1 <u>Bisphenol A exposure is not associated with area level socioeconomic index in Australian children using pooled</u>

2 <u>urine samples</u>

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17

18   **Abstract**

19   Bisphenol A (BPA) is used extensively in food-contact materials and has been detected routinely in populations

20   worldwide, and this exposure has been linked to a range of negative health outcomes in humans. There is some

21   evidence of an association between BPA and different socioeconomic variables which may be the result of

22   different dietary patterns. The aim of this study was to conduct a preliminary investigation of the association

23   between BPA and socioeconomic status in Australian children using pooled urine specimens and an area level

24   socioeconomic index. Surplus pathology urine specimens collected from children aged 0-15 years in

25   Queensland, Australia as samples of convenience (n = 469) were pooled by age, sex and area level

26   socioeconomic index (n = 67 pools), and analysed for total BPA using online solid phase extraction LC-MS/MS.

27   Concentration ranged from 1.08-27.4 ng/ml with geometric mean 2.57 ng/ml, and geometric mean exposure was

28   estimated as 70.3 ng/kg d^{-1}. Neither BPA concentration nor excretion was associated with age or sex, and the

29   authors found no evidence of an association with socioeconomic status. These results suggest that BPA

30   exposure is not associated with socioeconomic status in the Australian population due to relatively homogenous

31   exposures in Australia, or that the socioeconomic gradient is relatively slight in Australia compared with other

32   OECD countries.

33

34   **Keywords:** human biomonitoring; urine; bisphenol A; BPA; socioeconomic status; socioeconomic position;

35   children

Introduction

Bisphenol A (4,4'-(propane-2,2-diyl)diphenol, or BPA) is a chemical intermediate in the manufacture of polycarbonate plastics and epoxy resins used extensively in food contact items, and is a ubiquitous contaminant in the developed world. Measured levels of BPA in human tissues and fluids have been associated with a range of adverse health outcomes and chronic disease in humans (recently reviewed in Rochester (2013)). Chemical exposures during critical windows of development such as infancy, childhood and adolescence are of particular concern because of the unique susceptibility and disproportionate exposure during this time, which can differ significantly from that of adults; and the longer latency period for the development of chronic disease in later life (Scheuplein et al. 2002; WHO 2011; WHO 2004).

The relative concept of socioeconomic status, socioeconomic position or social class (herein referred to as socioeconomic status (SES)) refers to the social and economic position of an individual or a group within the larger society. There is evidence for disparity in BPA exposures along the socioeconomic gradient, with some studies in USA (Nelson et al. 2012; Calafat et al. 2008), China (He et al. 2009) and Spain (Casas et al. 2013) reporting associations between BPA and socioeconomic variables. Oral exposure is assumed to be the dominant exposure route (Koch and Calafat 2009; Vandenberg et al. 2007) and the most important exposure source is polycarbonate baby bottles and canned food, for infants and adolescents/adults, respectively (Von Goetz et al. 2010). There is consistent evidence from industrialised countries that people from disadvantaged or low SES groups are more likely to consume more energy-dense, processed and canned or packaged foods (Darmon and Drewnowski 2008; Monsivais and Drewnowski 2009), and consume fewer fresh fruits and vegetables (reviewed by Kamphuis et al. (2006)). Studies have demonstrated an association between canned food or beverage consumption and urinary BPA concentration (Braun et al. 2011a; Matsumoto et al. 2003; Casas et al. 2013), and dietary intervention studies limiting pre-packaged foods and maximising fresh foods show decreased BPA levels post-intervention (Rudel et al. 2011; Carwile et al. 2009; Carwile et al. 2011).

A number of food survey studies investigating the BPA content of packaged foods available in Australia have been conducted (ACCC 2010; Choice 2010; FSANZ 2010b), and the results are generally consistent with similar studies performed in other counties (Consumer Reports 2009; Environmental Working Group 2007; Noonan et al. 2011; Goodson et al. 2002; Thomson and Grounds 2005). To date there have been no studies of the Australian population to investigate the potential link between BPA exposure and SES, although there is

66 some evidence for differences in dietary patterns between socioeconomic groups (AIWH 2012a; Ambrosini et

67 al. 2009), for example, the association of high income (Giskes et al. 2002) and higher education (Ball et al.

68 2006) with increased fruit and vegetable consumption. Assessing exposure to a range of environmental

69 chemicals is important for developing strategies to address and prevent health inequality and for the

70 identification of susceptible populations in the broader community. The aim of this study was to conduct a

71 preliminary investigation of the potential association between urinary BPA concentration and SES in Australian

72 children relying on minimal resources, by using pooled pathology specimens and an area level socioeconomic

73 index.

74

75 **Materials and methods**

76 Study population and sample collection

77 De-identified urine specimens were obtained from a community-based pathology laboratory (Sullivan

78 Nicolaides Pathology, Taringa, Australia) from surplus stored urine that had been collected and analysed as part

79 of routine testing as previously described (Heffernan et al. 2013a). Urine specimens were collected in sterile

80 polyethylene urine specimen containers, refrigerated immediately following collection, and sent to the

81 pathology laboratory for testing within 12 hours where they were stored in monitored cold rooms for a

82 maximum of three days. Specimens were frozen immediately following collection by researchers. Urine

83 specimens were collected by participants as samples of convenience, and as this was a pre-existing, convenience

84 population no specific sampling protocols were employed. Descriptive information about each specimen was

85 limited to age, sex and post code. Specimens were collected and pooled from February to November 2012, and

86 analysed in March 2013. This project was approved by the University of Queensland ethics committee (approval

87 number 2002000656).

88

89 Measuring SES

90 The Socioeconomic Indexes for Areas (SEIFA) is a publicly-available area-based measure of SES developed by

91 the Australia Bureau of Statistics. The Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD)

92 is one of four SEIFA indices, and measures relative advantage and relative disadvantage, and includes

93 information collected from the census related to income, internet connection, occupation and education (for a

94 more detailed explanation refer to Online Resource 1). Geographical areas are ranked and given a score, where

95 a low IRSAD score indicates that an area has low SES compared to an area with a higher score (Pink 2008a,

96 <u>2008b; ABS 2011).</u> Using <u>IRSAD</u> scores and adjusting for the population fraction in each postal area, the

97 population was divided into quintiles, where quintile 1 (Q1) contains the fraction of the population with the

98 highest SES and Q5 contains those with the lowest SES. Postal codes were then classified into one of the five

99 quintiles (refer to online resource <u>2</u>). Individual urine specimens were then assigned <u>an area level</u>

100 <u>socioeconomic index quintile (Q1 – Q5)</u> based on the postal code from which that specimen was drawn.

101

102 <u>Pooling protocol</u>

103 Specimens were stratified by age, sex and <u>area level socioeconomic index quintile</u> for pooling (refer to <u>online</u>

104 <u>resource 3</u>). Individual urine specimens were thawed, homogenised, aliquoted <u>into amber glass vials</u> and

105 refrozen until analysis. Seven individual specimens were combined to create one pool, where each individual

106 contributed the same volume to the pool. A total of 469 individual specimens were collected and combined into

107 67 pools. Replicate pools per strata (same age, sex and postal code) were constructed where sufficient unique

108 specimens were available. No individual urine specimens contributed to more than one pool.

109

110 <u>Chemical analysis</u>

111 Fifty microliter aliquots of each pooled sample were analysed for total BPA (free plus conjugated species) at the

112 National Research Centre for Environmental Toxicology, University of Queensland, Australia using an online

113 solid-phase extraction liquid chromatography tandem mass spectrometry method described previously

114 (Heffernan et al. 2013a). Synthetic urine (Calafat and Sampson 2009) was used for quality control. Fortified

115 synthetic urine (1 ng/ml) was used to monitor instrument performance (0.79 ± 0.12 ng/ml, $n = 31$), and

116 background contamination was monitored by repeated measures of un-fortified synthetic urine (0.086 ± 0.033

117 ng/ml, $n = 35$). The limit of detection (LOD) was 0.1ng/ml (calculated as 3*standard deviation of the blank).

118 Due to unavoidable low but consistent background contamination, a conservative limit of reporting (LOR) was

119 calculated as 3*average blank, and set as 0.3 ng/ml. No blank subtraction was performed.

120

121 <u>Exposure estimates</u>

122 Daily urinary excretion of BPA on a per kg bodyweight basis (ng/kg-d), was calculated for each pool using

123 measured pool concentrations (ng/ml); and model-predicted, age-specific urinary flow (ml/kg-d) described

124 previously (Heffernan et al. 2013a). Under a steady-state assumption, daily urinary excretion of BPA is equal to

125 daily intake (Volkel et al. 2002), and so the estimated daily excretion of BPA in this study can be taken as an

126 estimate of daily BPA exposure in the population covered by this study.

127

128 <u>Statistical analysis</u>

129 Generalised linear analyses using univariate and multivariate models were implemented to determine the

130 association between ln-transformed urinary BPA concentration or exposure estimate and age, sex and SES. An

131 interaction term between age group and sex was included in the multivariate models, as follows:

132

133 $$\ln BPA = \text{intercept} + \beta_1 * \text{quintile} + \beta_2 * \text{age} + \beta_3 * \text{sex} + \beta_4 * (\text{age*sex})$$

134 *(Equation 1)*

135 Data were analysed using SAS Version 9.3 (SAS Institute Inc., Cary, NC, USA). Results were deemed

136 statistically significant for p values <0.05.

137

138 **Results**

139 When using pooled samples comprised of equal volumes from each individual contributing to the pool, the

140 concentration measured in each pool is equivalent to the arithmetic mean of the concentration in each individual

141 specimen contributing to the pool (Mary-Huard 2007; Caudill 2010). BPA was detected in all pooled samples,

142 ranging from 1.08 to 27.4 ng/ml urine across all strata. The geometric mean urinary concentrations for each age

143 group (0-5, 5-10 and 10-15 years), area level socioeconomic index quintile (Q1-Q5) and sex (M/F) are

144 summarized in Table 1. Table 2 shows a condensed view of the data grouped by area level socioeconomic index

145 quintile only with age and sex strata combined. Table 3 presents the data pooled by age and sex only.

146

147 Due to age-related differences in urine flow a model described previously (Heffernan et al. 2013a) was used to

148 estimate BPA exposure. Correction for 24 hour urine volume is recommended for young children because

149 volume-based measures of concentration for environmental chemicals may significantly underestimate actual

150 exposures for young age groups relative to older age groups (Heffernan et al. 2013a). Daily exposure estimates

151 ranged from 31.1 to 1080 ng/kg d^{-1} across all pools (Tables 1 – 3). No measurements of creatinine or specific

152 gravity were available.

153

154   The association of BPA concentration and exposure with SES, age and sex was investigated using univariate

155   and multivariate models. SES was not associated with BPA concentration or exposure in either model. In the

156   multivariate model there was a slight effect of age and sex on BPA concentration (p = 0.021 and p = 0.003,

157   respectively) with significant interaction between the two (p = 0.006), where a 5-year increase in age results in a

158   decrease in BPA concentration by factor 0.47 (Table 4). Similar results with respect to SES and sex were

159   obtained using BPA exposure in place of concentration, but the age-exposure association was stronger (p =

160   0.004, see online resource 4).

161

162   The data set contains four extreme values (identified by visual inspection; see Figure 1), at 19.4, 17.5, 27.4 and

163   19.6 ng/ml (in strata 1, 2, 3 and 15 respectively, see online resource 3). To ensure the samples were not

164   contaminated during sample collection, all samples exceeding the ninety-fifth percentile were reanalysed

165   separately for free and total BPA. Free BPA was not detected above the reporting limit in any sample,

166   confirming that the quality control procedures were adequate to prevent and assess potential contamination with

167   the free species, and the values reported provide a reliable estimate of the pool mean total BPA. The extreme

168   values are within the range of values reported previously for children (Braun et al. 2011b; Morgan et al. 2011;

169   Heffernan et al. 2013a) but omission of these data points from the model affects the results. The effects are seen

170   particularly with respect to BPA concentration associations with age and sex because all four extreme values are

171   male, and three of the four extreme values occur in the youngest age category (0-5 years). When the extreme

172   values are excluded from the multivariate model (n = 63) the age trend is reversed and BPA concentration is

173   positively but not significantly associated with age; and there is no longer any interaction between age and sex

174   variables (Table 4). Similar results were obtained in multivariate and univariate models using BPA exposure in

175   place of urinary concentration (with extreme values excluded), and no significant differences by SES, age or sex

176   were found.

177

178   **Discussion**

179   BPA (as BPA glucuronide) is present in measurable quantities in the urine of the general population of multiple

180   countries worldwide (reviewed by Vandenberg et al. (2010); Dekant and Volkel (2008)), but limited information

181   exists on BPA exposures in the Australian population (Heffernan et al. 2013a; Callan et al. 2012). BPA

182   concentrations in the pools analysed in this study ranged from 1.08 to 4.14 ng/ml with GM 2.57 ± 4.66 ng/ml (n

183   $= 67$), with GM 2.65 ± 6.62, 2.32 ± 1.31 and 2.82 ± 4.17 ng/ml for 0-5, 5-10 and 10-15 years age strata,

184   respectively. The results are consistent with a previous study of pooled urine samples from Australian children

185   (0-5 years, *n* = 67; range 0.65 – 265 ng/ml across pools; GM across pools 2.98 ng/ml) (Heffernan et al. 2013a).

186   Exposure estimates based on pool concentrations ranged from 36.3 to 159 ng/kg d^{-1} for 0-15 year olds (GM

187   across pools: 60.9 ± 29.0 ng/kg d^{-1}; extreme values excluded) and from 36.3 to 127 ng/kg d^{-1} for 0-5 year olds

188   specifically (GM across pools 65.1 ± 24.1 ng/kg d^{-1}; extreme values excluded, see also Table 3). All estimated

189   exposures in this study were ≤1 µg/kg d^{-1}, which is well below the European Food Safety Authority tolerable

190   daily intake of 50 µg/kg bw (EFSA 2006, 2010). Australian regulatory bodies, including Food Standards

191   Australia and New Zealand (FSANZ) and the Australian Competition and Consumer Commission (ACCC)

192   support the current guideline and have concluded that BPA concentrations in Australian foods do not pose a

193   health risk to consumers (ACCC 2012). However, the Australian Government did introduce a voluntary phase

194   out of BPA use in polycarbonate baby bottles in 2010 (FSANZ 2010a), which is consistent with similar actions

195   in the United States, Canada and selected European countries.

196

197   Although concentration and exposure were both associated with age, neither relationship reached significance.

198   This is in contrast to previous findings which demonstrated a significant inverse association (Heffernan et al.

199   2013a). This could be explained by a loss of resolution of the age trend due to the use of comparatively larger

200   age brackets in the pooling strategy for the current study. From the urinary flow model, we do not expect a large

201   flow-driven, age-related difference in exposure estimates for children >5 years as the predicted flow rates begin

202   to plateau at this point (refer to Heffernan et al. (2013a)).

203

204   *Comparison of urinary concentrations with existing literature*

205   Few previous studies have examined urinary BPA concentrations in young children (see Table 5). The German

206   Environmental Survey (GerES) reported results for children aged 3 to 14 years. Results from the GerES were

207   generally consistent, although we find lower concentrations in the youngest age group (GM of 2.65 ng/ml across

208   pools for 0-5 year olds in our study compared with GM 3.55 ng/ml for 3-5 year olds in GerES) (Becker et al.

209   2009). The Canadian Health Measures Survey reports geometric mean urinary concentrations of 1.3 and 1.5

210   ng/ml for 6-12 and 12-19 year olds, respectively, with significantly higher levels reported in the youngest age

211   bracket when the results were corrected for creatinine (2.0 µg/g creatinine for 6-12 year olds) (Bushnik et al.

212   2010). Slightly higher levels were measured by Kasper-Sonnenberg et al. (2012) in 6-8 year old German

213   children at 2.4 ng/ml (2.3µg/g creatinine), ranging from 0.3 to 50.5 ng/ml. Higher mean values of 3.6 ng/ml and

214   3.7 ng/ml were measured in 6-11 year old children and 12-19 year old adolescents, respectively, as part of the

215   2003-2004 NHANES survey cycle in the United States (Calafat et al. 2008).

216

217   *Reported associations between BPA and socioeconomic variables*

218   The data did not show an association of BPA concentration or estimated exposure with SES. Few studies have

219   set out to explicitly examine the relationship between BPA exposure and SES, and even fewer studies report

220   results for young children. In the literature BPA exposure has been linked to a range of demographic factors,

221   including income (Nelson et al. 2012), education (Nelson et al. 2012; Braun et al. 2011a) and race/ethnicity

222   (Kasper-Sonnenberg et al. 2012; Becker et al. 2009) as typical indicators of SES, but the results are inconsistent

223   (see Table 6). Using data from the 2003-2004 and 2005-2006 NHANES cycles Nelson et al. (2012) examined

224   the association between urinary BPA and multiple measures of SES including family income, education,

225   occupation and food security. Overall, people with lower incomes had higher body burdens of BPA, and that

226   after adjusting for family size, income was the strongest predictor of chemical concentration of all the different

227   SES measures studied. Conversely, Bushnik et al report no association with household education or household

228   income in the Canadian Health Measures Survey (Bushnik et al. 2010). Although those in the third income

229   quartile and with the third highest level of education had higher BPA concentrations compared to their reference

230   groups. Hoepner et al. (2013), Braun et al. (2011a) and Ye et al. (2008) also report no association with

231   household income. The inconsistencies also prevail for education and race/ethnicity/migrant status. Only two

232   studies assessed occupation, but this variable is likely to be irrelevant for the present study population.

233

234   A comparison of literature results from studies that characterise SES demonstrates the significant variation in

235   methodologies used to quantify socioeconomic variables (discussed in Braveman et al. (2005)). For example,

236   occupation is frequently used as a measure of SES in Europe, whereas education is more commonly used in

237   United States (Braveman et al. 2005; Galobardes et al. 2001). There is often an interaction between SES and

238   ethnicity, and social inequalities exist such that ethnic differences exist even within a given occupation, income

239   or educational level (Shavers 2007; Nelson et al. 2012). Consequently, occupation and education may not be

240   adequate measures of income and wealth in ethnically-diverse populations (Daly et al. 2002; Shavers 2007).

241   Further, Braveman et al. (2005) suggests that correlations between income and education are not strong enough

242   to replace one with the other, and that neither of these are a proxy for SES. Accordingly, a composite measure of

243   SES is most desirable. SEIFA is a compound evaluation based on information collected from the Census of

244   Population and Housing conducted every five years in Australia, and includes information on income, wealth,

245   education and employment - some of the key concepts used to measure SES (Pink 2008a, 2008b; ABS 2011)

246   (see also Online Resource 1). However, even when using SES indices there is no consistency or agreement on

247   the preferred method of measurement and assessment (Bradley and Corwyn 2002). For example, the Townsend

248   and Carstairs Indices are used in the United Kingdom; Duncan's Socioeconomic index is more likely used in the

249   United States, and the Socio-Economic Risk index tends to be used most often in Canada (Shavers 2007).

250

251   Despite the suggestion of differences in BPA exposure along the socioeconomic gradient in other studies, we

252   find no supporting evidence in this subset of the Australian population. There are two possible explanations for

253   this observation: (1) BPA exposure is not associated with SES in the Australian population; or (2) the study

254   methodology lacks the sensitivity needed to assess the true association between BPA and SES. In the 2013

255   World Wealth Report Australia is reported as having the highest median and second highest mean wealth in the

256   world and the proportion of Australians with wealth above USD 100,000 is eight times the world average

257   (Keating et al. 2013). The ratio of mean-to-median wealth in Australia is 1.83 compared with 6.71 in the United

258   States, and the ratio of people living below the poverty line in each country is 0.124 and 0.171, respectively

259   (OECD 2010). So, the proportion of Australians living in poverty is less than in the US, the mean wealth is

260   higher, and the ratio of mean-to-median wealth is smaller, meaning that overall, the disparity between

261   disadvantaged and advantaged people is less in Australia than in the US. This suggests that the SES gradient in

262   Australia is less than in the US, so differences in behaviour (i.e. canned food consumption) between Q1 and Q5

263   in Australia may not be as evident as in the US.

264

265   The assumption that consumption of fresh foods will result in decreased BPA exposure is flawed if one of those

266   fresh food sources is highly contaminated (e.g. in the experience of Sathyanarayana et al. (2013)), or if canned

267   food consumption (as the major contributing source) is equal across different SES groups (see discussion

268   above). Alternatively, there may be significant non-food exposures to BPA (Stahlhut et al. 2009), such as non-

269   nutritive ingestion or dermal absorption, which are not associated with SES. While there are notable differences

270   in dietary patterns along the socioeconomic gradient, BPA exposure may be strongly associated with food

271   preparation practices (reviewed in Hoekstra and Simoneau (2013)), rather than the type of food consumed.

272

273   *Study limitations*

274 There are a number of limitations to the study design that must be considered when interpreting the results of the

275 study, and the following assumptions have been made: (1) pathology specimens do not introduce significant bias

276 into the study population; (2) pooled samples provide an accurate measurement of mean urinary BPA

277 concentration; and (3) IRSAD provides an accurate assessment of SES for the Australian population.

278

279   *The use of pooled, pathology specimens*

280 The study population consisted of samples of convenience collected during the course of routine pathology

281 testing (with no significant medical intervention). The samples are not statistically representative of the

282 Australian population as a whole, but there is no reason to expect BPA exposures to be different in this

283 community pathology-sourced population than in the general population. Pooled pathology specimens have

284 been used successfully in a previous study to measure urinary BPA (Heffernan et al. 2013a) and a discussion of

285 the opportunities and limitations of using pooled samples for biomonitoring has been published recently

286 (Heffernan et al. 2013b). However, we do not know the extent to which socially disadvantaged Australians have

287 access to pathology services. The availability of more samples from individuals in the top two quintiles (Q1 and

288 Q2, n=37 pools) compared with the bottom two quintiles (Q4 and Q5, n = 19 pools) possibly reflects inequality

289 in access to healthcare, and fewer data points in the bottom quintiles provide a limited description of the

290 variability in these strata compared with the top quintiles.

291

292   *The use of an area-level index to characterise SES*

293 The use of an area-level index as a measure of SES introduces the risk for ecological fallacy, where an

294 individual may be misclassified at the area level (Pink 2008b; Baker and Adhikari 2007), for example, a

295 relatively advantaged person living in an area classified as relatively disadvantaged would be misclassified. The

296 use of pooled samples mitigates this to some extent because the pool concentration is an average of the

297 individual samples contributing to the pool, and SEIFA scores have been shown to correlate with the proportion

298 of people living in an area that report poor health or other health risk factors (Adhikari, 2006). SEIFA indices

299 can be used to compare relative socioeconomic advantage and disadvantage at an area level, but the caveat

300 applies that IRSAD is an area-level index, and the score for a particular area should not be presumed to apply to

301 all individuals living in that area (Adhikari, 2006). Further, as a consequence of being a composite assessment,

302 indices do not allow the study of how specific SES factors may influence health (Braveman et al. 2005), and this

303 may be particularly relevant for BPA exposure where behaviour modification such as dietary intervention or

304 product replacement may be effective in reducing exposure where ingestion is the dominant exposure route

305 (Wilson et al. 2007). Alternatively, there may be other social determinants of health (AIWH 2012b) that

306 contribute to chemical exposures that are not captured by the socioeconomic index.

307

308 *Concluding remarks*

309 To the best of our knowledge, this is the first study investigating BPA and SES in Australian children, and we

310 report no significant association with urinary concentration or exposure. BPA exposures in Australia may be

311 more homogenous than what is seen in countries that do report such an association, such as the United States

312 (e.g. Calafat et al. 2008; Nelson et al. 2012), or IRSAD may not be sensitive enough to measure SES for this

313 purpose. However, there is no alternative currently available in Australia, with the exception of conducting a

314 prohibitively large and expensive random sampling population survey of the general population, complete with

315 biomonitoring samples, comprehensive food frequency questionnaire and detailed food packaging and

316 preparation procedures. The data presented here do not provide justification for such a study. A standardised

317 method of quantifying SES across different populations is required for accurate comparison between studies,

318 and the lack of such a method may explain some of the inconsistencies reported in the literature.

319

326

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Tables & Figures

Table 1: Summary of urinary BPA urinary concentration (total of free and conjugated species), average urinary flow (in ml/kg d^{-1}, from flow model); and BPA exposure (ng/kg d^{-1}) for pooled samples stratified by age, sex and quintile of area level SES (n = 67)

Table 2: Summary of urinary BPA concentration (total of free and conjugated species, ng/ml), and BPA exposure (ng/kg d^{-1}) for stratified pooled samples by area level socioeconomic index quintile, with age strata combined (n = 67)

Table 3: Summary of urinary BPA urinary concentration (total of free and conjugated species), average urinary flow (in ml/kg d^{-1}, from flow model); and BPA exposure (ng/kg d^{-1}) for pooled samples stratified by age and sex (n = 67)

Table 4 Univariate and multivariate statistical analysis of ln-transformed BPA concentration (ng/ml urine) associations with area level socioeconomic index quintile (SES), age and sex. Data presented for all data points (n=67) and with extreme values excluded (n=63)

Table 5: Summary of literature reporting urinary concentrations of total BPA (sum of free and conjugated species) in children and adolescents

Table 6 Summary of associations between urinary bisphenol A and various demographic variables from published literature; asterisk denotes statistical significance

Fig. 1 Urinary concentrations of bisphenol A in pooled samples (n = 67) grouped by area level socioeconomic index quintile (Q1-Q5). Each open circle represents one pooled sample, where seven individual urine specimens contribute to each pool. Horizontal line denotes geometric mean. Four extreme values identified by visual inspection

Table 1: Summary of urinary BPA urinary concentration (total of free and conjugated species), average urinary flow (in ml/kg d^{-1}, from flow model); and BPA exposure (ng/kg d^{-1}) for pooled samples stratified by age, sex and quintile of area level SES (n = 67)

Description	Age bracket (years)	Av. Age (years)	Quintile of area level SES[b]	Number of pools	Av. urinary flow (ml/kg d^{-1})	GM[a] (ng/ml)	GM[a] exposure (ng/kg d^{-1})
Male ‡	>0 – <5	3.68	Q1	2		8.68	262
Female		3.11		7		2.03	67.1
All		3.23		9	32.4	2.81	90.8
Male ‡	>0 – <5	2.63	Q2	2		5.95	220
Female		3.16		4		1.60	52.4
All		2.99		6	34.1	2.48	84.5
Male ‡	>0 – <5	2.99	Q3	2		6.47	222
Female		2.94		2		1.41	48.0
All		2.96		4	34.2	3.02	103
Male	>0 – <5	3.15	Q4	2		2.01	66.7
Female		3.21		1		1.42	45.8
All		3.17		3	32.9	1.79	58.8
Male	>0 – <5	3.56	Q5	1		4.14	127
Female		3.36		2		2.82	89.5
All		3.42		3	31.3	3.21	100
Male	≥5 – <10	7.17	Q1	3		1.63	40.3
Female		7.27		2		1.80	44.5
All		7.21		5	24.8	1.70	41.9
Male	≥5 – <10	7.08	Q2	3		3.34	82.6
Female		7.00		5		2.62	65.0
All		7.03		8	24.8	2.87	71.1
Male	≥5 – <10	7.14	Q3	2		1.85	45.9
Female		6.60		2		1.32	32.9
All		6.87		4	24.9	1.56	38.8
Male	≥5 – <10	7.58	Q4	2		2.25	55.4
Female		7.79		2		4.15	102
All		7.68		4	24.6	3.06	75.1
Male	≥5 – <10	7.02	Q5	1		2.35	58.3
Female		7.88		2		2.69	65.9
All		7.59		3	24.6	2.57	63.2
Male	≥10 – <15	12.4	Q1	2		2.39	57.8
Female		13.3		3		2.24	54.3
All		12.9		5	24.2	2.30	55.7
Male	≥10 – <15	12.6	Q2	2		5.16	125
Female		12.4		2		1.75	42.2
All		12.5		4	24.2	3.00	72.6
Male	≥10 – <15	12.7	Q3	1		1.99	48.1
Female		12.4		2		2.18	52.6
All		12.5		3	24.2	2.11	51.1
Male	≥10 – <15	12.3	Q4	2		2.30	55.5
Female		13.1		1		2.41	58.2
All		12.6		3	24.2	2.33	56.4
Male ‡	≥10 – <15	12.3	Q5	2		6.11	148
Female		13.0		1		5.49	133
All		12.5		3	24.2	5.89	143

[a] geometric mean; [b] Q1 contains 20% of the population with the highest SEIFA scores, and represents the least disadvantaged geographical areas. Q5 contains 20% of the population with the lowest SEIFA scores, and represents the most disadvantaged geographical areas. ‡ strata contains extreme value

Table 2: Summary of urinary BPA concentration (total of free and conjugated species, ng/ml), and BPA exposure (ng/kg d^{-1}) for stratified pooled samples by area level socioeconomic index quintile, with age strata combined (n = 67)

Description	Quintile of area level SES[b]	Number of pools	GM[a] conc. (ng/ml)	GM[a] exposure (ng/kg d^{-1})
Male ǂ	Q1	7	2.93	76.3
Female		12	2.04	59.4
All		19	2.33	65.1
Male ǂ	Q2	7	4.46	123
Female		11	2.03	55.6
All		18	2.76	75.7
Male ǂ	Q3	5	3.10	87.1
Female		6	1.59	43.6
All		11	2.16	59.7
Male	Q4	6	2.18	59.0
Female		4	2.77	72.5
All		10	2.40	64.1
Male ǂ	Q5	4	4.37	113
Female		5	3.16	85.7
All		9	3.65	96.8
Male ǂ	All	29	3.25	87.6
Female		38	2.14	59.5
All		67	2.57	70.3

[a] geometric mean; [b] Q1 contains 20% of the population with the highest SEIFA scores, and represents the least disadvantaged geographical areas. Q5 contains 20% of the population with the lowest SEIFA scores, and represents the most disadvantaged geographical areas; ǂ strata contains extreme value

Table 3: Summary of urinary BPA urinary concentration (total of free and conjugated species), average urinary flow (in ml/kg d^{-1}, from flow model); and BPA exposure (ng/kg d^{-1}) for pooled samples stratified by age and sex (n = 67)

Description	Age bracket (years)	Av. Age (years)	Number of pools	Av. urinary flow (ml/kg d^{-1})	GM[a] (ng/ml)	GM[a] exposure (ng/kg d^{-1})
Male ‡	>0 – <5	3.16	9		4.98	165
Female		3.14	16		1.86	61.2
All		3.15	25	33.0	2.65	87.5
Male	≥5 – <10	7.20	11		2.22	55.0
Female		7.23	13		2.40	59.3
All		7.22	24	24.7	2.32	57.3
Male ‡	≥10 – <15	12.44	9		3.39	82.0
Female		12.84	9		2.35	56.7
All		12.64	18	24.2	2.82	68.2
Male	>0 – <15	7.57	29		3.25	87.6
Female		6.84	38		2.14	59.5
All		7.15	67	27.7	2.57	70.3

[a] geometric mean; ‡ strata contains extreme value

Table 4: Univariate and multivariate statistical analysis of ln-transformed BPA concentration (ng/ml urine) associations with area level socioeconomic index quintile (SES), age and sex. Data presented for all data points (n=67) and with extreme values excluded (n=63)

	Variable	All data points (*n*=67)		Extreme values excluded (*n*=63)	
		β (95% CI)	p-value	β (95% CI)	p-value
Univariate	SES quintile	-0.076 (-0.292-0.139)	0.487	-0.064 (-0.144-0.016)	0.119
	Age	-0.159 (-0.564-0.246)	0.442	0.122 (-0.022-0.266)	0.097
	Sex[a]	0.803 (0.126-1.479)	0.020	0.136 (-0.094 -0.365)	0.248
Multivariate	SES quintile	0.058 (0.139-0.256)	0.562	-0.055 (-0.134-0.024)	0.169
	Age	-0.468 (0.368-1.808)	0.021	0.111 (-0.032-0.254)	0.129
	Sex[a]	1.088 (0.368-1.808)	0.003	0.069 (-0.156-0.294)	0.546
	Sex*age	-0.694 (-1.188 -0.200)	0.006	-0.054(-0.344-0.235)	0.714

[a] where 'female' is the reference group

Table 5: Summary of literature reporting urinary concentrations of total BPA (sum of free and conjugated species) in children and adolescents

Reference	Country	Year of sample collection	Total BPA[a] concentration (ng/ml) *(µg/g Cr)*		N	Participant age range (years)
			GM	Median		
This study	Australia	2012	2.65	N/A	25[b]	0 – 5
			2.32	N/A	24[b]	5 – 10
			2.82	N/A	18[b]	10 – 15
Mendonca et al (2014)	United States	2006 – 2008	2.3	1.8	29	0.25 – 1.25
Hoepner et al (2013)	United States	2001 – 2010	3.7	3.8	408	3
			3.2	3.1	401	5
			2.9	2.7	318	7
Heffernan et al. (2013a)	Australia	2010 – 2011	2.97	N/A	65[b]	0 – 5
Pirard et al (2012)	Belgium	2011	2.71 *(3.63)*	N/A	21	0 – 6
			3.27 *(3.04)*	N/A	21	7-11
			2.61 *(2.96)*	N/A	22	12-19
Kasper-Sonnenberg et al. (2012)	Germany	2007 – 2009	2.4 *(2.3)*	2.3 *(2.1)*	104	6 – 8
Casas et al (2011)	Spain	2004 – 2008	N/A	4.2	30	4
Volkel et al. (2011)	Germany	2008	N/A	<0.45	91	0.083 – 0.42
Braun et al. (2011b)	United States	2004 – 2009	N/A	3.9 *(18)*	213	1
			N/A	2.9 *(9.6)*	195	2
			N/A	2.9 *(5.3)*	222	3
Morgan et al. (2011)	United States	2001	4.8 *(6.6)*	5.2	81	2 – 5
Bushnik et al. (2010)	Canada	2007 – 2009	1.30 *(2.00)*	N/A	N/A[c]	6 – 11
			1.50 *(1.31)*	N/A	N/A[c]	12 – 19
Becker et al. (2009)	Germany	2003 – 2006	3.55	3.53	137	3 – 5
			2.72	2.81	145	6 – 8
			2.22	2.13	149	9 – 11
			2.42	2.60	168	12 – 14
Calafat et al. (2008)	United States	2003 – 2004	3.6 *(4.3)*	3.7 *(4.2)*	314	6 – 11
			3.7 *(2.8)*	4.2 *(2.7)*	715	12 – 19

GM geometric mean; N/A not available; Cr creatinine; [a] total BPA (free + conjugated species); [b] pooled samples, where each pool contains 7 individual samples; [c] 5476 participants across all age ranges (6 – 79 years)

Table 6: Summary of associations between urinary bisphenol A and various demographic variables from published literature; asterisk denotes statistical significance

Study	Country	Year of sample collection	Total BPA[a], GM, ng/ml (µg/g Cr)	Participant age, years (number)	Association with selected SES variables			Additional Notes
					Income	Education	Ethnicity	
This study	Australia	2012	2.00 (N/A)	0 – 15 (n=67[b])	N/A	N/A	N/A	No association with SEIFA score (area-level index measure of SES)
Hoepner et al. (2013)	United States	1999 – 2010	1.8 – 3.7 (N/A)	0 - 7 (n=568)	None	None	Inconsistent	Higher concentrations in children of unmarried mothers
Kasper-Sonnenberg et al. (2012)	Germany	2007 – 2009	2.1 (1.8)	34 – 44 (n=104)	N/A	None	Some*	Positive association* with non-German nationality
Nelson et al. (2012)	United States	2003 – 2004	N/A (2.6)	≥6 – ≥60 (n=3953)	Negative*	Negative	Some	Negative association* with food security. Inconsistent association with occupation. Lower concentrations in Mexican-Americans than non-Hispanic whites.
		2005 – 2006	N/A (1.7)					
Bushnik et al. (2010)	Canada	2007 – 2009	1.16 (1.40)	6 – 79 (n=5476)	None	None	None	
Becker et al. (2009)	Germany	2003 – 2006	2.66 (N/A)	3 – 14 (n=599)	None	N/A	Some	No correlation with *"socioeconomic status which includes income"*. Lower levels reported in children of migrant families.
He et al. (2009)	China	N/A	0.87 (0.38)	24 – 43 (n=952)	N/A	Positive	N/A	
Calafat et al. (2008)	United States	2003 – 2004	2.6 (2.6)	≥6 – ≥60 (n=2517)	Negative	N/A	Some*	Lower concentrations* in Mexican-Americans than in non-Hispanic blacks and non-Hispanic whites.
Pregnancy cohorts								
Casas et al (2013)	Spain	2004 – 2006	2.1 (2.6)	≥16 (n=479)	None	Negative	N/A	
Braun et al. (2011)	United States	2006 – 2006	N/A (2.0)	N/A (n=388)	None	Negative	None	No association with marital status. Concentration varied by occupation (highest is cashiers)
Ye et al. (2008)	Netherlands	2002 – 2006	1.1 (N/A)	18-41 (n=99)	None	None	None	

GM, geometric mean; N/A, data not available; [a] total BPA (free + conjugated species); [b] pooled samples, where each pool contains 7 individual sample