numbers when RHS shifted from Q1 to Q4.

Supplementary Material, Table S-4 includes the top 100 rules with both LHS and RHS being demographic variables, minimum support value 0.01, and lift greater than 1. Highest poverty score was associated with average population age of 20-30 years old and the lowest education score. On the other hand, lowest poverty score was related to high educationscores and low race minority scores.

318 To explore further the one-to-one relationship between the LHS and 319 RHS, the rule size was set to be 2 on top of other predefined criteria such as 320 LHS being socio-demographic variables, RHS chemical variables, minimum 321 support value 0.01 and lift greater than 1 (see sample rules in 322 Supplementary Material, Table S-5). Table 4 lists complementary pairs of 323 rules with high and low race scores for given high/low chemical guartiles. 324 The rule with highest odds ratio (5.534, estimated 95% CI 5.102-6.008) had 325 an LHS race score of 10 and RHS fourth quartile diesel. The rule with the 326 same LHS and RHS but low race and exposure values was 'Race Minority' 327 Score = $1 \rightarrow$ Diesel = Q1' for which the odds ratio was 2.893 (estimated 95%) 328 CI 2.818-2.969). The general form of these rules is that 'Race Minority Score 329 = 10 \rightarrow Chemical = Q4' and 'Race Minority Score = 1 \rightarrow Chemical = Q1'. In 330 addition, average population age of 20-30 and 30-35 years old were 331 associated with 'Diesel = Q4' but average population age of 40-50 and 50-100 with Q1 chemical concentrations. All estimated 95% CI for the OR of all 332 333 rules in Table 4 were well above 1 suggesting positive associations.

334

335

337 Student's t-tests

338 Regarding educational attainment, in general, chemical exposure 339 concentration levels for different education scores were statistically different 340 (Bonferroni's corrected a level = 1.79×10^{-3}) except for cyanide compounds 341 (see Supplementary Material, Table S-6). Also, differences between chemical 342 concentration levels for each poverty score were statistically significant for 343 all chemicals (details in Supplementary Material, Table S-7). Except for 344 several pairs of race score categories associated with cyanide and 345 acetaldehyde concentrations, statistically significant differences between 346 different race scores in terms of chemical exposure concentration levels were 347 observed (Supplementary Material, Table S-8).

348 **DISCUSSION**

349 Overview

350 Major Association Rules

351 Among the 212 rules with minimum support value greater than 0.1, 13 major rules were found with the strength measure 'lift' greater than 1 that 352 353 contained socio-demographic variables as their LHS and chemical variables as 354 their RHS. Results presented in Table 1 convey the main message that 355 census tracts with low non-white population percentages (0-10%) or average 356 population age of 40 and 50 years old (which happens to be associated with low poverty and low non-white populations, details in Table 2) are associated 357 with low chemical exposure concentrations (mostly at the first quartiles). 358

359 Six major rules were also found when setting both the RHS and LHS to 360 be socio-demographic variables with similar criteria (in Table 2). As with the 361 results in Table 1, in addition to low percentage of non-white population and 362 average population age of 40-50, poverty score 2 (or, 10% - 20% of the 363 residents within a census tract having income below one-and-a-half times the 364 poverty level) appeared and demonstrated key interactions with the other 365 two socio-demographic variables. This suggests that income level is probably 366 associated with chemical exposure concentration level. Another perspective is 367 that predominantly white census tracts of middle aged people are directly

related to lower exposure levels, and they happen to have low poverty levels,which are thus indirectly related to exposures.

370 Association Rules and EJ Interpretation

371 When the minimum support value was lowered to 0.01 and held other 372 criteria the same, several interesting trends were found regarding the 373 association between demographic variables and exposure concentration 374 levels. Greater proportions of non-white populations and poorer census tracts 375 tended to be exposed to higher chemical concentrations, while tracts with low 376 non-white percentages, wealthy tracts, and those with average population 377 age of 38 to 50 were more likely to have low chemical exposure 378 concentrations (Table 3). Particularly, the number of stronger (lift > 1) and 379 applicable (support > 0.01) association rules with high race score, high 380 poverty score, and higher education scores (contrary to expectations) 381 increased as the chemical exposure concentrations increased from the first to 382 the fourth quartiles; while rules with low race score, low poverty score, and 383 average population age of 38 to 50 decreased as chemical concentrations 384 became higher.

Educational attainment did not show a clear inverse relationship with chemical concentrations when considered by itself on the LHS (Table 3). These may represent a limited sample of highly educated census tracts that were exposed to increased concentrations. However, in general, according to

389 results when comparing socio-demographic variables as both LHS and RHS, 390 (Table S-4), high education was associated with low poverty and low non-391 white population percentages, which experienced lower concentration levels 392 and appeared to be more influential to exposures. Also, when considering 393 multiple socio-demographic variables on the LHS and chemical concentrations 394 on the RHS, educational scores were no greater than 4, suggesting that the 395 majority of tracts that were associated with chemical concentrations (high or 396 low) had populations where less than 40% of the residents have an 397 associate's degree, and were likely driven by the other EJ factors, especially 398 race, income, and age. Wealthier, middle aged, white population experienced 399 lower exposures, and low-income, younger, minority population experienced 400 higher exposures. Education may not be as influential, as long as race and 401 poverty had low scores (i.e., more non-white with higher incomes). 402 Education could vary and still represent lower exposures but itself cannot 403 sufficiently address environmental disparities.

404 Graph-based Visualization

Graph-based visualization of the identified association rules offers better illustrations of the combined effects of multiple chemical and sociodemographic variables. It can be rather useful in displaying associations between variables, especially when the number of involved variables increased and the size of a rule was more than 2 (see Supplementary Material, Figures S-1 & S-2). In conjunction with using other statistical methods such as regression analysis, the combined effects of multiple
stressors upon one response variable can be identified and quantified,
provided that the number of explanatory variables was small (<4) and the
association of interest was statistically significant.

415 The graph-based visualization of the association rules can also serve as 416 the basis for developing more complex mathematical models for 417 environmental studies such as a system dynamic model^{42, 43} or multi-418 objective model^{44, 45}, and provide hints for better ways of clustering and 419 classifications (Supplementary Material, Figures S-1 & S-2). It may also shed 420 lights on potential contributors to disproportionate environmental burdens for 421 certain vulnerable populations such as pregnant women or children who 422 suffer from obesity⁴⁶.

Along with the method developed to explore and identify a group of important variables⁴⁷, this approach can be applied to evaluate the internal relationships among a large number of multiple stressors, and potentially provides a systemic perspective into the environmental issues at hand.

427 *Limitations*

There are three limitations of this study. First, NATA exposure
concentration are simulated data rather than actual observations. The results
presented here may not perfectly reflect the actual chemical exposure levels.
Second, ARM cannot provide exact quantitative relationships between

variables. Therefore, the results cannot be directly compared with those from
other studies. Third, interpretation of other measures such as OR and RR can
be an issue when the rule size is greater than 2.

435 **Conclusion**

Unsupervised data mining methods such as ARM can be applied to EJrelated evaluations of the combined effects of multiple stressors. It
highlights some of the main variables associated with chemical exposures, in
this case race, income, and population age, and suggests that other
variables, such as education, may be less associated with exposures and
more a secondary component of the other socio-demographic variables.

442 Other variables that could be included in future studies include pre-443 existing health conditions, access to health care, epigenetic predisposition, 444 chemical mixtures, and chemical/non-chemical synergistic interactions (e.g., 445 radon and smoking, or toluene and noise). ARM has proven to be an 446 effective methodology for finding associations between specific categories/values (i.e., binned ranges) of EJ variables, which provides more 447 insight into the specifically affected populations. In general, middle aged, 448 449 white, non-poor tracts were associated with lower exposures, and younger, 450 higher poverty, non-white tracts with higher exposures. ARM allows us to 451 investigate each of these variables with respect to their associations to not

452 only chemical exposures but to each other as well. This method could thus453 be used to target solutions to the most applicable variables.

454

455 Supplementary information is available at Journal of Exposure Science and456 Environmental Epidemiology's website.

457

458 Disclaimer

459 This article has been subject to review by the EPA and approved for

460 publication. Although this work was performed as research for the U.S.

461 Environmental Protection Agency, it does not necessarily represent

462 endorsement of official Agency policies.

463 All authors declare no actual or potential competing financial interests.

464

466 **References**

467 1. Callahan MA, Sexton K. If cumulative risk assessment is the answer, what
468 is the question? Environmental Health Perspectives. 2007;115(5):799469 806.

470 2. U.S. EPA (Environmental Protection Agency). Concepts, methods and data

471 sources for cumulative health risk assessment of multiple chemicals,

472 exposures and effects: A resource document. U.S. EPA, National Center

473 for Environmental Assessment, Cincinnati, OH. EPA/600/R-06/013F2007.

474 3. Taylor WC, Poston WSC, Jones L, Kraft MK. Environmental justice:

475 obesity, physical activity, and healthy eating. Journal of Physical Activity

476 & Health. 2006; 3: 30-54.

477 4. Sexton K, Linder SH. The role of cumulative risk assessment in decisions

478 about environmental justice. International Journal of Environmental

479 Research and Public Health. 2010;7(11):4037-49.

480 5. Sexton K. Cumulative risk assessment: an overview of methodological

481 approaches for evaluating combined health effects from exposure to

482 multiple environmental stressors. International Journal of Environmental
483 Research and Public Health. 2012;9(2):370-90.

484 6. Sexton K. Cumulative health risk assessment: finding new ideas and

485 escaping from the old ones. Human and Ecological Risk Assessment: An

486 International Journal. 2014;21(4):934-51.

- 487 7. Alexeeff GV, Faust JB, August LM, Milanes C, Randles K, Zeise L, et al. A
- screening method for assessing cumulative impacts. International Journal
- 489 of Environmental Research and Public Health. 2012;9(2):648-59.
- 490 8. Apelberg BJ, Buckley TJ, White RH. Socioeconomic and racial disparities in
- 491 cancer risk from air toxics in Maryland. Environmental Health
- 492 Perspectives. 2005; 113(6): 693-9.
- 493 9. Barzyk TM, White BM, Millard M, Martin M, Perlmutt LD, Harris F, et al.
- Linking socio-economic status, adverse health outcome, and
- 495 environmental pollution information to develop a set of environmental
- 496 justice indicators with three case study applications. Environmental
- 497 Justice. 2011; 4(3): 171-7.
- 498 10. Bell ML, Ebisu K. Environmental inequality in exposures to airborne
- 499 particulate matter components in the United States. Environmental Health
- 500 Perspectives. 2012; 120(12): 1699-704.
- 501 11. Clougherty JE, Levy JI, Kubzansky LD, Ryan PB, Suglia SF, Canner MJ, et
- al. Synergistic effects of traffic-related air pollution and exposure to
- 503 violence on urban asthma etiology. Environmental Health Perspectives.
- 504 2007; 115(8): 1140-6.
- 505 12. Cutter SL, Boruff BJ, Shirley WL. Social vulnerability to environmental
 506 hazards. Social Science Quarterly. 2003;84(2):242-61.
- 507 13. Harner J, Warner K, Pierce J, Huber T. Urban environmental justice
- indices. The Professional Geographer. 2002;54(3):318-31.

509	14. Linder SH, Marko D, Sexton K. Cumulative cancer risk from air pollution
510	in Houston: Disparities in risk burden and social disadvantage.
511	Environmental Science & Technology. 2008;42(12):4312-22.
512	15. Morello-Frosch R, Pastor Jr M, Porras C, Sadd J. Environmental justice
513	and regional inequality in southern California: implications for future
514	research. Environmental Health Perspectives. 2002;110:149-54.
515	16. Perlin SA, Sexton K, Wong DW. An examination of race and poverty for
516	populations living near industrial sources of air pollution. Journal of
517	Exposure Analysis and Environmental Epidemiology. 1998;9(1):29-48.
518	17. Sadd JL, Pastor M, Morello-Frosch R, Scoggins J, Jesdale B. Playing it
519	safe: assessing cumulative impact and social vulnerability through an
520	environmental justice screening method in the South Coast air basin,
521	California. International Journal of Environmental Research and Public
522	Health. 2011;8(5):1441-59.
523	18. Sexton K, Linder SH. Cumulative risk assessment for combined health
524	effects from chemical and nonchemical stressors. American Journal of
525	Public Health. 2011;101(S1):81-8.
526	19. Chahine T, Schultz BD, Zartarian VG, Xue J, Subramanian SV, Levy JI.
527	Modeling joint exposures and health outcomes for cumulative risk
528	assessment: the case of radon and smoking. International Journal of
529	Environmental Research and Public Health. 2011;8(9):3688-711.

530	20. Fox MA, J.D. G, Burke TA. Evaluating cumulative risk assessment for
531	environmental justice: a community case study. Environmental Health
532	Perspectives. 2002;110:203-9.
533	21. Morello-Frosch R, Pastor M, Sadd J. Environmental justice and southern
534	california's "riskscape": the distribution of air toxics exposures and
535	health risks among diverse communities. Urban Affairs Review.
536	2001;36(4):551-78.
537	22. Dawson JF, Richter AW. Probing three-way interactions in moderated
538	multiple regression: development and application of a slope difference
539	test. Journal of Applied Psychology. 2006;91(4):917.
540	23. Hastie T, Tibshirani R, Friedman J. The elements of statistical learning:
541	data mining, inference and prediction. Springer; 2005.
542	24. Agrawal R, Imieliński T, Swami A, editors. Mining association rules
543	between sets of items in large databases. ACM SIGMOD 1993.
544	25. Becquet C, Blachon S, Jeudy B, Boulicaut J, Gandrillon O. Strong-
545	association-rule mining for large-scale gene-expression data analysis: a
546	case study on human SAGE data. Genome Biology. 2002;3(12):0067. 1
547	16.
548	26. Chen TJ, Chou LF, Hwang SJ. Application of a data-mining technique to
549	analyze coprescription patterns for antacids in Taiwan. Clinical
550	Therapeutics. 2003;25(9):2453-63.

551	27. Jiao J, Zhang Y. Product portfolio identification based on association rule
552	mining. Computer-Aided Design. 2005;37(2):149-72.

28. Rajak A, Gupta MK, editors. Association rule mining-applications in
various areas. International conference on data management. 2008.
Ghaziabad, India.

- 556 29. Treinen JJ, Thurimella R. A framework for the application of association
 557 rule mining in large intrusion detection infrastructures. In International
 558 Workshop on Recent Advances in Intrusion Detection. Springer Berlin
- 559 Heidelberg. 2006:1-18.
- 560 30. Bell SM, Edwards SW. Identification and prioritization of relationships
- 561 between environmental stressors and adverse human health impacts.

562 Environmental Health Perspectives. 2015;123(11):1193-9.

563 31. Bell SM, Edwards SW, editors. Building associations between markers of

564 environmental stressors and adverse human health impacts using

- 565 frequent itemset mining. Society for Industrial and Applied Mathematics
- 566 (SIAM) international conference on data mining; 2014.

567 32. U.S. Census Bureau. A compass for understanding and using American

568 Community Survey data: What general data users need to know.

- 569 Washington, DC: U.S. government printing office; 2008.
- 570 33. Habermann M, Souza M, Prado R, Gouveia N. Socioeconomic inequalities

and exposure to traffic-related air pollution in the city of São Paulo,

572 Brazil. Cadernos de Saúde Pública. 2014; 30(1): 119-25.

573	34. Thompson U, Caquard S. Compiling a geographic database to study
574	environmental injustice in Montréal: process, results, and lessons. In
575	Mapping Environmental Issues in the City. Springer Berlin Heidelberg.
576	2011:10-29.
577	35. Hahsler M, Grün B, Hornik K, Buchta C. Introduction to arules-A
578	computational environment for mining association rules and frequent
579	item sets. 2009.
580	36. Hahsler M, Chelluboina S. Visualizing association rules: Introduction to
581	the R-extension package arulesViz. 2011.
582	37. Borgelt C. Frequent item set mining. Wiley interdisciplinary reviews: data
583	mining and knowledge discovery. 2012;2(6):437-56.
584	38. Ramsey F, Schafer D. The statistical sleuth: a course in methods of data
585	analysis. Third ed. Boston, MA: Cengage Learning; 2012.
586	39. Zhang J, Kai FY. What's the relative risk? A method of correcting the
587	odds ratio in cohort studies of common outcomes. JAMA.
588	1998;280(19):1690-1.
589	40. U.S. Census Bureau. American community survey and puerto rico
590	community survey 2014 subject definitions. Available from:
591	https://www2.census.gov/programs-
592	surveys/acs/tech_docs/subject_definitions/2014_ACSSubjectDefinitions.
593	pdf.

594	41. Hillis DM, Bull JJ. An empirical test of bootstrapping as a method for
595	assessing confidence in phylogenetic analysis. Systematic biology.
596	1993;42(2):182-92.
597	42. Martínez-Fernández J, Esteve-Selma MA, Calvo-Sendín JF. Environmental
598	and socioeconomic interactions in the evolution of traditional irrigated
599	lands: a dynamic system model. Human Ecology. 2000;28(2):279-99.
600	43. Patterson T, Gulden T, Cousins K, Kraev E. Integrating environmental,
601	social and economic systems: a dynamic model of tourism in Dominica.
602	Ecological Modelling. 2004;175(2):121-36.
603	44. Kenney MA, Hobbs BF, Mohrig D, Huang H, Nittrouer JA, Kim W, et al.
604	Cost analysis of water and sediment diversions to optimize land building
605	in the Mississippi River delta. Water Resources Research.
606	2013;49(6):3388-405.
607	45. Trujillo-Ventura A, Ellis JH. Multiobjective air pollution monitoring
608	network design. Atmospheric Environment. Part A. General Topics.
609	1991;25(2):469-79.
610	46. Nau C, Ellis H, Huang H, Schwartz BS, Hirsch A, Bailey-Davis L, et al.
611	Exploring the forest instead of the trees: An innovative method for
612	defining obesogenic and obesoprotective environments. Health & Place.
613	2015;35:136-46.
614	47. Huang H, Fava A, Guhr T, Cimbro R, Rosen A, Boin F, et al. A

615 methodology for exploring biomarker--phenotype associations:

- 616 application to flow cytometry data and systemic sclerosis clinical
- 617 manifestations. BMC bioinformatics. 2015;16:293.

619 620	Table 1. Association Rules (LHS socio-demographic variables and RHSchemical variables, minimum support value of 0.1, lift > 1)
621 622	Table 2. Association Rules (both LHS and RHS are socio-demographicvariables, minimum support value of 0.1, lift > 1)
623 624	Table 3. Summary of Association Rules (LHS socio-demographic variables and RHS chemical variables, minimum support value of 0.01, lift > 1)
625 626 627	Table 4. Complementary Pairs of Rules with One-to-One Relationship (LHS socio-demographic variables and RHS chemical variables, minimum support value of 0.01, lift > 1, Size = 2)
628	

Table 1. Association Rules (LHS socio-demographic variables and RHS chemical variables, minimum
 support value of 0.1, lift > 1)

LHS		RHS	Support	Confidence	Lift	Relative Risk	Odds Ratio
Race Minority Score 1	=>	BUTADIENE=Q1	0.146	0.448	1.793	2.074	2.947
Race Minority Score 1	=>	DIESEL=Q1	0.145	0.445	1.780	2.051	2.893
Race Minority Score 1	=>	TOLUENE=Q1	0.141	0.435	1.740	1.981	2.737
Race Minority Score 1	=>	BENZENE=Q1	0.134	0.412	1.647	1.830	2.411
Race Minority Score 1	=>	ACETALDEHYDE=Q1	0.129	0.396	1.585	1.734	2.216
Age=40-50	=>	DIESEL=Q1	0.125	0.375	1.499	1.615	1.984
Age=40-50	=>	BUTADIENE=Q1	0.119	0.356	1.425	1.512	1.795
Age=40-50	=>	TOLUENE=Q1	0.117	0.349	1.396	1.473	1.726
Age=40-50	=>	BENZENE=Q1	0.115	0.344	1.375	1.445	1.679
Race Minority Score 1	=>	CYANIDE=Q3	0.108	0.332	1.328	1.383	1.573
Age=40-50	=>	ACETALDEHYDE=Q1	0.109	0.324	1.297	1.346	1.512
Race Minority Score 1	=>	DIESEL=Q2	0.102	0.315	1.259	1.297	1.433
Race Minority Score 1	=>	TOLUENE=Q2	0.102	0.315	1.258	1.297	1.433

Table 2. Association Rules (both LHS and RHS are socio-demographic variables, minimum support value of 0.1, lift > 1)

LHS		RHS	Support	Confidence	Lift	Relative Risk	Odds Ratio
Race Minority Score 1	=>	Age=40-50	0.172	0.530	1.583	1.801	2.704
Age=40-50	=>	Race Minority Score 1	0.172	0.514	1.583	1.801	2.650
Poverty Score 2	=>	Race Minority Score 1	0.110	0.435	1.338	1.397	1.702
Poverty Score 2	=>	Age=40-50	0.110	0.433	1.295	1.344	1.607
Race Minority Score 1	=>	Poverty Score 2	0.110	0.340	1.338	1.397	1.601
Age=40-50	=>	Poverty Score 2	0.110	0.329	1.295	1.344	1.512

Table 3. Summary of Association Rules (LHS socio-demographic variables and RHS chemical variables,
 minimum support value of 0.01, lift > 1)

	Number of Rules	Low Exposure (Q1)	Q2	Q3	High Exposure (Q4)
Race Minority Score 7 or 8 or 9 or 10	29	0 (0%)	1 (3.45%)	8 (27.59%)	20 (68.97%)
Race Minority Score 1 or 2	342	139 (40.64%)	129 (37.72%)	58 (16.96%)	16 (4.68%)
Poverty Score 7-10	14	1 (7.14%)	1 (7.14%)	3 (21.43%)	9 (64.29%)
Poverty Score 1 or 2 or 3	354	140 (39.55%)	118 (33.33%)	69 (19.49%)	27 (7.63%)
Education Score 8-10	24	2 (8.33%)	3 (12.5%)	8 (33.33%)	11 (45.83%)
Education Score 1 or 2 or 3	237	116 (48.95%)	31 (13.08%)	39 (16.46%)	51 (21.52%)
Age 40-50	213	106 (49.77%)	69 (32.39%)	34 (15.96%)	4 (1.88%)
Age 38-40	83	31 (37.35%)	28 (33.73%)	16 (19.28%)	8 (9.64%)

Table 4. Complementary Pairs of Rules with One-to-One Relationship (LHS socio-demographic variables and RHS chemical variables, minimum support value of 0.01, lift > 1, Size = 2)

LHS	5		Support	Confidence	Lift	Odds Ratio	Est. 9	5% CI
Race Minority Score 10	=>	DIESEL=Q4	0.023	0.637	2.549	5.534	5.102	6.008
Race Minority Score 1	=>	DIESEL=Q1	0.145	0.445	1.780	2.893	2.818	2.969
Race Minority Score 10	=>	TOLUENE=Q4	0.018	0.501	2.002	3.081	2.851	3.335
Race Minority Score 1	=>	TOLUENE=Q1	0.141	0.435	1.740	2.737	2.666	2.809
Race Minority Score 10	=>	BUTADIENE=Q4	0.017	0.489	1.958	2.942	2.722	3.177
Race Minority Score 1	=>	BUTADIENE=Q1	0.146	0.448	1.793	2.947	2.869	3.025
Race Minority Score 10	=>	BENZENE=Q4	0.017	0.468	1.870	2.687	2.484	2.902
Race Minority Score 1	=>	BENZENE=Q1	0.134	0.412	1.647	2.411	2.351	2.472
Race Minority Score 10	=>	ACETALDEHYDE=Q4	0.013	0.369	1.475	1.768	1.636	1.914
Race Minority Score 1	=>	ACETALDEHYDE=Q1	0.129	0.396	1.585	2.216	2.161	2.272



Figure 1. Graph-based Visualization of Association Rules (LHS is socio demographic variables and RHS is chemical variables, minimum support
 value of 0.1, lift > 1)