Toddler exposure to flame retardant chemicals: magnitude, health concern and potential risk- or protective factors of exposure: observational studies summarized in a systematic review
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Introduction
Many flame retardant (FR) chemicals are endocrine disrupting and thereby a human health concern (1, 2). Exposure is mostly investigated for adult- and early life exposure. Prenatal FR exposure has been assessed previously in maternal blood (3, 4), or in umbilical cord blood and placental tissue at birth (4-6). Neonatal exposure, of which the main is consumption of contaminated breastmilk, has been studied in numerous studies across Europe, the United States of America (USA), the Pacific and Asia as reviewed by Fromme et al. (7). However, human development does neither stop at birth nor at the end of the neonatal period, and human exposure to FRs is not a one-time event but a cumulative process. Toddlerhood is a critical developmental period. Furthermore, toddlers are at an increased risk of exposure because of their specific behavior, such as often being close to the floor, mouthing of hands and objects (8), and their different body proportions with a relatively higher total body surface compared to adults (9). An overview of studies on toddler exposure and health effects is hardly existing. This systematic narrative review primarily presents an overview of the magnitude of toddler exposure worldwide and secondarily health effects and potential environmental, demographic or behavioral risk- or protective factors for toddler exposure.

Materials and methods
A systematic literature search in four databases (PubMed, Embase.com, The Cochrane Library (via Wiley) and Web of Science Core collection) was carried out in collaboration with a medical librarian. Studies were included if FRs were measured in or on toddlers (e.g. serum, urine or body wipe samples) and if the study population included toddlers aged 8 to 24 months.

Results and discussion
The comprehensive search resulted in 1474 records after removing duplicates. Title and abstract screening identified 60 full-text articles that were assessed for eligibility. After full-text screening, 10 studies were included and subsequently 50 articles were excluded (see figure 1). The included studies measured several types of FRs in toddlers’ serum, urine, hand wipes and feces. We identified five studies that measured polybrominated diphenyl ethers (PBDEs), one that measured hexabromocyclododecane (HBCDs), one that measured new/emerging brominated FRs (NBFRs), and two that measured phosphorus FRs (PFRs) Concentrations of PBDEs occurring most are presented in table 1.
BDE-47 was the main congener in studies from the USA whereas BDE-209 was the most abundant congener in studies performed in Sweden, which is in line with the literature (10). Concentrations of NBFRs, new FRs replacing banned PBDEs, are presented in table 2. Most concentrations are lower in comparison to PBDEs. However, two contaminants, decabromodiphenyl ethane (DBDPE) and (bis(2-ethylhexyl) tetrabromophthalate (BEH-TEBP) were detected at approximately 50–fold higher concentrations than PBDEs (except for BDE-209). PFRs are nowadays also frequently being used as alternatives for PBDEs. Concentrations of PFR metabolites measured in urine are summarized in table 3. One study assessed health effects and reported thyroid hormone disturbance, as BDE-47 and -99 were positively correlated with Thyroid Stimulating Hormone (TSH) concentrations (11). Comparable studies were not available for toddlers, however the above described findings were in line with a study from South Korea including much younger children (1-3 months) (12). Owning a certain amount of infant furniture and toys that contain polyurethane foam such as a highchair or swing, or playing with plastic toys affected respectively PBDE levels and PFR metabolite levels (13, 14). FR levels were higher in toddlers compared to their mothers. Moreover, the exposure pathway for the various congeners is suspected to be different for some congeners. For example, BDE-153 in mothers’ and toddlers’ serum was correlated and concentrations were similar, which implies same source and/or exposure route, whereas BDE-209 in mothers’ and toddlers’ serum was not correlated and toddlers had a higher serum concentration compared to their mothers, which implies that toddlers were more exposed to BDE-209 via another exposure route (15).

Studies were not uniform on whether exposure differs for age as some studies found increasing exposure with age (16, 17), whereas others found the highest levels in younger children (11, 18). Results on gender were also not unambiguous, two studies reporting higher levels in girls (13, 15) and three studies reported higher levels in boys (17-19).
Considering the limited amount of studies and their variation in biological matrices, FRs and associating factors, results did not reveal a uniform pattern of toddler exposure and further research is necessary for this particular age group. However, we can conclude that toddlers are exposed to PBDEs, NBFRs, PFRs and HBCDs (the latter not reported here). Especially the new FRs, NBFRs and PFRs are of concern as not much research on exposure and its health effects is available. Factors in the indoor environment such as playing with plastic toys are associated with increased exposure. Alternation of these factors can result in a reduction of indoor exposure to FRs in toddlers which enables a healthy development.
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