Intake of Phthalate-tainted Foods and Microalbuminuria in Children: The 2011 Taiwan Food Scandal

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Outline

- Brief history of Taiwan food scandal in 2011
- NHRI, like NIH, initiated nationwide survey
- DEHP-tainted foods and renal damage
- Conclusion

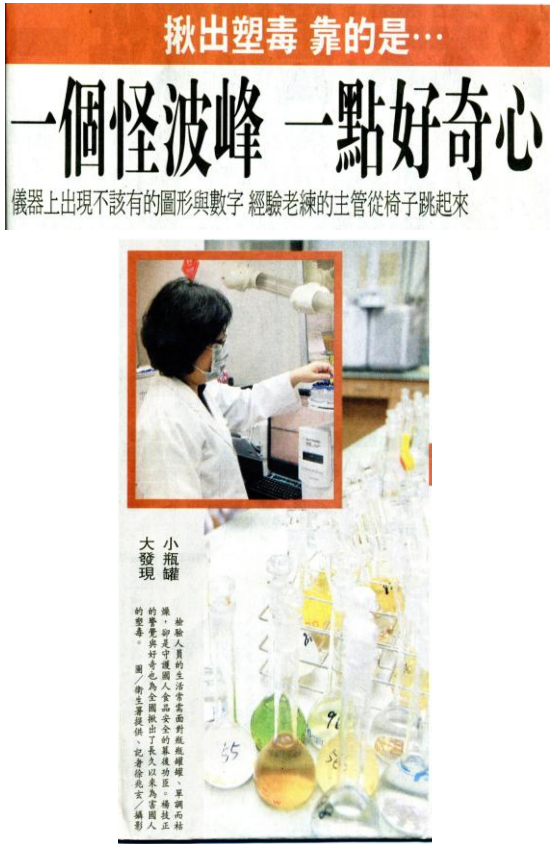
History of Taiwan Food Scandal (I)

- In April 2011, a laboratory staff member from the Taiwan's FDA, accidentally detected ~600 ppm DEHP (Di-(2-ethylhexyl)phthalate) in a probiotic supplement.

- Two perfumery-chemical companies: illegally adding DEHP and DINP (Di-isononyl phthalate), as substitutes for more costly emulsifiers (clouding agents), into their upstream products for more than 10 years.

- Five major food categories were contaminated: (I) sports drinks, (II) fruit beverages, (III) tea drinks, (IV) fruit jam or jelly, and (V) health food or supplements in tablet or powder form.

- Some phthalate-tainted foodstuffs (34 manufacturers and 206 food products in total) had been exported to as many as 22 countries, including the USA and European Union (Germany).



History of Taiwan Food Scandal (II)

- D-day (31 May 2011): all items of those 5 categories on the shelf were needed to have certificates (DEHP, DIDP, DNOP DINP, DBP, and BBP < 1 ppm).

- 13 July 2011: DOH officially limit
TDI (mg/kg bw/day) for DEHP to
0.01, DINP to < 0.15, BBP to < 0.
0.15.

- 01 August 2011: Taiwan governme
need of phthalate-free certificatior

Phthalate-free Certificate

Figure S1. The phthalates-free certificate was posted before the beverages.

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The public health threat of phthalate-tainted foodstuffs in Taiwan: The policies the government implemented and the lessons we learned☆

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V. Probiotics

Phalate-tainted Food Items posted on the website; DEHP ≥ 1.0 ppm; 05/28/2011

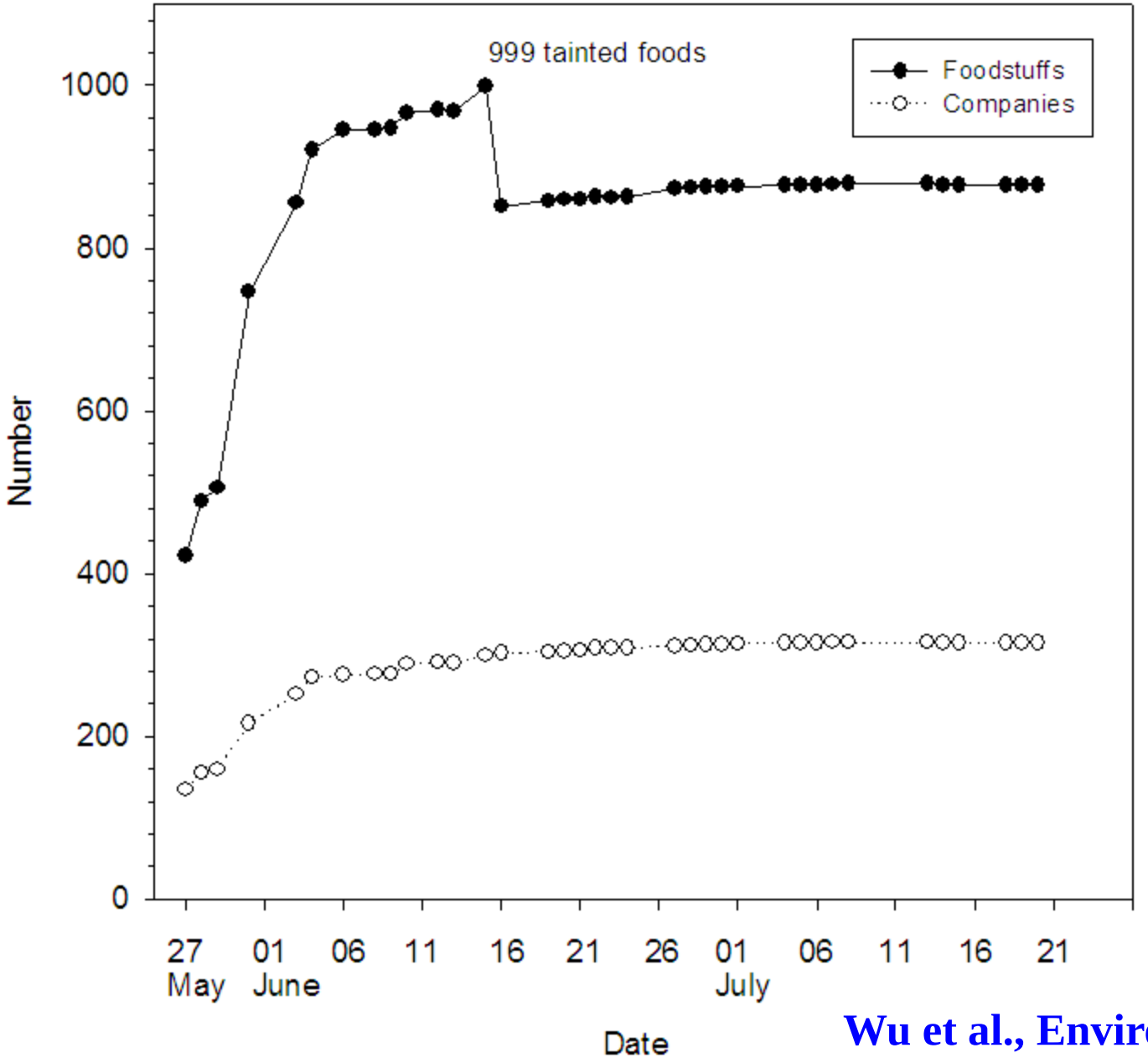
食品中檢出塑化劑DEHP累計清單

100.05.28 製表

	No.	檢體名稱	DEHP（ppm）	抽驗廠商	來源廠商	製造日期
膠囊／錠	15	檸檬酵素沖泡飲品	7.8	德康生物科技	德康生物科技	製造日期2010/01/11 有效日期2013/01/10
	16	通暢包酵素飲品	31.7	德康生物科技	德康生物科技	有效日期2013/12/12
	17	固樂好	362	欣茂實業	鴻仲生物科技	2011/04/02
	18	EC-12乳酸菌末	15.6	欣茂實業	鴻仲生物科技	不詳
	19	纖果園木寡糖乳酸菌	1.7	黑松股份有限公司		有效日期2012/06/25
	20	威敏Power-Lac粉末營養食品	527	百晟生物科技股份有限公司		有效日期2013/03/14

食品中檢出塑化劑DINP累計清單 **DINP ≥ 1.0 ppm** 00.05.28 製表

	No.	檢體名稱	DINP（ppm）	抽驗廠商	來源廠商	製造日期
膠囊／錠狀／粉劑類	15	威敏Power-Lac粉末營養食品	約8713	百晟生物科技股份有限公司		2013/03/14
	16	超級龍根菌Best Bifidus Plus 五合一加強版	約205.2	順傑生物科技(股)公司		2012/01/05
	17	柔護益生菌複方膠囊食品	約604.5	台塑生醫科技股份有限公司		2012/09/13



Wu et al., Environ Int, 2012

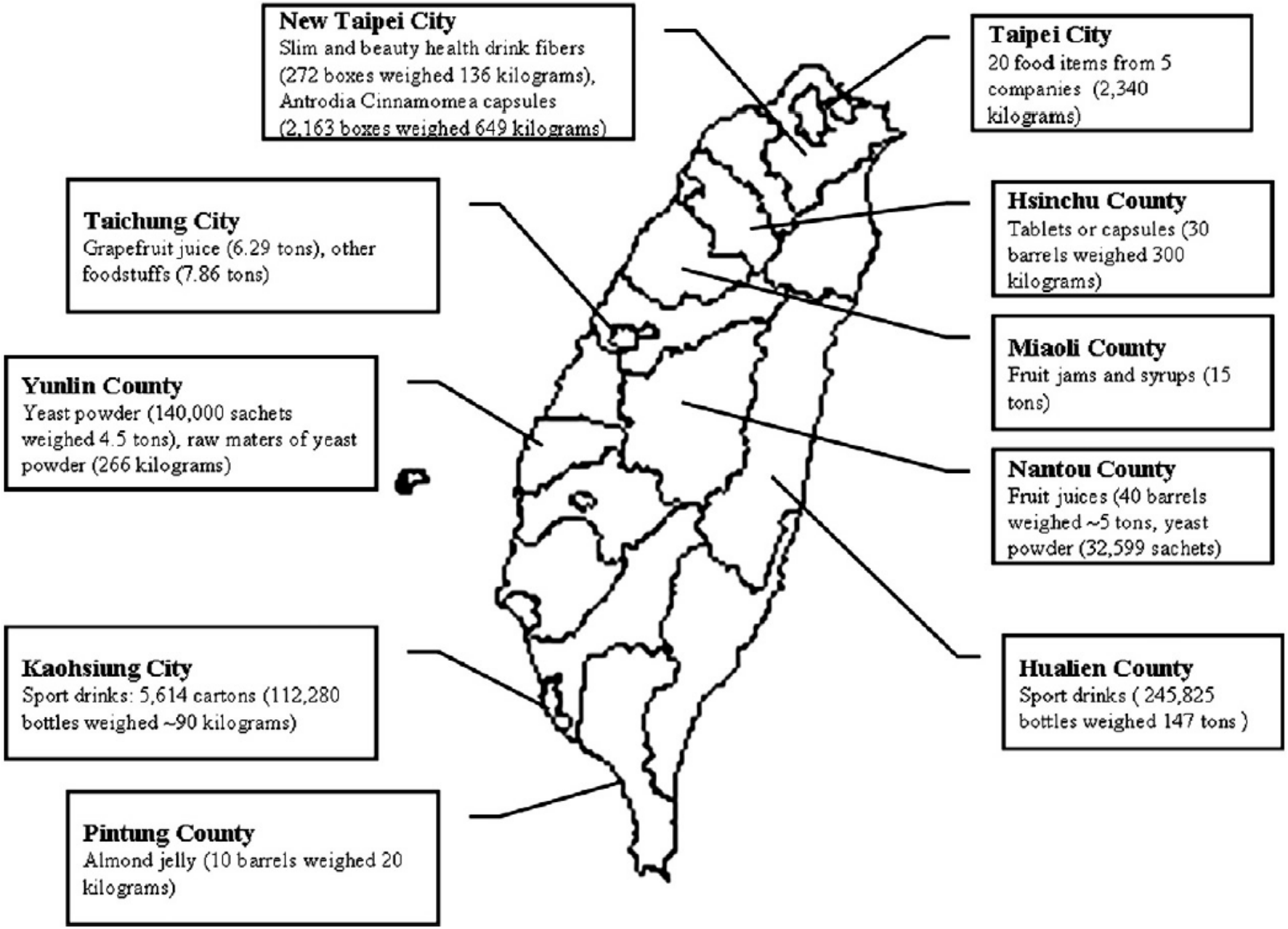


Fig. 2. The phthalate-tainted raw materials and/or final food products weighing ~286.44 t were ceremonially destroyed in public all over Taiwan on 11 June 2011.

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New Taipei City
Slim and beauty health drink fibers (272 boxes weighed 136 kilograms), Antrodia Cinnamomea capsules (2,163 boxes weighed 649 kilograms)

Taipei City
20 food items from 5 companies (2,340 kilograms)

Taichung City
Grapefruit juice (6.29 tons), other foodstuffs (7.86 tons)

Hsinchu County
Tablets or capsules (30 barrels weighed 300 kilograms)

Miaoli County
Fruit jams and syrups (15 tons)

Yunlin County
Yeast powder (140,000 sachets weighed 4.5 tons), raw maters of yeast powder (266 kilograms)

Nantou County
Fruit juices (40 barrels

Kaohsiung City
Sport drinks: 5,614 cartons (112,280 bottles weighed ~90 kilograms)

Pintung County
Almond jelly (10 barrels weighed 20 kilograms)

NHRI, like NIH

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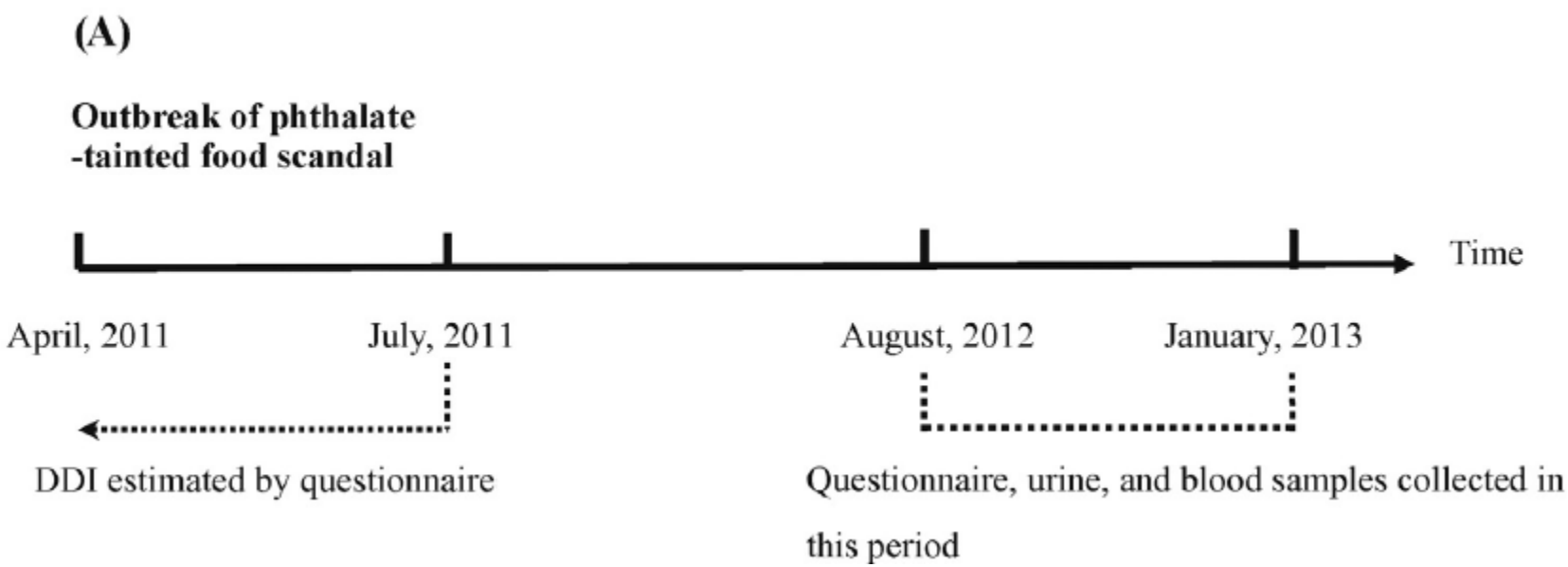
Intake of phthalate-tainted foods and microalbuminuria in children: The 2011 Taiwan food scandal

Hui-Ju Tsai [a,b,1], Bai-Hsiun Chen [c,d,1], Chia-Fang Wu [b,e], Shu-Li Wang [f], Po-Chin Huang [f], Yi-Chun Tsai [g], Mei-Lien Chen [h], Chi-Kung Ho [b,i], Chao A. Hsiung [j,*], Ming-Tsang Wu [b,d,e,k,l,**]

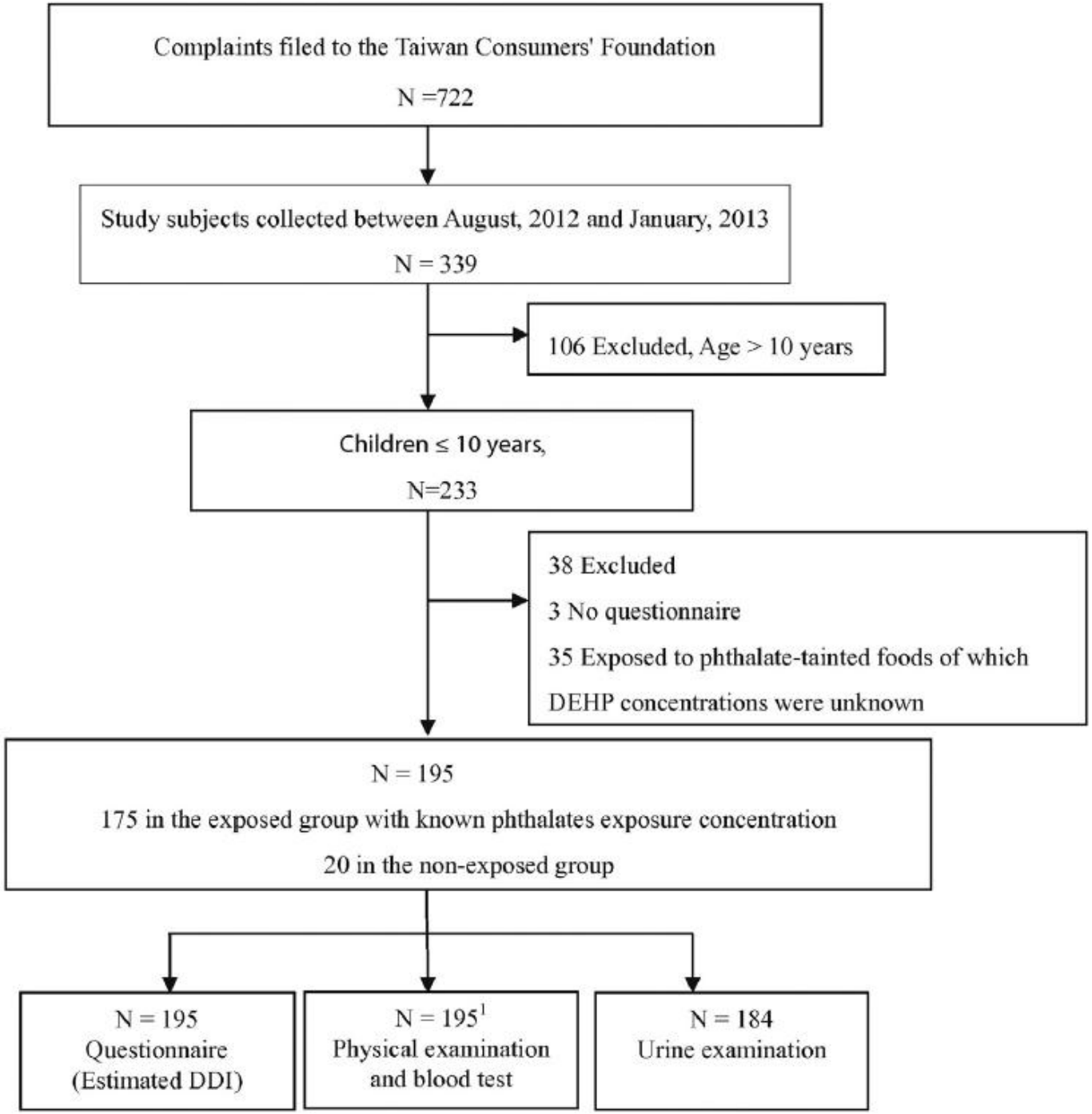


Introduction

- Phthalates are well known as endocrine-disrupting chemicals (Halden, 2010; Pak et al., 2011).

- For renal function, animal studies suggested that some phthalates, such as DEHP and DINP, can damage kidney (Kaufmann et al., 2002; Ito et al., 2007).

- One human study, the 2009-2010 National Health and Nutrition Examination Survey (NHANES), has investigated the association between exposure to phthalates and renal function in children and adolescent (Trasande et al., 2014).
  - Studied 667 children aged 6-19 years old and found a positive association between metabolites of HMW phthalates and urine ACR.


Complaints filed to the Taiwan Consumers' Foundation
N =722
Study subjects collected between August, 2012 and January, 2013
N = 339
106 Excluded, Age > 10 years
Children ≤ 10 years,
N=233
38 Excluded
3 No questionnaire
35 Exposed to phthalate-tainted foods of which
DEHP concentrations were unknown
N = 195
175 in the exposed group with known phthalates exposure concentration
20 in the non-exposed group
N = 195
Questionnaire
(Estimated DDI)
N = 195[1]
Physical examination
and blood test
N = 184
Urine examination

Phthalates Special Clinic for Children

Environmental Science & Technology
Article
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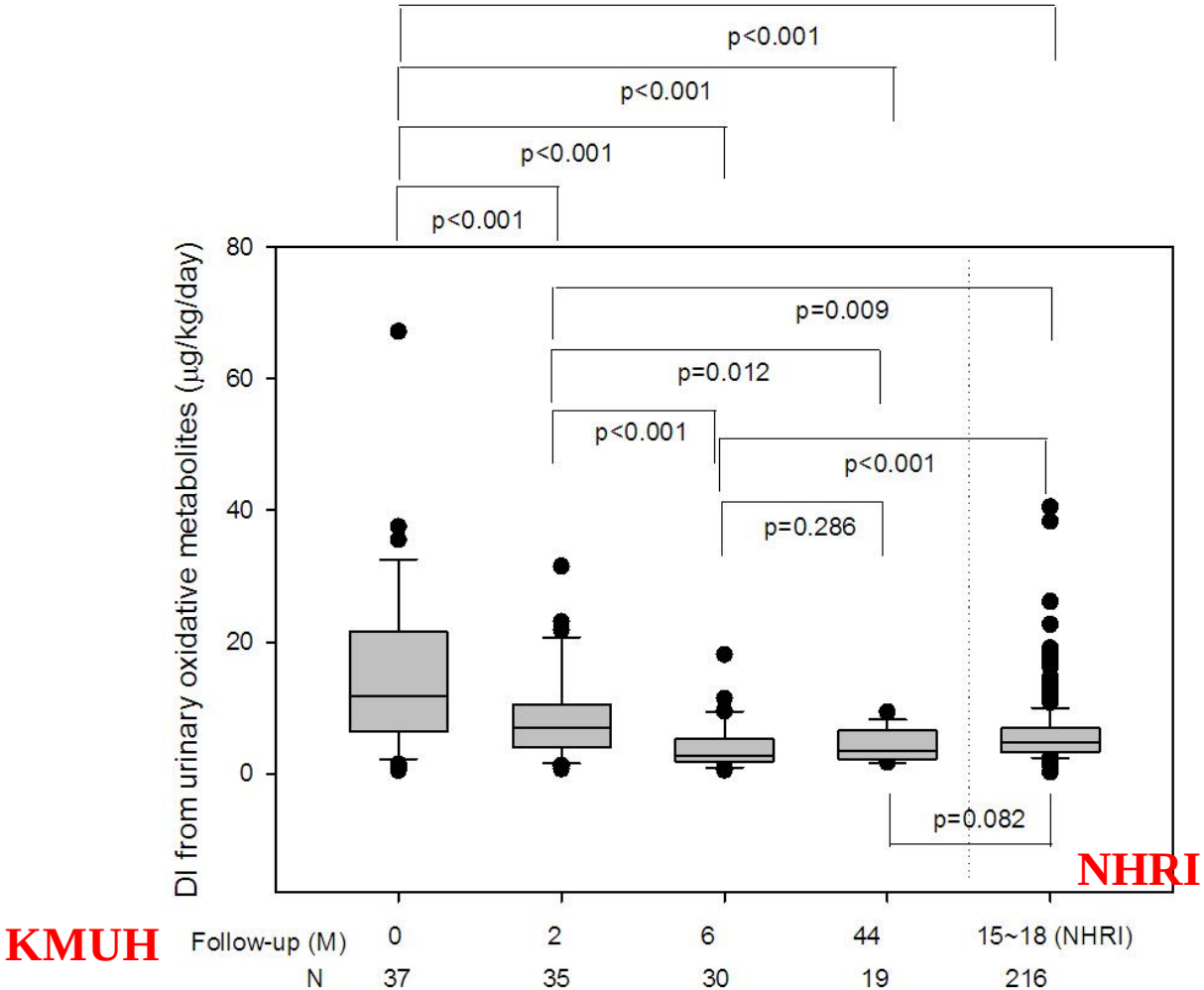
Temporal Changes of Urinary Oxidative Metabolites of Di(2-ethylhexyl)phthalate After the 2011 Phthalate Incident in Taiwanese Children: Findings of a Six Month Follow-Up

Chia-Fang Wu,[†] Bai-Hsiun Chen,[‡,§] Jentaie Shiea,[∥] Eric K. Chen,[⊥] Ching-Kuan Liu,[#] Mei-Chyn Chao,[§] Chi-Kung Ho,[†] Jiunn-Ren Wu,[§] and Ming-Tsang Wu[*,†,∇,○]



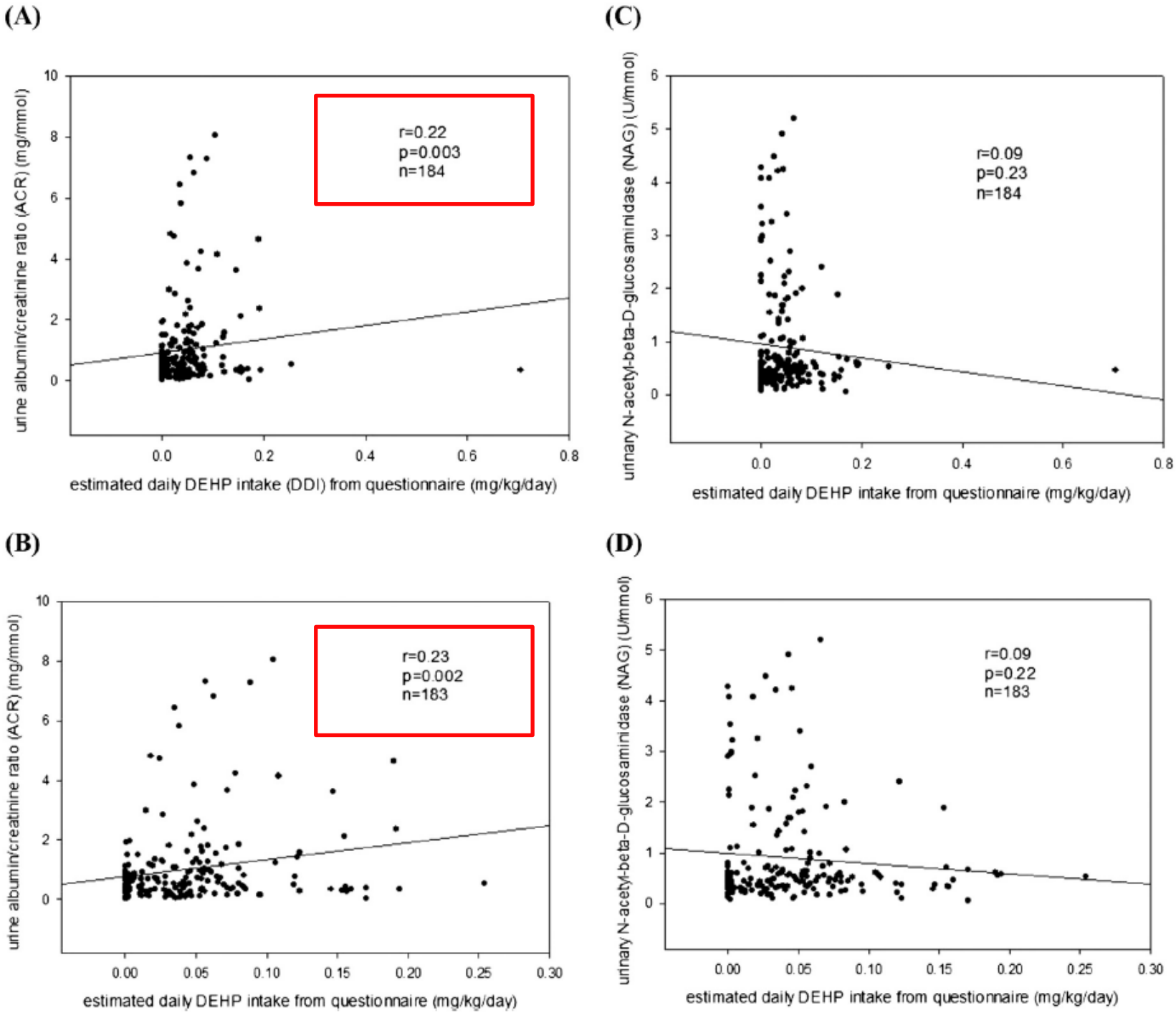

(A)
r=0.22
p=0.003
n=184
urine albumin/creatinine ratio (ACR) (mg/mmol)
estimated daily DEHP intake (DDI) from questionnaire (mg/kg/day)
(C)
r=0.09
p=0.23
n=184
urinary N-acetyl-beta-D-glucosaminidase (NAG) (U/mmol)
estimated daily DEHP intake from questionnaire (mg/kg/day)
(B)
r=0.23
p=0.002
n=183
urine albumin/creatinine ratio (ACR) (mg/mmol)
estimated daily DEHP intake from questionnaire (mg/kg/day)
(D)
r=0.09
p=0.22
n=183
urinary N-acetyl-beta-D-glucosaminidase (NAG) (U/mmol)
estimated daily DEHP intake from questionnaire (mg/kg/day)

Table 3
Relationship of log-transformed urine microalbumin/creatinine ratio (ACR) with the category of the recommended tolerable daily intake (TDI) of di-(2-ethylhexyl) phthalate (DEHP) by questionnaire in multivariable linear regression models.

DDI	Crude			Model 1[a]			Model 2[b]			Model 3[c]		
	β	SE	P	β	SE	P	β	SE	P	β	SE	P
Non-exposure	1	–	–	1	–	–	1	–	–	1	–	–
≤0.02, >0	0.160	0.135	0.235	0.155	0.137	0.260	0.169	0.139	0.226	0.194	0.143	0.179
≤0.05, >0.02	0.222	0.134	0.100	0.203	0.135	0.134	0.197	0.136	0.150	0.222	0.141	0.171
>0.05	0.418	0.128	0.001	0.414	0.131	0.002	0.408	0.132	0.002	0.440	0.139	0.002

Abbreviations: BMI: body mass index; DDI: daily DEHP intake; MAP: mean arterial pressure; MBzP: mono-benzyl phthalate; MEHHP: mono (2-ethyl-5-hydroxyhexyl) phthalate; MEHP: mono-(2-ethylhexyl) phthalate; MEOHP: mono-(2-ethyl-5-oxohexyl) phthalate; MEP: mono-ethyl phthalate; MMP: mono-methyl phthalate; MiBP: mono-isobutyl phthalate; MnBP: mono-n-butyl phthalate.

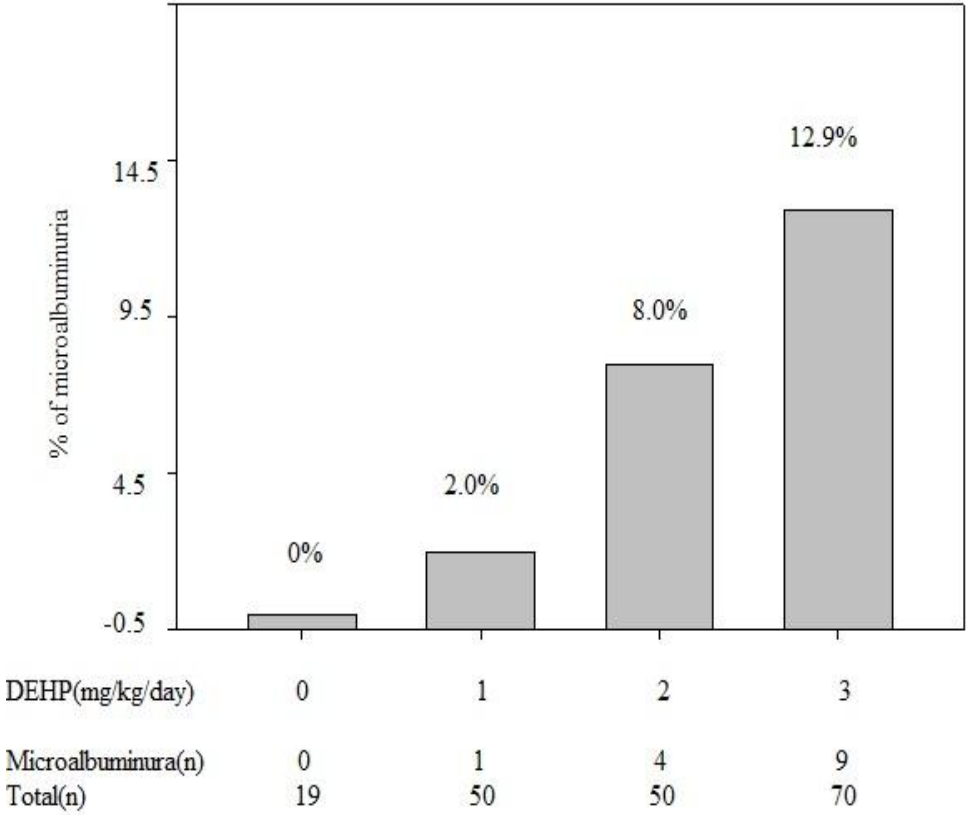
[a] Adjusting for age, gender, BMI.

[b] Adjusting for age, gender, BMI, MAP, insulin resistance, cholesterol, and uric acid.

[c] Adjusting for age, gender, BMI, MAP, insulin resistance, cholesterol, uric acid, MMP, MEP, MnBP, MBzP, MEHP, MEHHP, MEOHP, and MiBP.

Table 2
Urinary biomarkers of renal injury categorized by the recommended tolerable daily intake (TDI) of di-(2-ethylhexyl) phthalate (DEHP) (N = 184).[a]

DDI (mg/kg/day)	Exposed groups >0.05 N = 70	≤0.05, >0.02 N = 49	≤0.02, >0 N = 47	Non-exposed Group N = 18	P value[b]	P value for trend
Mean ± SD (Median, IQR) or N (%)						
ACR (mg/mmol)	1.43 ± 1.80 (0.76, 0.35–1.64)[e]	1.02 ± 1.42 (0.53, 0.23–1.15)[d]	0.72 ± 0.84 (0.47, 0.27–0.85)[c]	0.47 ± 0.33 (0.38, 0.20–0.75)	0.007	<0.001
NAG (U/mmol)	0.79 ± 0.84 (0.54, 0.37–0.74)[e]	1.06 ± 1.21 (0.57,0.34–1.38)[d]	0.97 ± 1.13 (0.43, 0.26–1.11)[c]	0.75 ± 1.07 (0.34, 0.28–0.64)	0.32	0.72
Microalbuminuria						
Yes	9 (12.9)[f]	4 (8.2)[f]	1 (2.1)	0 (0)	0.12	0.02
No	61 (87.1)	45 (91.8)	46 (97.9)	18 (100)		



After multiple imputation

Table 4. Relationship of microalbuminuria (> 3.5 mg/mmol creatinine) with the category of the recommended tolerable daily intake (TDI) of di-(2-ethylhexyl) phthalate (DEHP) by questionnaire in multivariable logistic regression models.

	Microalbuminuria		Crude			Model 1[1]			Model 2[2]			Model 3[3]		
	Yes	No	OR	95%CI	*P*	OR	95%CI	*P*	OR	95%CI	*P*	OR	95%CI	*P*
	N (%)													
DDI ≤ 0.02	**1 (1.5)**	**64 (98.5)**	**1**	**-**	**-**	**1**	**-**	**-**	**1**	**-**	**-**	**1**	**-**	**-**
≤ 0.05, > 0.02	**4 (8.2)**	**45 (91.8)**	**5.689**	**0.615-52.602**	**0.126**	**5.527**	**0.584-52.321**	**0.136**	**5.005**	**0.520-48.170**	**0.163**	**5.883**	**0.567-61.062**	**0.138**
>0.05	**9 (12.9)**	**61 (87.1)**	**9.443**	**1.161-76.767**	**0.036[4]**	**10.769**	**1.226-94.615**	**0.032**	**10.019**	**1.138-88.249**	**0.038**	**10.395**	**1.096-98.580**	**0.041[5]**
Covariates														
MEHP														
First tertile	5 (8.1)	57 (91.9)	1	-	-									
Second tertile	4 (6.7)	56 (93.3)	0.814	0.208-3.190	0.768									
Third tertile	5 (8.1)	57 (91.9)	1.000	0.274-3.643	1.000									
MEOHP														
First tertile	3 (4.9)	58 (95.1)	1	-	-									
Second tertile	5 (8.1)	57 (91.9)	1.696	0.387-7.430	0.483									
Third tertile	6 (9.8)	55 (90.2)	2.109	0.503-8.850	0.308									
MEHHP														
First tertile	2 (3.2)	60 (96.8)	1	-	-							1	-	-
Second tertile	8 (13.1)	53 (86.9)	4.528	0.921-22.271	0.063							4.643	0.815-26.446	0.084
Third tertile	4 (6.6)	57 (93.7)	2.105	0.371-11.942	0.401							2.017	0.314-12.969	0.460

Abbreviations: ACR: albumin/creatinine ratio; BMI: body mass index; DDI: daily DEHP intake; DEHP: di-(2-ethylhexyl) phthalate; MBzP: mono-benzyl phthalate; MEHHP: mono (2-ethyl-5-hydroxyhexyl) phthalate; MEHP: mono-(2-ethylhexyl) phthalate; MEOHP: mono-(2-ethyl-5-oxohexyl) phthalate; MEP: mono-ethyl phthalate; MMP: mono-methyl phthalate; MiBP: mono-isobutyl phthalate; MnBP: mono-n-butyl phthalate

Conclusion

- A major health threat from phthalate-tainted foodstuffs occurred in Taiwan in 2011.
- DEHP-tainted food intake increases the excretion of urinary ACR in children.
- DEHP-tainted food intake may increase the risk of microalbuminuria.

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