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## Personal care products use and phthalate exposure levels among pregnant women

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#### HIGHLIGHTS

### GRAPHICAL ABSTRACT

- · Most phthalate metabolites were detected in >80% of pregnant women's urine samples.
- · Phthalate metabolites showed weak to moderate reproducibility across the pregnancy.
- · MEP was associated with increasing uses leave-on personal care products (PCPs).
- The more number the use of leave-on PCPs, the higher concentrations of MEP in urine.
- · Use of leave-on PCPs was considered a relevant phthalate source in Taiwan.

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#### ABSTRACT

Background: Fetuses are susceptible to phthalates, known endocrine disrupting chemicals, within sensitive windows of development. It is crucial to determine the major sources of phthalates to reduce exposure. This study aims to examine the associations between usage patterns of personal care products (PCPs) and urinary levels of phthalate metabolites across pregnancy in a multi-hospital based birth cohort.

Methods: During 2012–2015, we conducted a birth cohort study named the Taiwan Mother Infant Cohort Study

Abbreviations: PCPs, personal care products; TMICS, Taiwan Mother Infant Cohort Study; ICCs, intraclass correlation coefficients; MMP, mono-methyl phthalate; MEP, mono-ethyl phthalate; MnBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MiNP, mono-isononyl phthalate; MBZP, mono-benzyl phthalate; MEHP, mono-2-ethylhexyl phthalate; MEHHP, mono-2-ethyl-5-hydroxyhexyl phthalate; MEOHP, mono-2-ethyl-5-oxohexyl phthalate; MECPP, mono-2-ethyl-5-carboxypentyl phthalate; MCMHP, mono-2carboxymethylhexyl phthalate; DMP, di-methyl phthalate; DEP, di-ethyl phthalate; DnBP, di-n-butyl phthalate; DiBP, di-isobutyl phthalate; DiNP, di-isononyl phthalate; BzBP, benzyl butyl phthalate; DEHP, di-2-ethylhexyl phthalate; LOD, limit of detection; GMs, geometric means; CIs, confidence intervals; GEE, generalized estimating equation.

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*Keywords:* Phthalate Pregnancy Personal care product Urine Repeated measurement (TMICS). Usage patterns of PCPs were obtained using structured questionnaires during the third trimester of pregnancy. Spot urine samples were collected at each trimester, and levels of eleven phthalate metabolites were measured by liquid chromatography tandem mass spectrometry. The association of PCPs use with urinary phthalate metabolite concentrations was assessed using GEE models.

*Results*: Among the 1676 pregnant women participated in TMICS, 281 who provided two or three urine samples across pregnancy were included. The levels of several phthalate metabolites were significantly associated with the use of PCPs, particularly leave-on PCPs. With the increasing use of skin toners (11.7%; 95% CI: 1.5%, 22.9%), lipsticks (13.2%; 95% CI: 4.6%, 22.5%), and essential oils (21.8%; 95% CI: 9.1%, 36.0%), individuals are exposed to higher concentrations of mono-ethyl phthalate (MEP). Additionally, a positive trend was found regarding the number of leave-on PCPs used and the measured change in MEP concentrations (P for trend = 0.01). Other positive associations included MBzP and body lotions (7.9%; 95% CI: 0.1%, 16.2%). With regard to rinse-off PCPs, we found a positive association between urinary MBzP and shampoo use, and a negative association between urinary MMP and face wash.

*Conclusion:* Leave-on PCPs were found to be a more probable source of phthalate exposure than the use of rinseoff PCPs. We suggest pregnant women reduce the frequency of leave-on PCPs use during pregnancy to avoid such phthalate exposure.

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#### 1. Introduction

Phthalates are well-known endocrine disrupting chemicals that remain ubiquitous in the environment (Braun, 2017). Despite having short half-lives in the human body, inevitable and constant exposure to phthalates results in high detection frequencies of their metabolites in biological samples (Koch et al., 2013). People get exposed to various phthalates through different routes based on the types of products they use. For example, exposure to phthalates may occur through eating food stored in plastic containers (ingestion), spraying perfumes (inhalation and dermal contact), and applying lotions (dermal contact). Mouthing behavior in children is an additional type of phthalate ingestion exposure (Juberg et al., 2001).

Diet is considered a major route of exposure to high molecular weight (HMW) phthalates (≥250 Dalton (Da)) such as di-2-ethylhexyl phthalate (DEHP) as a result of migration from food containers and/or packaging materials (Cao, 2010; Koch et al., 2013; Serrano et al., 2014). By contrast, the use of consumer products, specifically personal care products (PCPs), is suggested to be the dominant exposure pathway of low molecular weight (LMW) phthalates (<250 Da), such as diethyl phthalate (DEP) (Guo and Kannan, 2013; Koniecki et al., 2011; Parlett et al., 2013; Sakhi et al., 2017). High detection rates of LMW phthalates in PCPs (~100% DEP in perfumes from the United States) have been reported (Braun, 2017; Guo and Kannan, 2013; Kamrin, 2009; Paulsen, 2015). However, phthalates in PCPs are not as wellregulated as consumer products such as food contact materials, toys, and child care products.

The application types of PCPs, including rinse-off and leave-on, can influence the absorbed doses of phthalates (Guo and Kannan, 2013; Paulsen, 2015). Exposure to multiple phthalates was found to increase adverse health effects in animal studies (Howdeshell et al., 2008). Thus, the risks of phthalate exposure caused by PCPs must be investigated.

Exposure to phthalates has been linked to adverse reproductive and developmental effects (Chevrier et al., 2012; Ejaredar et al., 2015; Huang et al., 2012; Kamrin, 2009). A significant correlation between phthalate metabolite concentrations in pregnant women's urine and their corresponding cord blood emphasizes the potential impact of maternal exposure on fetal health (Lin et al., 2011). Prenatal exposure to phthalates, particularly during a critical period of fetal development, is of great concern. In pregnant women, biomonitoring studies that assess prenatal phthalate exposure have found positive associations between the frequent use of PCPs and urinary levels of phthalate metabolites, particularly LMW phthalates (Arbuckle et al., 2014; Braun et al., 2014; Buckley et al., 2012; Cantonwine et al., 2014; Parlett et al., 2013; Sakhi et al., 2017). Although these studies indicate that PCPs contribute to the phthalate body burden during pregnancy, most of them primarily

used a 24- or 48-hour recall questionnaire for PCPs use to link the results to one-spot urinary phthalate metabolites, which may not capture the temporal variation of phthalate exposure during pregnancy because of their short half-lives. Thus, this study aimed to investigate the relationship of usage patterns of PCPs with urinary phthalate metabolites by measuring multiple urine samples across the period of pregnancy in a Taiwan birth cohort.

#### 2. Methods

#### 2.1. Study population

A birth cohort study, called the Taiwan Mother Infant Cohort Study (TMICS), was conducted for the general population that covered the northern, central, southern, and eastern parts of Taiwan in the years 2012-2015. The detailed study protocol was described previously (Wu et al., 2018). In short, pregnant women who received prenatal care at nine collaborative hospitals were invited to participate in the TMICS (Fig. 1). Pregnant women who underwent a prenatal examination in selected hospitals were invited to join this study in their 1st (4-12 weeks), 2nd (13-27 weeks) or 3rd (28-42 weeks) trimester of pregnancy. In total, 1676 participants participated in this cohort study and answered our questionnaires. The study protocol was approved by the Institutional Review Boards of the National Health Research Institutes and the 9 collaborative hospitals. After obtaining written informed consent, the participants provided one-spot urine samples at each trimester of pregnancy, particularly in the third trimester. One-spot urine samples were collected in a 15 mL polypropylene (PP) tube (northern, central, and southern sites) or a glass container (eastern site) and immediately transferred and aliquoted into several 12 mL amber glass bottles. All the glassware was washed in MeOH, ACN and acetone, and then sealed with aluminum foil in order to prevent possible contamination of the urine samples from the environment. Urine samples were collected at the same time as serum samples, and all samples were stored at -80 °C before analysis. Our previous study has found that the median levels of studied urinary phthalate metabolites in the glass cups were not significantly different from those in PP tubes in the eleven healthy volunteer females (Kuo et al., 2015).

#### 2.2. Questionnaires for PCPs

Structured questionnaires were via face-to-face interviews by welltrained staff members during the third trimester of pregnancy. Exposure information on the use of 11 PCPs during pregnancy was obtained and categorized as rinse-off (body washes, shampoos, face washes, and hand washes) and leave-on (body lotions, skin toners, lipsticks, cosmetics, essential oils, perfumes, and hair sprays) products. Information Download English Version:

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