
Critical Reviews in Toxicology

ISSN: 1040-8444 (Print) 1547-6898 (Online) Journal homepage: https://www.tandfonline.com/loi/itxc20

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**To cite this article:** Laura Campo, Petra Bechtold, Lucia Borsari & Silvia Fustinoni (2019): A systematic review on biomonitoring of individuals living near or working at solid waste incinerator plants, Critical Reviews in Toxicology, DOI: 10.1080/10408444.2019.1630362

**To link to this article:** https://doi.org/10.1080/10408444.2019.1630362



Published online: 16 Sep 2019.

CRITICAL REVIEWS IN TOXICOLOGY
https://doi.org/10.1080/10408444.2019.1630362

REVIEW ARTICLE

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# A systematic review on biomonitoring of individuals living near or working at solid waste incinerator plants

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**ABSTRACT**

**Background:** Solid waste incinerators (SWI) emit several pollutants among which polychlorodibenzo-dioxins and furans (PCDD/Fs), polychlorobiphenyls, metals, monocyclic and polycyclic aromatic hydrocarbons (PAHs).

**Aim of the study:** To present a systematic review of peer-reviewed literature on human biological monitoring of exposure and effect following potential exposure to SWI pollutants to bring together evidences and to highlight strengths and deficiencies of the studies conducted so far.

**Methods:** Relevant studies on biomonitoring of individuals living near or working at SWIs were selected through three steps: (1) a literature search in the Medline, CAplus, and Embase database; (2) the retrieved abstracts were screened by four independent reviewers; (3) the full text of the relevant papers was read, papers were pooled in studies, and then analyzed to highlight strengths and weaknesses. Studies with the strongest epidemiological design and/or the largest sample size were identified as reference studies.

**Results:** One hundred and thirty-two papers, pooled in 82 studies, were included in the review: 67 on general population, 52 on SWI workers, and 14 on both groups. The most frequently investigated biomarkers were PCDD/Fs in plasma (87). Several studies presented limitations, such as a small samples size, scarce information on confounders, and a poor statistical analysis. Some earlier studies showed an increase of PCDD/Fs, lead, and PAHs in individuals (mainly workers) exposed to emissions from old SWIs; studies from the year 2000 showed no increase of biomarkers or biomarkers within the range of the general population; decreasing trends were observed in prospective studies.

**Conclusions:** Most studies presented methodological pitfalls; reference studies showed no or a limited evidence of the impact of SWI on exposure and effect biomarkers.

**Abbreviations:** 1-OHPYR: 1-hydroxypyrene; 2-NAPOH: 2-hydroxynaphtalene; 8-OH-dG: 8-hydroxy-deoxyguanosine; ACGIH: American Conference of Governmental Industrial Hygienists; BAT: Best Available Technologies; BEI: Biological exposure Index; BMI: Body Mass Index; BTEX: Benzene, toluene, ethylbenzene and xylenes; Co-PCB: non-ortho coplanar polychlorobiphenyls; DCP: dichlorophenols; DDE: p,p′-dichlorodiphenyldichloroethylene; EPP: erythrocyte protoporphyrin; FLEHS: Flemish Environment and Health Study; GGT: γ-glutamyl transpeptidase; HBM: human biomonitoring; HCB: hexachlorobenzene; HSWI: hazard solid waste incinerator; IED: Industrial Emission Directive; MCP: monochlorophenol; MDA: malondialdheyde; MSWI: municipal solid waste incinerator; PAHs: polycyclic aromatic hydrocarbons; PBDE: polybromodibenzodioxins; PCB: polychlorobiphenyls; PCDD/F: polychlorodibenzodioxins/furans; PCP: polychlorophenols; PM: Particulate Matter; POPs: Persistent Organic Pollutants; SPMA: S-phenylmercapturic acid; SWI: solid waste incinerator; *t,t*-MA: *t,t*-muconic acid; TCDD: 2,3,7,8-tetra-chlorodibenzo-*p*-dioxine; TCP: threechlorophenols; TEF: toxic equivalency factor; TEQ: toxic equivalency of a mixture; VOCs: Volatile Organic compounds; ZPP: zinc protoporphyrin; GSTM1: Glutathione S-transferase Mu 1

**ARTICLE HISTORY**
Received 31 May 2019
Accepted 7 June 2019

**KEYWORDS**
Solid waste incinerators; human biomonitoring; biomarkers of exposure; biomarkers of effect; dioxins; metals; polycyclic aromatic hydrocarbons; volatile organic compounds; general population exposure; occupational exposure

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## Introduction

### *SWI and air pollution*

Waste incineration is a thermal process leading to the combustion of organic substances contained in waste material. Solid waste incinerators (SWIs) can treat both municipal (MSWI) and industrial/hospital hazardous waste (HSWI). Waste materials feeding the plant may be thus crude urban waste, residual from differentiated waste collection and treated or untreated waste from industrial processes or hospitals. As a consequence of the combustion process, emissions are spread into the environment containing both inorganic and organic substances, among which carbon oxide (CO), carbon dioxide ($CO_2$), sulfur and nitrogen oxides ($SO_X$, $NO_X$), soot, metal elements, and their oxides and salts, volatile organic compounds (VOC), dioxins [polychlorinated dibenzo-p-dioxin (PCDDs) and polychlorinated dibenzofuran (PCDFs), together PCDD/Fs)], polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), particulate matter (PM) and ultrafine particles (World Health Organization 2007). These substances may be emitted as vapors (i.e. Hg, VOC, 2-, and 3-ring-PAHs) or adsorbed onto particulate matters; as such, they can be present as airborne pollutants and enter the human body through inhalation, or they can deposit on the ground. Ground contaminants can be directly ingested with contaminated food, that is vegetables or animals grown in the deposition area of the incineration plume, or with contaminated water, after dissolution by atmospheric precipitations and leaching into the groundwater.

Due to the potential toxic effects of these pollutants on human health and environment, there is a lot of public concern over the global sustainability of the waste incineration process. In particular, people living near SWIs need to be reassured about health risk possibly associated with both short- and long-term exposure to SWI emissions, the safety of such facilities, and their compliance with regulations under normal or abnormal operations. Concern may be higher for potentially sensitive populations, such as young children, adolescents, and pregnant women. In addition, incinerator workers may be exposed to toxic chemicals at higher levels than the general population.

### *Regulation*

In the framework of the so-called 3 R policy, that is reduction of production, re-use of waste, and recovery in terms of material and energy, modern waste incineration technology aims to treat waste so as to reduce its volume and hazard, to capture, concentrate and destroy potentially harmful substances and to recover energy from combustion (World Health Organization 2007). Regulations are in force in most countries to regulate SWI emissions, technical requirements, and operating conditions. Different guiding principles for setting environmental standards are adopted in the different countries, among which the "prudence avoidance principle", the "precautionary principle", the "Best Available Technology" (BAT) and the "as low as reasonably achievable" principle (Liu et al. 2015).

In Europe, the Industrial Emissions Directive (IED) 2010/75/EU of the European Parliament and the Council is the main instrument regulating pollutant emissions from industrial installations. This Directive replaces seven previously existing directives among which the Integrated Pollution Prevention and Control (2008/1/EC), the Waste Incineration (2000/76/EC) and the Large Combustion Plants (2001/80/EC) Directive. Plants are required to operate in accordance with a permit including emission limit values based on Best Available Techniques, and addressing the whole environmental performance of the plant, that is pollutant emissions, generation of waste, use of raw materials, energy efficiency, noise, prevention of accidents, and restoration of the site upon closure. Moreover, environmental inspections on site are required at least every 1 to 3 years, and the public has a right to participate in the decision-making process, and to be informed of its consequences (European Commission 2010).

In the US, a combination of federal, state, and local regulations apply to waste incinerators: minimal standards are set by federal laws that the states must implement and enforce. The Clean Air Act, in particular, requires the Environmental Protection Agency to establish new source performance standards for new incineration facilities and emission guidelines for existing facilities on the basis of best-demonstrated technology, while the Maximum Achievable Control Technology standards establish control requirements (National Research Council 2010).

As regards Asian countries, in Japan, the Waste Management and Public Cleansing Law (Law 137, effective in 1970, lastly reviewed in 2006) sets, among others, the technical standards on SWI facilities. Plants are required to operate under a license, released by the Prefectural Governor, which is granted if the facility meets the applicable technical standards to preserve the living environment of the surrounding area. In Taiwan, the Waste Disposal Act (effective 1974, latest revised in 2017) is formulated for the effective clearance and disposal of waste, improvement of environmental sanitation and maintenance of public health. The Act set standards for municipal waste treatment and recycling and hazardous waste identification. The Taiwan Environmental Protection Administration is the competent authority to deal with waste management. In South Korea, the Integrated Control of Environmental Pollution-Generating Facilities, that has introduced several components of the European IED in Korean legislation, is in force since October 2017. The Ministry of Environment has provided the BAT Reference Document for waste incineration facility that suggests techniques for the integrated control of environmental pollution.

## Health effects and biomonitoring

Several epidemiological studies have been conducted over the past years to elucidate the possible associations between adverse health outcome and SWI emission exposures. Some health effects were studied, including birth outcomes, reduction of thyroid hormones, and cancer. However, studies were often affected by methodological weaknesses, such as a scarce exposure characterization, the lack of information on possible confounders, and the lack of statistical power (Franchini et al. 2004; World Health Organization 2007; Porta et al. 2009; National Research Council 2010; Ashworth et al. 2014).

A powerful tool to help in define personal exposure to toxic substances or biological effect related to such exposure is human biomonitoring (HBM), which is the quantification of metabolites, of the chemicals themselves, or of effect biomarkers in biological fluids from the exposed individuals. Although HBM offers the unique opportunity to investigate the actual body burden of specific substances or the presence of effects that may be related to a previous exposure, several challenges should be dealt with, such as the need for reliable assays, the interpretation issues deriving from multiple sources of exposure, and the genetic and environmental factors affecting the individual response. No exposure biomarker uniquely related to SWI emissions as a whole is available; however, several biomarkers related to pollutants potentially emitted from SWIs are measurable to date, including dioxins, PCBs, metals, PAHs and VOCs.

PCDD/Fs and PCBs are included in the broad class of persistent organic pollutants (POPs), together with mono and polychlorophenols (MCP and PCP), hexachlorobenzene (HCB) and other chlorobenzenes, polybrominated diphenylethers (PBDE), and dichlorodiphenyldichloroethylene (DDE) (http://chm.pops.int). PCDD/Fs and PCBs contain several congeners (e.g. there are 209 PCBs). Exposure to POPs can be assessed by measuring their levels in blood, in breast milk, and in urine (the last limited to MCP and PCP). Given the complexity of dealing with so many chemicals at once, a simplified approach to assess the toxicity of these mixtures has been developed. This is based on the identification of an indices of relative toxicity (TEF) for each dioxin and dioxin-like PCBs, taking 2,3,7,8-tetrachlorodibenzo p-dioxin as reference; the toxic equivalency of a mixture (TEQ) is calculated as the sum of the concentrations of individual compounds multiplied by their TEF (Van den Berg et al. 2006). The concern regarding POPs has been associated with both their long life and their biomagnification in the environment and to several different toxic effects, among which carcinogenicity. The International Agency for Research on Cancer (IARC) has classified both 2,3,7,8-tetrachlorodibenzo p-dioxin and PCBs as group 1 carcinogens (carcinogenic to human) (IARC 2012, 2016). PCDD/Fs and PCBs were studied in association with SWI exposure in some large population studies in Flanders, France, Spain, Japan, South Korea, and North Taiwan (Kitamura et al. 2001; Tajimi et al. 2005; Chen, Su, and Lee 2006; Huang et al. 2007; Frery et al. 2007a, 2007b; Schroijen et al. 2008; Zubero et al. 2011, 2017; Park et al. 2014), and in several occupational studies (Angerer et al. 1992; Wrbitzky et al. 1996; Kitamura et al. 2000; Hu et al. 2004; Yoshida et al. 2006; Mari et al. 2013).

Mid- or short-term exposure to metals can be assessed by biological monitoring, measuring the levels of metals in blood or urine; for some metals, such as mercury (Hg), long-term exposure can be assessed using hair, where they can accumulate. Among metals, the most relevant for toxicity and widespread diffusion are lead (Pb), cadmium (Cd), nickel (Ni), arsenic (As), and Hg. They can be associated to a plethora of health effects such as neurotoxicity (Pb and Hg), kidney toxicity (Cd), and carcinogenicity (Cd, As, Cr) (Nordberg et al. 2014). The exposure to metals in association with SWI was studied in some large population studies (Reis et al. 2007a, 2007b, 2007c; Lee et al. 2012; Martorell et al. 2015; Deng et al. 2016; Gatti et al. 2017), and in occupational studies (Bresnitz et al. 1992; Wrbitzky et al. 1996; Hours et al. 2003; Chao and Hwang 2005).

Benzene, toluene, ethylbenzene, and xylenes (BTEX), are monocyclic aromatic hydrocarbons, belonging to the wide class of volatile organic compounds (VOCs). Once adsorbed into the body, they are extensively metabolized to polar compounds excreted in urine, therefore biomonitoring of BTEX is mostly performed by measuring urinary metabolites, and specifically *t,t*-muconic acid (*t,t*-MA) and S-phenylmercapturic acid (SPMA) for benzene, *o*-cresol for toluene, and methylhyppuric acids for xylenes (ACGIH 2017). Tiny amount of BTEX can also be measured as unmetabolized chemicals in blood and urine (Fustinoni et al. 2005, 2010). BTEX are neurotoxic, moreover, benzene is also classified as a known carcinogen to human, being able to cause acute myeloid leukemia (IARC 2012). The exposure to BTEX in association to SWI was studied in a limited number of population studies (Staessen et al. 2001; Schroijen et al. 2008; Ranzi et al. 2013), and in some occupational studies (Angerer et al. 1992; Wrbitzky et al. 1996).

Polycyclic aromatic hydrocarbons are a group of chemicals that includes more than 100 congeners. One absorbed into the body, PAHs are metabolized to phenols and excreted as glucuronyl or glutathione conjugates in urine or feces (Grover 1986). Biological monitoring is usually performed by measuring urinary hydroxylated metabolites, among which 1-hydroxypyrene (1-OHPYR) is mostly used. A small percentage of absorbed PAHs is excreted unmetabolized (Waidyanatha et al. 2003; Campo et al. 2010). Some PAHs are genotoxic and known human carcinogens (IARC 2010). The exposure to PAHs in association with SWI was studied in limited number of studies in the general population (Schroijen et al. 2008; Gatti et al. 2017) and in workers (Angerer et al. 1992; Wrbitzky et al. 1996; Lee et al. 2003; Mari et al. 2013)

Various biomarkers of effect were measured in individuals living near or working at SWI: for example, urinary 8-hydroxy-deoxy-guanosine (8-OH-dG) and/or malondialdheide (MDA) in association with oxidative stress (Leem et al. 2003; Yoshida et al. 2003; De Coster et al. 2008); zinc and erythrocyte protoporphyrins (ZPP and EPP), markers of alterations of the biosynthesis of heme, in association with exposure to Pb (Bresnitz et al. 1992); thyroid and sex hormones in association with the exposure to POPs, Cd, and Hg (Osius et al. 1999; Croes et al. 2009); markers of kidney function (i.e. ß2-microglobuline) in association with exposure to Cd (Staessen et al. 2001); thioethers, comet assay, micronuclei, DNA strand breaks, DNA adducts, and urinary mutagenicity in association with exposure to electrophilic and/or genotoxic compounds (Scarlett et al. 1990; Ardévol et al. 1999; Lee, Kang, et al. 2002); tumor associated proteins and immunological parameters in association with carcinogens and immunosuppressive agents (Oh et al. 2005; De Coster et al. 2008).

A relevant issue in biomonitoring is the presence of several sources of exposure in the living environment and/or associated with personal habits, that concur to the final level of biomarker and that should be taken into account for a correct interpretation of data. Among them is worth to mention: diet for PCBs, dioxins, PAHs, Hg, As, and others metals; tobacco smoke for BTEX, PAHs, and Cd; traffic pollution for BTEX; industrial emissions for various pollutants, and open fires for PAHs (IARC 2004, 2010, 2014; Domingo 2010; Nordberg et al. 2014; González et al. 2019).

### *Aims of the review*

A systematic review of peer-reviewed literature on biomonitoring of the general population living near solid waste incinerators and of incinerator workers was conducted: the aim is to bring together evidences associating modification of biomarkers in relation to SWI exposure and to highlight strength and deficiencies of the studies conducted so far.

## Methods

### *Search strategy and study inclusion criteria*

The process for the selection of relevant studies was made of three steps. In the first step, literature searches were performed in the Medline, CAplus, and Embase database, through PubMed and SciFinder Scholar interfaces. A filter on English language and "humans" was used.

For PubMed, searches were conducted using both keywords and MESH terms. Alternative nomenclature for SWI were tested, such as "incinerators", "waste-to-energy plants", and WTE plants. The following search string was finally used: (residues OR waste OR hazardous substances [Mesh]) AND (Incineration [Mesh] OR incinerat* OR "waste to energy") AND (expos* OR biomarker* OR biomonitoring OR biological monitoring OR biological markers [Mesh]) AND (environmental pollut*[Mesh] OR environmental exposure [Mesh] OR epidemiological monitoring [Mesh] OR environmental monitoring [Mesh] OR occupational exposure [Mesh]). The search is updated to 21 February 2018.

For SciFinder Scholar, the research topic "waste" was used, followed by the index term "incineration", and by the research term "humans" and then "blood" or "urine" or "hair" or "milk". The search is updated to 20 February 2018.

For Embase the search query comprised ("biological monitoring"/exp OR "biological monitoring" OR biomarker* OR "biomonitoring"/exp OR biomonitoring OR "urine"/exp OR "urine" OR "blood"/exp OR "blood" OR "plasma"/exp OR plasma OR "serum"/exp OR "serum" OR "milk"/exp OR "milk" OR "hair"/exp OR "hair" OR "nail"/exp OR "nail" OR "tissue"/exp OR "tissue") AND ("waste"/exp OR waste) AND (incinerat* OR "waste-to-energy"/exp OR "waste-to-energy") AND [english]/lim AND [humans]/lim AND [embase]/lim. The search is updated to 26$^{th}$ February 2018.

In the second step, the retrieved abstracts/titles were screened by four independent reviewers (two reviewers for each abstract) who selected papers that met the following inclusion criteria: (1) a MSWI or an HSWI was present in the investigated area and was indicated as a potential source of exposure (excluded: baseline studies, open-air incineration), (2) they were human studies with living subjects (excluded: studies on cells or autopsy), (3) biological monitoring results were reported (excluded: studies reporting only results on environmental monitoring or only health outcome), (4) they were full papers (excluded: conference abstracts, reviews, and books). A study was retained if it was considered relevant by at least one reviewer.

In the third step, the full texts of the selected papers were obtained and examined using the study inclusion criteria above reported. Each paper was read by two reviewers and discussed by the four reviewers together in case of disagreement for its final inclusion. The reference lists of the selected papers were screened to gather other potential interesting papers.

### Quality of reporting and study design assessment

To assess the reporting and general standard of each paper, a quantitative modification of the STrengthening Reporting of Observational studies in Epidemiology-Molecular Epidemiology (STROBE-ME) statement was used. The STROBE initiative aims to provide a guidance to improve the reporting of a research and provides a list of reporting recommendations (Gallo et al. 2012). The modified version here used comprises 28 items, with each item assigned a score of 0 (not reported or not fulfilled), 0.5 (partially fulfilled), 1 (completely fulfilled) by the reviewer. The checklist used is reported in the Supplementary Appendix material, Table A1. No paper was excluded on this basis, but for each the quality score is provided.

A further evaluation was performed to assess study design and methodology. Acknowledging that a large number of investigated individuals is a basic requirement for performing a statistical analysis that can take into consideration the confounding factors, studies/papers with at least about 140 exposed individuals for the general population and 40 individuals for workers, were extracted. Studies with a repeated measurement design, even if with a small sample size, were also considered. These studies were further examined to collect information regarding the method of selection of exposed/control individuals, the exposure assessment, the collection of information on personal characteristics, exposure duration, diet, and alternative exposure sources, chemical analysis of individual or pooled samples (for dioxins and PCB), and the use of statistical regression analysis taking in account possible confounders.

## Results and discussion

### Search strategy

The workflow of the selection process is represented in Figure 1. The first step (literature search) led to 790 papers, 430 of which were retrieved by PubMed, 220 by Embase, and 140 by SciFinder Scholar. The exclusion of duplicates led to 547 abstracts to be examined.

The second step of the selection process (abstract/title screening) resulted in the identification of 154 papers meeting the inclusion criteria. The agreement between reviewers was 93.9%, with 121 papers selected and 393 papers rejected by both reviewers. Five papers, previously available to our review, were not retrieved by any database and were added to the 154 group; moreover, the screening of the reference list of these papers led to the inclusion of additional 27 papers, so the final number of papers identified for the third selection step was 186.

The third step of the selection process (full-text reading) resulted in the identification of 132 papers meeting the inclusion criteria.

### Quality of reporting

The results of the general quality and reporting assessment are shown in Table A2. The mean value of the quality score assigned to each item by two reviewers is reported.

Table 1 shows a summary of the 132 papers meeting the inclusion criteria. About the same percentage of papers (40%) was focalized on adults of the general population or workers, while only 8% of papers were dedicated to children or adolescents. Most papers were published in European countries (56%), followed by Asian (36%), and American countries (8%). Most papers (60%) included MSWIs as potential sources of exposure, while about one third (28%) included HSWIs. As regards the biomarkers, the most investigated biomarkers of exposure were PCDD/Fs (66%), followed by PCB (42%), metals (26%), PAHs (15%), MCP, PCP, and HCB (11%) and VOCs (6%). In addition, biomarkers of effect were reported (21%), among which oxidative stress biomarkers, DNA damage and mutagenicity biomarkers, thyroid and sex hormones and others (porphyrins, immunochemistry parameters, thioethers, tumor proteins, and beta-2-microglobulin). Blood was the most assayed biological mean (85%), followed by urine (28%), breast milk (11%), hair (4%), and others (adipose tissue, cord blood, sperm, and exhaled breath).

### Description of studies by country and investigated population

A description of the selected papers, grouped by the country where the study was conducted and by target population (general population or workers), is reported in the following paragraphs. As a number of different papers were in some

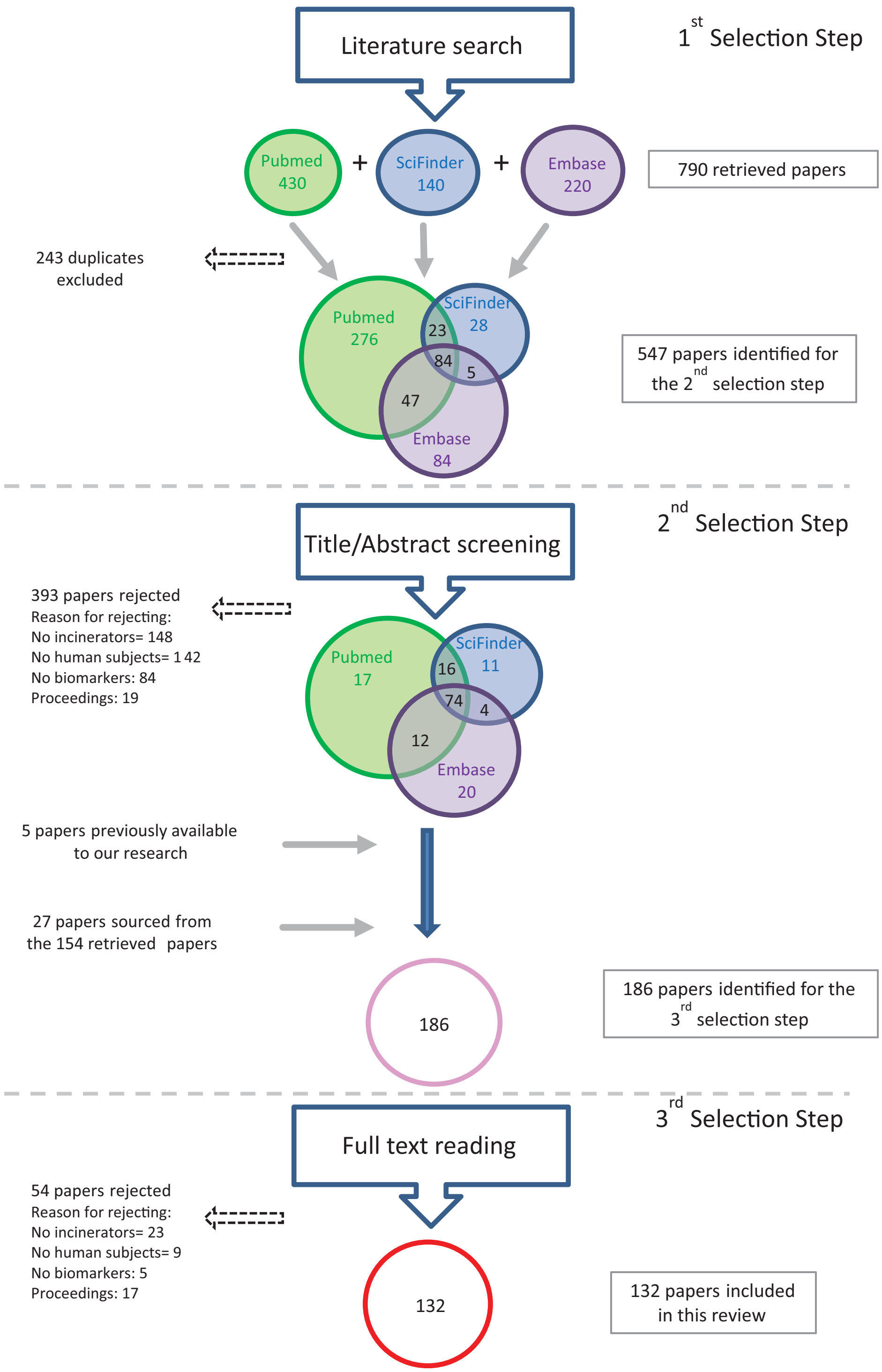


**Figure 1.** Workflow of the selection process for all identified papers.

cases published for a unique study, an attempt was made to group the papers according to the pertinent study. Unfortunately, the information on the SWI or on the area actually investigated is not always clearly reported in papers, so this grouping was not always possible.

A summary of the retrieved information from each study/paper is reported in Table 2 for the general population and in Table 3 for workers. Table 4 shows the results of the assessment of study design for 14 studies on the general population conducted on more than 140 individuals.

## European countries

### *Austria*

#### *Workers*

Metal exposure and genotoxic effects were studied in 23 workers who were temporarily conducting cleaning operations, residual transfer, and disposal operations in a MSWI; study year was not reported (Wultsch et al. 2011). The mean concentration of urinary Cr, Mn, Ni, and As, and the genotoxic effects investigated by measuring DNA migration and

**Table 1.** Summary of papers included in the review stratified by country.

| | *N* papers | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | European countries | | | | | | | | | | | American countries | | Asian countries | | | | |
| | AT | BE | FI | FR | DE | IT | PT | SK | ES | SE | NL | BR | US | CN | JP | KR | TW | All |
| *N* papers | 1 | 11 | 4 | 7 | 7 | 3 | 12 | 1 | 24 | 2 | 2 | 2 | 8 | 2 | 16 | 19 | 11 | 132 |
| Investigated subjects | | | | | | | | | | | | | | | | | | |
| General population >18 years | | 5 | | 5 | 1 | 3 | 11 | 1 | 13 | | | | 1 | 1 | 4 | 4 | 7 | 56 |
| General population <18 years | | 5 | | | 1 | | 1 | | 4 | | | | | | | | | 11 |
| Workers | 1 | 1 | 3 | 2 | 5 | | | | 6 | 2 | 1 | 1 | 7 | | 11 | 8 | 4 | 52 |
| Workers + general population | | | 1 | | | | | | 2 | | 1 | 1 | | 1 | 1 | 7 | | 14 |
| Type of SWI | | | | | | | | | | | | | | | | | | |
| Municipal | 1 | 11 | | 6 | 3 | 3 | 9 | 1 | 7 | | 1 | | 6 | 2 | 12 | 7 | 11 | 80 |
| Hazard | | | 4 | | 3 | | | | 17 | 2 | 1 | 2 | 1 | | 1 | 6 | | 37 |
| Municipal + hazard | | | | 1 | 1 | | 3 | | | | | | | | 1 | 3 | | 9 |
| Not known | | | | | | | | | | | | | 1 | | 2 | 3 | | 6 |
| Investigated biomarkers | | | | | | | | | | | | | | | | | | |
| PCDD/Fs | | 7 | 1 | 5 | 4 | 1 | 9 | 1 | 18 | 1 | 1 | | 2 | | 15 | 12 | 10 | 87 |
| PCB | | 10 | 3 | 4 | 3 | 1 | 3 | 1 | 13 | 1 | | | | | 11 | 5 | | 55 |
| MCP/PCP/DDE/HCD/and other chlorobenzenes, PDBE | | 1 | | | 2 | | | 1 | 9 | 1 | | | | | | 1 | | 15 |
| Metals | 1 | 6 | 1 | 2 | 2 | 2 | 3 | | 8 | | | 1 | 3 | 2 | | 2 | 2 | 35 |
| PAHs | | 4 | | 1 | 2 | 2 | | | 6 | | | | | | | 5 | | 20 |
| VOC | | 3 | | 1 | 2 | 1 | | | | | | | 1 | | | | | 8 |
| Effects | 1 | 6 | | | 1 | | | | 1 | | 1 | 2 | 5 | | 6 | 6 | 2 | 31 |
| Biological fluids | | | | | | | | | | | | | | | | | | |
| Blood | 1 | 11 | 4 | 6 | 7 | 2 | 7 | 1 | 17 | 2 | 1 | 2 | 5 | 2 | 14 | 19 | 11 | 112 |
| Urine | 1 | 5 | | 1 | 3 | 2 | | | 9 | | 1 | 1 | 4 | | 3 | 6 | 1 | 37 |
| Hair | | | 1 | | | | | | 3 | | | | | | 1 | | | 5 |
| Breast milk | | | | | 1 | | 6 | | 6 | | | | | | 1 | | | 14 |
| Others | | | | | | | 1 | | 1 | | | | 1 | | | 1 | | 4 |

AT: Austria; BE: Belgium; FI: Finland; FR: France; DE: Germany; IT: Italy; PT: Portugal; SK: Slovakia; ES: Spain; SE: Sweden; NL: the Netherlands; BR: Brazil; US: United States; CN: China; JP: Japan; KR: South Korea; TW: Taiwan.

**Table 2.** Human biomonitoring studies on exposure to SWI performed in the adult general population, if not otherwise specified.

| Study name or place/country | Year | SWI type | *N.* and type of exposed subjects | *N.* and type of control subjects | PCDD/Fs, PCB, HCB, PBDE | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|
| FLEHS I/ Belgium | 1999 | MSWI | 42 adolescents | 100 adolescents | Blood: PCDD/Fs, PCB_B | Urine: Cd, Pb, Blood: Pb, Cd, Cu, Zn, Se | | Urine: t,t-MA, o-cresol | Blood: Cystatin-C, comet assay, sex hormones, tumor-associated proteins Urine: B2 microglobulin, 8-OH-dG | Staessen et al. 2001; Den Hond et al. 2002; Nawrot et al. 2002 |
| | | | 39 women | 100 women | Blood: PCDD/Fs, PCB_B | Urine: Cd Blood: Pb, Cd, Cu, Zn, Se | Urine: 1-OHPYR | | Blood or urine: Tumor-associated proteins | Van Larebeke et al. 2006 |
| FLEHS II/ Belgium | 2002–2006 | 6 MSWI | 198–207 adolescents | Mean biomarkers values measured on 1583–1679 adolescents (including exposed subjects) | Blood: PCB, HCB, DDE | Blood: Pb, Cd | Urine: 1-OHPYR | Urine: t,t-MA, o-cresol | Blood: sex hormones, thyroid hormones, PSA, carcinoembryonic antigen, mutated p53, anti-p53 antibody, micronuclei, DNA-strand breaks Urine:8-OH-dG | Schroijen et al. 2008; Croes et al. 2009; De Coster et al. 2008 |
| Wallonia/Belgium | 2000–2005 | MSWI | 84 | 63 | Blood: PCDD/Fs, PCB | Blood: Pb Urine: Cd, Hg | | | | Fierens et al. 2003, 2006, 2007 |
| Finland | 1984–1994 | HSWI | 113 (<5 km) | 55 (30 km) | | Hair: Hg | | | | Kurttio et al. 1998 |
| French Dioxins and Incinerator study/France | 2005 | 8 MSWI | 1030 | | Blood: PCDD/Fs, PCB | | | | | Frery et al. 2007a, 2007b Zeghnoun et al. 2007 |
| Maincy/France | 2003 | MSWI | 10 | | Blood: PCDD/Fs, PCB | | | | | Pirard et al. 2005 |
| Besançon/France | 2003–2005 | MSWI | 34 newly diagnosed non-Hodgkin lymphoma cases | 34 randomly selected controls | Blood: PCDD/Fs, PCB, HCB | | | | | Viel et al. 2011 |
| Schawandorf/Germany | 1993 | MSWI | 46 | | Blood: PCDD/Fs Breast milk: PCDD/Fs | | | | | Deml et al. 1996 |
| Rhine area/Germany | ns | HSWI | 186 children | 144 children | Blood: PCB | Blood: Pb, Cd Urine: Hg | | | Blood: thyroid Hormones | Osius et al. 1999 |
| Tuscany/Italy | 2005–2006 | MSWI | 35 | 39 | Blood: PCDD/Fs, PCB | | | | | De Felip et al. 2008 |
| AIA Study/Modena Italy | 2010 | MSWI | 65 | 103 | | Blood: Pb, Cd, Hg, Mn, Ni, Cu, Zn Urine: Pb, Cd, Hg, Mn, Ni, Cu, Zn | Urinary PAH | Urine: BTEX, SPMA | | Ranzi et al. 2013 |
| | 2012 | | 497 | | | Urine: Pb, Cd, Hg, Mn, Ni, Cu, Zn | Urinary PAH, 1-OHPYR | | | Gatti et al. 2017 |
| External monitoring plan Lipor II plant/ Oporto Portugal | 2001 | MSWI | 46 + 19 mothers | | Blood: PCDD/Fs Breast milk: PCDD/Fs | | | | | Calheiros et al. 2002 |

(*continued*)

**Table 2.** Continued.

| Study name or place/country | Year | SWI type | *N.* and type of exposed subjects | *N.* and type of control subjects | PCDD/Fs, PCB, HCB, PBDE | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|
| Valursul Environmental Health Survey/ Lisbon Portugal | 1999–2004 | MSWI | 60 adults + 51 mothers (<5 km) | 58 adults + 72 mothers | Blood: PCDD/Fs Breast milk: PCDD/Fs | | | | | Sampaio, Reis, et al. 2004 |
| | | | 15 (<5 km) | 15 | Blood: PCDD/Fs | | | | | Reis et al. 2005 |
| | | | 31 mothers (<5 km) | 18 mothers | Breast milk: PCDD/Fs, PCB | | | | | Sampaio, Murk, et al. 2004 |
| | | | 21 mothers (<5 km) | 52 mothers | Breast milk: PCDD/Fs | | | | | Reis et al. 2002 |
| Environmental Health Survey/ Madeira Portugal | 2002 | MSWI + HSWI | 55 (<3 km) | 55 (>20 km) | Blood: PCDD/Fs, PCB | | | | | Reis, Miguel, et al. 2004 |
| | | | 22 mothers | 36 mothers (>20 km) | Breast milk: PCDD/Fs, PCB | | | | | Reis, Sampaio, et al. 2004 |
| Environmental Health Survey/ Lisbon vs Madeira Portugal | 1999–2004 | MSWI + HSWI | 65 | 51 | Blood: PCDD/Fs | | | | | Reis, Miguel, et al. 2007 |
| | | | 73 mothers | 108 mothers | Blood: PCDD/Fs | | | | | Reis, Sampaio, et al. 2007 |
| | | | 398 (<3–5 km) | 290 | | Blood: Pb, Cd, Hg | | | | Reis et al. 2007a |
| | | | 164 mothers | 253 mothers | | Blood: Pb Cord Blood: Pb | | | | Reis et al. 2007c |
| | | | 221 children (<6 years) | 276 children (<6 years) | | Blood: Pb | | | | Reis et al. 2007b |
| Slovakia | 2006–2007 | MSWI | 81 | 44 | Blood: PCDD/Fs, PCB, PBDE | | | | | Chovancová et al. 2012 |
| Constantì/Spain | 1996–2012 | HSWI | 9–40 | none-11 | Blood: PCDD/Fs | | | | | Schuhmacher et al. 1999; Bocio et al. 2004; Agramunt et al. 2005; Nadal et al. 2008; Nadal et al. 2013 |
| | | | 15–20 mothers | | Breast milk: PCDD/Fs, PCB, PBDE | | | | | Schuhmacher et al. 2004, 2007, 2009, 2013 |
| | | | 96–196 children (12–14 years) | | | Hair: As, Be, Cd, Cr, Hg, Mn, Ni, Pb, Sn, Tl, V | | | | Nadal et al. 2005; Ferré-Huguet et al. 2009 |
| | | | 144 adults | | | Blood: As, Be, Cd, Cr, Hg, Mn, Ni, Pb, Sn, Tl, V | | | | Martorell et al. 2015 |
| Matarò/Spain | 1995–2012 | MSWI | 68–104 (<1.5 km) | 97 (3–4 km) 86 (11 km) | Serum pooled samples: PCDD/Fs, PCB | Blood: Pb, Cd Urine: Cr, Hg | | | | Gonzalez et al. 2000 |
| | | | 46 mothers | | Pooled Breast milk: PCDD/Fs, PCB | | | | | Parera et al. 2013 |
| | | | 39 children (7–10 years) | 44 children (7–10 years) | | | | | Urine: thioethers | Ardévol et al. 1999 |
| Bilbao/Spain | 2006–2013 | MSWI | 163 (<2 km) | 163 (5–20 km) | Serum pooled samples: PCDD/Fs, PCB | | | | | Zubero et al. 2011 |
| | | | 57 (2 km) | 50 (5–20 km) | | Blood: Pb Urine: Cd, Cr, Hg | | | | Zubero et al. 2010 |
| | | | 61 (<2 km) | 66 (5–20 km) | individual samples: PCDD/Fs, PCB | | | | | Zubero et al. 2017 |

(*continued*)

**Table 2.** Continued.

| Study name or place/country | Year | SWI type | *N.* and type of exposed subjects | *N.* and type of control subjects | PCDD/Fs, PCB, HCB, PBDE | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|
| Duiven/The Netherlands | 1994 | MSWI | 5 | 5 | Blood: PCDDs | | | | | van den Hazel and Frankort 1996 |
| Capivari de Baixo/Brazil | 2001 | HSWI | 20 | 20 (>130 km) | | Blood: Pb, Cu, Fe, Mn, Zn | | | Blood: oxidative stress biomarkers | Possamai et al. 2009; Wilhelm Filho et al. 2010 |
| Times Beach, MO/US | 1992 | HSWI | 67 | 61 | Serum: PCDD/Fs, PCB | | | | | Evans et al. 2000 |
| Shenzhen/China | 2012–2014 | MSWI | 269 (<5 km)<br>195 (<3 km) | 143 (>5 km)<br>230 (5–10 km) | | Blood: Hg, Metil-Hg<br>Blood: Cr, Cd. Pb. Mn | | | | Deng et al. 2016<br>Li et al. 2017 |
| Japan | 2000 | HSWI | 13 | | Blood: PCDD/Fs, PCB | | | | | Aozasa et al. 2003 |
| Ryugasaky/Japan | 1996 | MSWI | 18 (<2 km) | | Blood: PCDD/Fs, PCB | | | | | Miyata et al. 1998 |
| Osaka/Japan | – | MSWI | 145 (<2 km) | 380 | Blood: PCDD/Fs, PCB | | | | | Kitamura et al. 2001 |
| Kansai + Kanto + Chugoku region/Japan | 1999–2000 | ns | 73 | 47 | Blood: PCDD/Fs, PCB | | | | Immunological parameters | Takei et al. 2001 |
| Tokio/Japan | 1999–2000 | MSWI + HSWI | 240 mothers | | Brest milk: PCDD/Fs, PCB | | | | | Tajimi et al. 2005 |
| Seoul + Pyongtack/South Korea | ns | 2 MSWI+ 1 HSWI | 16 (MSWI) + 10 (HSWI) | | Blood: PCDD/Fs | | | | Blood: oxidative stress biomarkers | Leem et al. 2003 |
| Different cities/South Korea | 2001–2002 | 4 MSWI | 75 (<0.3 km) | | Serum: PCDD/Fs | | | | | Moon et al. 2005 |
| Pyongtack/South Korea | 2002–2003 | HSWI | 40 (<5 km) | 25 (7–12 km) | Blood: PCDD/Fs | | | | | Park et al. 2004 Leem et al. 2006 |
| Seoul/South Korea | 2001 | 2 MSWI | 22 (<5km) | | Serum: PCDD/Fs, PCB, PBDE | | | | | Kim, Ikonomou et al. 2005 |
| Seoul/South Korea | 2003 | 3 MSWI | 50 (<0.3 km) | 10 (>10 km) | Serum: PCB | | | | | Park et al. 2007 |
| Seoul/South Korea | 2000–2002 | MSWI + 2 HSWI | 28 (MSWI)+ 10 (2 HSWI) | 7 (>10 km) | Serum: PCDD/Fs, PCB | | | | | Park et al. 2009 |
| South Korea | 2006 | MSWI | 49 (<0.3 km) | 11 (>10 km) | Serum: PCDD/Fs | | | | | Park et al. 2013 |
| Seoul/South Korea | 2001–2011 | MSWIs | 769 (<3 km) | 112 (>10 km) | Serum: PCDD/Fs, PCB | | | | | Park et al. 2014 |
| Seoul/South Korea | 2002–2006 | MSWI | 131 | 27 | Serum: PCDD/Fs | Blood: Pb, Cd, Hg | | | | Yang et al. 2007 |
| Seoul/South Korea | 2006–2009 | 3 MSWI | 841 (<0.3 km) | 105 | | Blood: Pb, Cd, Hg | | | | Lee et al. 2012 |
| North Taiwan | 1999–2004 | 3 MSWI<br>MSWI | 372 (<5 km)<br>95 (<5 km) | | Serum: PCDD/Fs | | | | | Chen et al. 2003<br>Chen et al. 2004; Lee et al. 2005 |
| | | 12 MSWI | 1034 (<5 km) | | | | | | Biochemical parameters of liver function and glucose production | Chen, Su, et al. 2006 |
| | | 19 MSWI<br>19 MSWI | 1658 (<5km)<br>1708 (<5 km) | | | | | | | Huang et al. 2007<br>Chen, Su, and Lee 2006 |
| Small town in central Taiwan | ns | MSWI | 68 (<4 km) | | Serum: PCDD/Fs | Blood: K, Al, Pb, Hg, Fe, Zn, Cd, Cu | | | | Chen et al. 2010 |

ns: not specified; MSWI: Municipal solid waste incinerator; HSWI: hazardous/hospital solid waste incinerator.

**Table 3.** Human biomonitoring studies/papers on exposure to SWI performed in occupationally exposed workers.

| Study name or place/country | Study year | SWI type | N. Exposed subjects | N. and type of control subjects | Sampling time | PCDD/Fs, PCB, PCP | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Austria | ns | MSWI | 23 | 19 office workers | Not reported | | Blood and urine: Cr, Mn, Ni, As | | | Blood: DNA migration and micronuclei (MN) frequency in lymphocytes | Wultsch et al. 2011 |
| Belgium | 2003–2004 | MSWI | 5 | | 10 days before and immediately after cleaning work and 6 days later | Blood: PCDD/Fs, PCB | | | | | Raemdonck et al. 2006 |
| Finland | 1991 | HSWI | 12 | 5 | | Blood: PCB, PCDD/Fs | | | | | Luotamo et al. 1993a, 1993b |
| Finland | ns | HSWI | 26 | 21 GP | At the end of the week of exposure | Blood: PCDD/Fs | | | | | Kontsas and Pekari 2003 |
| Finland | 1984 + 1994 | HSWI | 11 | 55 GP | ns | | Hair: Hg | | | | Kurtio et al. 1998 |
| France | 1995–1996 | MSWI + HSWI | 15 + 14 | 17 office workers | before shift end-shift | | Urine: Inorganic As, Cd, Cr, Ni, Mn | Urine: 1-OHPYR | Urine: t,t-MA, o-cresol, methylhippuric acids | | Maître et al. 2003 |
| | | 2MSWI + HSWI | 102 | | ns | | Blood: Pb | | | Blood: hematological parameters, hepatic functionality | Hours et al. 2003 |
| Germany | ns | MSWI | 53 | 431 GP | At the beginning of the work shift, after 3 work shifts | Blood: PCB, HCB, Urine: MCP, PCP | | Urine:1-OHPYR | Blood: benzene | | Angerer et al. 1992 |
| Germany | ns | 1–2 MSWI | 10 + 11 | 25 GP | ns | Blood: PCDD/Fs | | | | | Päpke et al. 1993; Schecter et al. 1995 |
| Germany | ns | 3 HSWI | 10 + 11 + 10 | 9 | ns | Blood: PCDD/Fs | | | | | Päpke et al. 1994 |
| Germany | ns | HSWI | 45 inceneration workers + 54 periphery workers | 23 management workers | ns | Blood: PCB, HCB, PCP Urine: PCP | Blood: Pb, Cr, Cd, Hg Urine: As, Cr, Ni, V | Urine: 1-OHPYR | Blood: BTEX | | Wrbitzky et al. 1996 |
| Constantì, Spain | 2000–2011 | HSWI | 16–29 | 11–14 | ns | Blood: PCDD/Fs, PCB, HCB Urine: PCP | Blood and Urine: Mn, Hg, Pb, Cd, Cr, Ni, V | Urine: 1-OHPYR | | | Schuhmacher et al. 2002; Agramunt et al. 2002, 2003; Mari et al. 2007, 2009, 2013 |
| Matarò, Spain | 1995–2012 | MSWI | 17 | 97 GP | ns | Blood: PCDD/Fs, PCB | Blood and Urine: Pb, Cr, Cd, Hg | | | | Gonzalez et al. 2000; Parera et al. 2013 |
| Norrto, Sweden | 1988–ns | HSWI | 10–29 | 0–60 | ns | Blood: PCDD/Fs; PCB, HCB | | | | | Rappe et al. 1992; Selden et al. 1997 |
| Duiven, The Netherlands | 1994 | MSWI | 4 | 5 | ns | Blood: PCDDs | | | | | Van den Hazel and Frankort 1996 |
| The Netherlands | ns | ns | 3 | 10 | before shift end-shift | | | | | Urine: thioethers | van Doorn et al. 1981 |
| Capivari de Baixo, Brazil | 2001 | HSWI | 20 | 20 | ns | | Urine: Pb, Cu, Fe, Mn, Zn | | | Blood: oxidative stress | Wilhelm Filho et al. 2010; Possamai et al. 2009 |
| USA, Philadelphia | 1988 | MSWI | 86 | | ns | | Blood and Urine: Pb, Hg, Cd, As | | | Blood: ZPP | Bresnitz et al. 1992 |
| USA | ns | 10 MSWI | 209–1404 samples from a not specified number of workers | | ns | | Blood and Urine: Pb, Cd | | | Blood: ZPP, EPP Urine: ß2-microglobuline | Hoffman et al. 1997 |

(*continued*)

**Table 3.** Continued.

| Study name or place/country | Study year | SWI type | N. Exposed subjects | N. and type of control subjects | Sampling time | PCDD/Fs, PCB, PCP | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|---|
| USA, New York City | 1989 | 3 MSWI | 56 | | ns | | Blood: Pb | | | Blood: EPP | Malkin et al. 1992 |
| | | | | 14 | ns | Blood: PCDD/Fs | | | | | Schecter et al. 1991 |
| USA | ns | ns | 6 | | Pre and post specific tasks | | | | exhaled air: benzene and toluene | | Thrall et al. 2001 |
| USA | 1988–1990 | MSWI | 37–104 | 35–61 | end-shift | | | | | Urine: mutagenicity | Scarlett et al. 1990; Ma et al. 1992 |
| Shenzhen, China | 2012 | MSWI | 35 | 143 | ns | | Blood: Hg and MeHg | | | | Deng et al. 2016 |
| Osaka, Bika Center Incinerator, Japan | 1998 | MSWI | 96 | | ns | Blood: PCDD/Fs, PCB | | | | Blood: hematological parameters | Kitamura et al. 2000, 2001 |
| Osaka, Japan | 1998 | MSWI | 20–30 | 20–30 | morning | Blood: PCDD/Fs | | | | | Kumagai et al. 2000, 2002 |
| Osaka, Japan | 2000 | HSWI | 5 | 5 | morning | Blood: PCDD/Fs | | | | | Kumagai and Koda 2005 |
| Osaka, Japan | 1995 | MSWI | 68 | 64 | ns | Hair: PCDD/Fs, PCB | | | | | Nakao et al. 2005 |
| Osaka, Japan | 2001 | MSWI | 57 | | morning | Blood: PCDD/Fs, PCB | | | | Urine: estrogens Blood and urine: Oxidative stress markers | Yoshida et al. 2005, 2006 |
| Japan | ns | | 81 | | morning before breakfast | | | | | Blood and Urine: Oxidative stress markers | Yoshida et al. 2003 |
| Osaka, Toyono-gun Clean Center Incinerator, Japan | 1998 | MSWI | 96 | | ns | Blood: PCDD/Fs | | | | Blood: chemistry and immunological parameters | Takata 2003 |
| Not specified, South Korea | ns | HSWI | 15 | 15 GP | ns | Blood: PCDD/Fs | | | | | Kim et al. 2001 |
| Not specified, South Korea | 2001 | ns | 23 (13 incinerator and 10 industrial workers | 22 GP | ns | Blood: PCDD/Fs, PCB | | | | | Kim et al. 2002 |
| Not specified, South Korea | ns | HSWI | 29–38 | 21–43 not exposed workers | ns | | | Urine: 1-OHPYRG | | Blood: DNA adducts Blood: GPA mutation | Lee, Kang et al. 2002; Lee, Lee et al. 2002 |
| Not specified South Korea | Ns | HSWI | 28 | – | Pre-shift (Monday a.m.) and post-shift (Friday p.m.) | | | Urine: 1-OHPYRG | | | Lee et al. 2003 |
| Ansan, South Korea | 2002 | ns | 28–31 | 43–84 GP | ns | | | Urine: 1-OHPYR, 2NAPOH | | Blood: DNA damage Blood: DNA damage, immunological parameters, Semen: sperm characteristics | Sul et al. 2003; Oh et al. 2005 |
| Seoul, South Korea | Ns | MSWI | 13 | | ns | Blood: PCDD/Fs | | | | Urine: Oxidative stress | Leem et al. 2003 |
| Seoul, South Korea | 2001 | 2 MSWIs | 13 | | ns | Blood: PCDD/Fs, PCB, PBDE | | | | | Kim, Ikonomou, et al. 2005 |
| Not specified, south Korea | Ns | HSWI | 3 plant workers | 2 office workers | ns | Blood: PCDD/Fs | | | | | Kim, Lee, et al. 2005 |
| Not specified large cities, South Korea | 2001–2002 | 4 MSWIs | 28 | – | ns | Blood: PCDD/Fs | | | | | Moon et al. 2005 |

(*continued*)

**Table 3.** Continued.

| Study name or place/country | Study year | SWI type | N. Exposed subjects | N. and type of control subjects | Sampling time | PCDD/Fs, PCB, PCP | Metals | PAHs | VOC | Effects and other biomarkers | References |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Seoul, South Korea | 2003 | 3 MSWIs | 25 | 10 living >10 km from plant | ns | Blood: PCB | | | | | Park et al. 2007 |
| Seoul, South Korea | 2000–2002 | HSWI + MSWI | 10 + 16 | 7 living >10 km from plant | ns | Blood: PCDD/Fs, PCB | | | | | Park et al. 2009 |
| Not specified, South Korea | 2006 | MSWI | 11 | 11 living >10 km from plant | ns | Blood: PCDD/Fs | | | | | Park et al. 2013 |
| Seoul, South Korea | 2001–2011 | MSWI | 73 | 112 living >10 km from plant | ns | Blood: PCDD/Fs, PCB | | | | | Park et al. 2014 |
| Taipei, Taiwan | ns | MSWI | 133 | – | ns | Blood: PCDD/Fs | | | | | Hu et al. 2003, 2004 |
| Taipei, Taiwan | 2004 | MSWI | 122 | 122 GP (age- and sex matched) | within 10 h after workshift | | Blood and Urine: As, Pb | | | | Chao and Hwang 2005 |
| Not specified Taiwan | ns | MSWI | 35 | – | Before and 1 month after maintenance work | Blood: PCDD/Fs | | | | | Shih et al. 2006 |

ns: not specified; MSWI: Municipal solid waste incinerator; HSWI: hazardous/hospital solid waste incinerator.

**Table 4.** Methodological features and main results for reference studies.

| Study (name/city or country, date) | Number of exposed subjects | Biomarkers | Method of selection | Exposure assessment method | Repeated surveys | Information on personal characteristics | Information on exposure duration | Information on diet | Information on other exposure sources | Analysis of individual vs. pooled samples | Use of regression methods taking in account all possible confounders | Main results | Papers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FLEHS II/ Belgium 2002–2006 | 207 Adolescents | PCB, Pb, Cd, PAHs, VOC, effects | volunteer | Distance from the source | no | Age, sex, BMI, education, residence history, health status, traffic, socio-economic situation | Living for at least 5 years in the municipality | Food frequency questionnaire (fruit, vegetables, fat-containing food, local food consumption) | Traffic exposure | individual | Yes: age, sex, smoking and BMI | Pb, Cd, PCB, DDE, HCB, 1-OH-pyrene, and t,t-MA were not different between residents in SWI areas and the total study sample. Testosterone, LH levels, and the proportion of boys having reached stadium 3 for sexual development were higher in the adolescents from the SWI areas. | Schroijen et al. 2008; Croes et al. 2009 |
| | 198 Adults | effects | random | Living in a limited area (mean surface 6.2 $km^2$) under the wind of a waste incinerator. Emission delineated in function of modeled, calculated emission of at least 1.2 mg smoke per $m^3$ from the SWI | no | Age, sex, BMI, education, smoking habit, residence history and characteristics, health status, traffic, socio-economic situation, occupational exposure, use of medication | Not reported | Food frequency questionnaire (fruit, vegetables, fat-containing food, local food consumption) | Other industries, traffic exposure | individual | Yes: age, sex, smoking and BMI | Significant higher values of micronuclei, DNA-strand breaks and oxidative DNA damage were found in those living near SWIs in comparison with the average values of the total study population. | De Coster et al. 2008 |
| French Dioxins and Incinerator study/France 2005 | 1030 Adults | PCDD/Fs, PCB | random | exposed subjects: defined as those under the incineration plume | no | Age, sex, smoking habit, burning activities, and recreational activities, diet, socio-demographic data | at least 10 years | Local food consumption | Burning activities | individual | Yes: age, body mass index, gender, recent change in weight, smoking status, background food intake, burning activities, and recreational activities | No difference between exposed and referents was found. Serum dioxins increased with the intake of food produced under the oldest incinerators' plume. The consumption of locally-produced animal food | Frèry et al. 2007a, 2007b; Zeghnoun et al. 2007 |

(*continued*)

**Table 4.** Continued.

| Study (name/city or country, date) | Number of exposed subjects | Biomarkers | Method of selection | Exposure assessment method | Repeated surveys | Information on personal characteristics | Information on exposure duration | Information on diet | Information on other exposure sources | Analysis of individual vs. pooled samples | Use of regression methods taking in account all possible confounders | Main results | Papers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | influenced the levels of specific dioxin and PCB congeners | |
| Rhine area/ Germany | 186 Children | PCB, metals, effects | volunteers | Distance from the source | no | Age, sex, BMI, ETS exposure | Not reported | Fish intake | Presence of other industries | individual | Yes: fish consumption, ETS exposure, age, sex | No difference in exposure or effect biomarkers between groups. Significant associations between some PCB congeners, or blood Cd and thyroid hormones. No association between SWI and biomarkers of exposure and of effects was shown. | Osius et al. 1999 |
| AIA/Modena, Italy, 2012 | 497 adults | Metals, PAHs | Census and random | Dispersion model based on fallout map of particulate matter | no | Sex, age, BMI, education, smoking habit, lifestyle, citizenship, residence zone and characteristics, traffic and heating exposure, diet, occupation | At least 3 years | Yes: fish, meat, vegetables, diary, cereals, alcohol | Traffic and other industries, urban environment | individual | Yes, all collected confounders | Biomarkers were in the range of the reference values of the general population. No metals showed a clear relationship with SWI exposure levels. Positive associations between SWI exposure and some urinary PAHs were found. | Gatti et al. 2017 |
| Environmental Health Survey Lisbon vs Madeira/ Portugal 1999–2004 | 783 Adults, Parturients Children | metals | volunteers | Distance from the source | yes | Age, sex | At least 1 year | Local food consumption | Not reported | individual | no | No differences between exposed and controls. The lack of information of other potential exposure sources and of adequate statistical analysis does not allow evaluating the actual contribute of the SWI to the total body burden of metals. | Reis et al. 2007a, 2007b, 2007c |

(*continued*)

**Table 4.** Continued.

| Study (name/city or country, date) | Number of exposed subjects | Biomarkers | Method of selection | Exposure assessment method | Repeated surveys | Information on personal characteristics | Information on exposure duration | Information on diet | Information on other exposure sources | Analysis of individual vs. pooled samples | Use of regression methods taking in account all possible confounders | Main results | Papers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Constantì/Spain, 1996–2012 | 96-196 Children and 144 adults | metals | Not reported | Distance from the source | Yes | age | Not reported | no | Presence of other industries and high traffic | individual | no | The results suggest a low exposure to metals, but several pitfalls in methodology and the lack of adequate statistical analysis does not allow evaluating the actual contribute of the SWI to the total body burden of metals. | Nadal et al. 2005; Ferré-Hugu et al. 2009; Martorell et al. 2015 |
| Bilbao/Spain 2006–2008 | 163 adults | PCDD/Fs, PCB | Census and volunteers | Distance from the source | yes | Sex, age, socioeconomic variables, education, anthropometric variables, smoking, | since the beginning of the SWI operation (1-3 years) | Yes: consumption of produce from local farms and gardens | High traffic density | 16 pooled samples per year grouped by age and sex (20 individuals for each pool) | no | No differences in PCDD/Fs levels as a function of the area of residence or proximity to the plant over the time. Results confirmed by a following but smaller study with better control of confounders and statistical analysis. | Zubero et al. 2011 |
| Shenzhen/China 2012–2014 | 269 adults | metals | volunteers | Distance from the source based on a previous environmental impact assessment | no | BMI, sex, age, residence duration, smoking, education level, income level | At least 3 years | Yes: fish, meat, rice intake | Not reported | individual | Yes: age, sex, BMI, education level, income, smoking habit, distance from SWI, residence time, gaseous mercury in air, fish intake | Blood Hg and methylmercury were correlated with the ingestion of local fish. Blood methylmercury was also correlated with mercury in air. | Deng et al. 2016 |
| | 195 adults | metals | Not reported | Distance from the source | no | BMI, sex, age, residence history, smoking, education level | At least 2 years | Yes: analysis on fish, meat, vegetables, and cereals | No other potential heavy metal pollution sources nearby could be found | individual | no | Blood Pb and Cr were higher in people living within 3 km from the plant than in referents. Food | Li et al. 2017 |

(*continued*)

**Table 4.** Continued.

| Study (name/city or country, date) | Number of exposed subjects | Biomarkers | Method of selection | Exposure assessment method | Repeated surveys | Information on personal characteristics | Information on exposure duration | Information on diet | Information on other exposure sources | Analysis of individual vs. pooled samples | Use of regression methods taking in account all possible confounders | Main results | Papers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | from local market resulted contaminated with Pb and Cr. Food ingestion played a major role to the total adsorbed daily dose. | |
| Osaka/Japan | 95 + 50 | PCDD/Fs, PCB | Not reported | Distance (<2 km) | no | Not reported | Not reported | Not reported | Not considered | individual | no | Higher PCDD/Fs levels were found in those subjects living near the SWI emitting high levels of dioxins | Kitamura et al. 2001 |
| Tokio/Japan 1999–2000 | 240 mothers | PCDD/Fs, PCB | Not reported | Distance between domicile and incinerators | no | age, history of delivery, height, and tobacco history and consumption of vegetables from a home garden. | Residents in Tokyo for more than 5 years. | Yes: frequency of fish consumption per week and vegetables from own garden | Not considered | individual | Yes: age, smoking, consumption of fish or vegetables from own garden. | No significant association between dioxins levels in breast milk and proximity of the domicile to an incinerator was found | Tajimi et al. 2005 |
| Seoul/Korea 2001–2011 | 769 adults | PCDD/Fs, PCB | volunteers | Distance from the source | no | Not reported | Not reported | no | Not reported | individual | no | No difference between exposed and controls. No clear reduction of PCDD/F or PCB along the study period was observed. | Park et al. 2014 |
| Seoul/Korea 2006–2009 | 841 adults | metals | Not reported | Distance from the source | no | sex, age, residence duration, smoking habit, marital status, education level, income level, risk perception variables | 4 groups of exposure duration: up to 5 yrs, 6-10 yrs, 11-15 yrs, 16 yrs or more | no | Not reported | individual | Yes: sex, age, residence duration, smoking habit, marital status, education level, income level, risk perception variables | Blood Cd and Pb levels were higher in those with longer residence duration. The diet impact was not evaluated. | Lee et al. 2012 |

(*continued*)

**Table 4.** Continued.

| Study (name/city or country, date) | Number of exposed subjects | Biomarkers | Method of selection | Exposure assessment method | Repeated surveys | Information on personal characteristics | Information on exposure duration | Information on diet | Information on other exposure sources | Analysis of individual vs. pooled samples | Use of regression methods taking in account all possible confounders | Main results | Papers |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| North Taiwan 2000–2004 | 341–1708 adults | PCDD/Fs, effects | Census and random | Dispersion model based on data on stack emission | no | Age, sex, smoking status, BMI, residence duration | Yes, at least 5 yrs. | yes | Not considered | individual | Yes; adjustment for age, sex, BMI and smoking status | No difference in PCDD/Fs serum levels were observed although PCDD/Fs air levels resulted different among the zones. Serum PCDD/Fs concentrations were not correlated with ambient air levels and residence duration. Eating locally produced animal and vegetable food was associated with PCDD/Fs serum levels. | Chen et al. 2003; Chen, Su, et al. 2006; Huang et al. 2007; Chen, Su, and Lee 2006 |

micronuclei (MN) frequency in lymphocytes were not different between 23 workers and 19 office workers from the same plant (controls), even stratifying the exposed individuals for the effective duration of the cleaning operations during the year (from 1 to 11 months/year). Data on alcohol consumption, tobacco smoking, physical activity, and drug intake showed no difference between exposed and controls. The authors concluded that no risk for health associated with DNA damage was found, but the small sample size and the limited information of confounding factors do not allow drawing firm conclusions.

## Belgium

### General population

In Belgium, the majority of studies were conducted in the Flanders, one of the most populated areas in Europe, with a dense network of traffic roads, industrial activities and intensive farming close to urban centers.

The pilot Flemish Environment and Health Survey (FLEHS) was performed in 1999 and included a small sample of 42 adolescents (Staessen et al. 2001; Den Hond et al. 2002; Nawrot et al. 2002) and 39 women (van Larebeke et al. 2006) living near two waste incinerators which started working in 1971 and 1980 and shut down in 1997 because of dioxin emissions exceeding recommendations. This study showed higher serum PCB concentration, higher urinary *t-t*-MA, and orthocresol, and delayed sexual maturation in subjects living near the incinerators than in the control group. Following these evidences, a larger scale 5-year (2002–2006) biomonitoring program was carried out (De Coster et al. 2008; Schroijen et al. 2008; Croes et al. 2009). Among the nine areas selected based on different type of pollution pressure, the "waste incineration area" included the immediate surroundings of six MSWIs spread out over the whole region. Exposure and effects biomarkers were measured in 14 to 15 years old adolescents and in the adult population. No significant differences were found between the mean biomarker values measured in serum/blood (Pb, Cd, PCB, DDE, HCB) and in urine (1-OH-pyrene, *t,t*-MA) from 207 adolescents living since at least 5 years in the waste incineration area and the average biomarker levels in Flanders' adolescents, measured on the total study sample (1679 adolescents). When considering the six areas individually, some areas had significant higher biomarker levels of metals, PCB, DDE, HCB, ad *t,t*-MA (after adjustment for confounders) than the reference values and differences among the areas were evident as well (Schroijen et al. 2008). However, individual groups were small (14–72 participants) and the influence of industrial plants other than SWI was not evaluated. In the same study, hormones levels (testosterone, LH, SHBG, estradiol, TSH, fT3, fT4) and sexual maturation were evaluated. In adolescents living in waste incineration area, testosterone and LH levels resulted higher than in the reference population and the proportion of boys having reached stadium 3 for sexual development was significantly higher than in the total study population (Croes et al. 2009) (Table 4). De Coster et al. reported results on effects biomarkers (PSA, CEA, p53, micronuclei, DNA damage, HDG) measured in 1583 adults selected in the same areas through a stratified clustered multi-stage design. The authors reported significant higher values of micronuclei, DNA-strand breaks and oxidative DNA damage among the 198 subjects living in the waste incineration area compared to the average values of the total study population, suggesting that residence near waste incinerators might be associated with an increase in the risk of cancer (De Coster et al. 2008). Strengths of this study are the large sample size, the random sampling and the consideration of important confounding factors in all the reported results, as age, sex, smoking, and BMI. Diet questionnaires were administered, but the authors apparently did not take into account the collected information for this analysis (Table 4).

In the region of Wallonia, two groups of subjects residing within 2 km from two old incinerators, one in a rural area (51 adults), and the other in an industrial area (33 adults), were compared with 63 controls from an unpolluted area. Subjects were recruited on a volunteer basis via mail in the year 2000. Information on personal characteristics, diet, residence history, smoking habits, and health status were collected by a self-administered questionnaire. Blood and urine concentrations of Cd, Hg, and Pb did not increase in exposed subjects in comparison with controls (Fierens et al. 2006, 2007). Individual serum levels of dioxins and PCB were higher in subjects residing in the rural area than in controls. Multiple regression models highlighted that the higher dioxin and PCB accumulation was related in part to local animal food consumption (Fierens et al. 2003, 2007). Five years later, a decrease in PCDD/F and PCB concentration was found in 20 of these volunteers (Fierens et al. 2006). Besides the small sample size, the inclusion of subjects on a voluntary base is a major weakness of this study.

### Workers

In Belgium, only one biomonitoring study was carried out to evaluate the exposure to dioxins of staff involved in incinerator cleaning work. This study involved only 5 workers at a MSWI. The authors measured serum dioxin-like activity by chemical-activated luciferase gene expression (CALUX test) during two of the annual stoppages of the plant for cleaning activities. They took blood samples at three different occasions: 10 days before the operation, immediately after the last shift and 6 days later. Serum concentration before the start of cleaning work resulted similarly to those found in Flemish general population, while increased levels were found at the end of the cleaning work. The extremely small sample size and the study design, together with the lack of analysis including confounding factors, make inconclusive these results (Raemdonck et al. 2006).

## Finland

### General population

In Finland, changes in Hg concentrations were investigated in the hair of 113 subjects living around an old HSWI and 55 controls, defined as subjects living at about 5 km from the plant. Baseline samples, taken in 1984, were compared to Hg levels measured in 1994. Slightly increased Hg levels were observed in resident than in controls, moreover, the Hg concentrations increased with decreasing residence distance from plant. Results were confirmed by multivariate logistic regression adjusting for age, sex, fish intake, and water source. This is one of the first studies performing a multivariate analysis, but the sample size is limited (Kurttio et al. 1998).

### Workers

Three small studies on workers were carried out in Finland.

An earlier study found higher PCDF and PCB levels in 12 HSWI and 5 capacitor manufacture workers than in 5 control subjects. They observed an increasing trend over a 7-year period (1985 to1991). However, the results may have occurred partially due to the impact of age, as PCBs accumulates in the human body (Luotamo et al. 1993a, 1993b).

As part of the study on the general population (see above), Kurttio et al. measured Hg in hair of 11 HSWI workers, observing Hg increase over the 10-year observation period (1984–1994) (Kurttio et al. 1998).

More recently, a study testing an analytical method for PCB measurement, reported higher PCB concentrations in 26 HSWI workers than in 21 general population controls (Kontsas and Pekari 2003).

The limited sample size and the insufficient confounder control make it difficult to draw conclusions from these small studies.

## France

### General population

In 2005, the French Dioxin and Incinerators Study was performed by the National Institute of Public Health Surveillance in collaboration with the France National Food Safety Agency. The study investigated 1030 subjects, including randomly selected adult residents living under the incinerator plume (exposed) and individuals residing at more than 20 km distance (referents) from the incinerator area of eight MSWIs. The definition of the area under the incinerator plume was not further specified, as well as the number of exposed subjects and referents. Enrolled exposed subjects were residing at least 10 years around the MSWIs, without occupational exposure and no breast-feeding within the past 15 years, for women. Validated questionnaires were adopted to collect information about general diet, locally produced food diet and production of cattle, poultry, eggs and milk in the area of the plume. Individual plasma levels of PCDD/Fs and PCB were measured. Statistical analysis using mono- and multivariate statistic was performed, taking into account potentially confounding factors such as age, body mass index, gender, recent change in weight, smoking status, background food intake, burning activities, and recreational activities (Frery et al. 2007a). No difference between exposed and referents was found. However, serum dioxins increased with the intake of food produced under the oldest incinerators' plume (Frery et al. 2007b). Moreover, the consumption of locally-produced animal food influenced the levels of specific dioxin and PCB congeners (Zeghnoun et al. 2007). Overall, inhalation seems to give a negligible contribution to exposure in comparison to dietary intake. Given the large number of involved subjects, the epidemiological design, with the careful consideration of confounding and exposure factors, including diet, and the statistical analysis, the results of this study are particularly robust and support the low impact of new SWIs on the body burden of PCDD/Fs and PCB; the lack of papers describing in details the study is, however, a major weakness (Table 4).

In 2003, a very small study was conducted in Maincy in 10 residents living for at least 25 y at less than 2 km from an old MSWI operating from 1974 until 2002, showing higher plasma dioxin levels in these subjects when compared to the general European population (Pirard et al. 2005). Authors showed that PCDD/Fs in eggs and soil sampled near the MSWI, under the prevailing wind stream, were higher than in samples taken outside this area, pointing out the impact of MSWI on the surrounding environment and in consumers of local food. However, it should be noted that study subjects were older than people usually studied (>51–75 years) and that their BMI was not indicated; both factors are known to play a role on dioxin levels and could, at least in part, explain findings.

Another small study involved 34 newly diagnosed non-Hodgkin lymphoma cases (2003–2005) residing in an area where in the past an old incinerator was releasing high levels of dioxins: plasma PCDD/Fs and PCBs in these subjects were higher than in 34 matched controls randomly selected from the donor registry of the regional blood bank (Viel et al. 2011).

### Workers

In 1995, the exposure to SWI emissions was investigated in 15 workers from a HSWI and 14 workers from a MSWI by measuring urinary Cd, Cr, Ni, Mn, and inorganic As (only for MSWI workers), 1-OHPYR, *t,t*-MA, *o*-cresol, and methyl hippuric acids in samples collected at the beginning and at the end of the work shift. Not occupationally exposed workers from a supermarket located 10 km aside, were included in the study for comparison. No difference was found comparing before and end of the shift levels for any metal. In comparison with controls, Cd, Cr, and Ni levels were similar in MSWI workers, and were higher in HSWI workers. Levels of Mn were comparable to those of controls, but levels of inorganic As were higher. The comparison with the French Biological Exposure Indices (BEI) showed levels lower than 25% of the BEI for Cd, and 2% for Cr; levels for inorganic As were as high as 65% of BEI. No control for diet was implemented for As intake. Median end-shift levels of 1-OHPYR were not different from controls; also the particulate PAH air concentration measured at the MSWI was not different from that measured at the control site. For urinary *t,t*-MA, *o*-cresol, and methyl hippuric acids, no difference was found comparing exposed and control subjects; levels of urinary metabolites were well below the French biological exposure indices (Maître et al. 2003). In 1996, a second study, including also workers from an additional MSWI, for a total of 102 subjects, was conducted; higher Pb in blood was found in subjects in the maintenance and effluents groups; moreover, there was a significant positive trend with respect to the duration of the job. Hepatic and hematological tests were well within the normal range, but higher white blood cells were observed in the exposed workers (Hours et al. 2003). Overall, exposure in SWI workers, assessed by urinary and blood biomarkers, was well below the French Biological Exposure Indices and/or comparable in SWI workers and controls.

### Germany

#### General population

In the Rhine area, Federal State of Hessen, a study investigated 187 children (7–10 years old) exposed to emissions from a HSWI that was burning PCB-contaminated material. The date of the study is not reported. Other industries, including a chemical plant, were present near the SWI. Children were recruited on a voluntary base in an area 30 km wide around the HSWI. Information on fish intake and ETS exposure were assessed by questionnaire. Two groups of children, the first from an industrialized area 20 Km far from the SWI and the second from a mountain area, for a total of 144 children, were also investigated as comparison groups. Blood PCBs, Pb and Cd, and urinary Hg were investigated together with serum thyroid hormones (TSH, FT3, and FT4) as biomarkers of effect. No differences between the groups were found, but the regression analysis, which accounted for fish consumption, ETS exposure, and age, highlighted significant associations between some PCB congeners, or blood Cd and thyroid hormones (Osius et al. 1999). No association between SWI exposure and biomarkers was reported (Table 4).

In 1993, 46 persons living for at least five years near a MSWI operating since 1983 in Schwandorf, Oberpfalz region, were involved in a biomonitoring study, following a recruitment based on regional newspapers advertising. Blood ($n = 39$) and breast milk ($n = 7$) samples were collected and tested for PCDD/Fs. No increase of PCDD/F body burden associated with the SWI was found in comparison with the background levels in the general population of Germany (Deml et al. 1996).

#### Workers

A bigger study included 122 workers of a modern HSWI (Wrbitzky et al. 1996) in the region of Franconia (southern Germany). Urinary PCB, HCB, MCP, PCP, BTEX and PAHs blood and urinary metals were assessed. Higher levels of blood toluene, Pb and Cd, and of urinary As, DCP and tetrachlorophenols were found in workers in contact with the incinerator ($N = 45$) compared with periphery workers ($n = 54$), and the management ($n = 23$). Nevertheless, elevations were always small and of interest from the environmental rather than from the occupational point of view; biomarkers never exceeded the German biological limit values. The authors associated the inconsistent elevation of biomarkers with the modern technology of the plant, based on an almost completely closed system (Wrbitzky et al. 1996).

At the beginning of the nineties, the exposure to PCB, HCB, MCP, PCP, BTEX, and PAHs, was assessed in 53 workers from a MSWI (Angerer et al. 1992). Urinary 1-OHPYR, DCP, TCP, and serum HCB were higher in workers than in 431 control subjects belonging to the general population. Conversely, urinary MCP and tetrachlorophenols were higher in controls than in workers, and no differences were detected for benzene and PCB in blood, and TCP, and pentachlorophenols in urine. Levels were well below German biological limit values for occupational risk assessment. Authors concluded that the increase of some of these biomarkers may have been caused by the incineration process, but they highlighted that the increases were small, and of interest mainly from the environmental point of view (Angerer et al. 1992).

Three different papers reported levels of PCDD/Fs in individual blood samples taken from few tens of workers from old and new MSWI/HSWI (Päpke et al. 1993; Schecter et al. 1995). The levels of some congeners were significantly higher in blood of workers of old MSWI and/or in HSWI than those of controls; this was mostly seen in locksmiths that performed repairs and inspection inside the oven (Päpke et al. 1994). Levels of blood PCDD/Fs of workers of the new plants were comparable to those found in the general population, indicating that the modern pollution controls can effectively limit exposure (Schecter et al. 1995). The small samples size and the poor study design limit the interpretation of these results.

### Italy

#### General population

The AIA study was conducted in the town of Modena, Emilia-Romagna region, in the year 2012/2013 and involved 496 volunteers (Gatti et al. 2017). Subjects were randomly selected among those living and working for at least 3 years within 4 km of the modern MSWI. Four sampling strata, based on quartiles of the annual median PM10 concentration fallout maps of SWI emissions, were defined and used for subject recruitment. Information on possible confounders, including zone classification, outdoor and residential traffic exposure, residence characteristics, diet, active and passive smoking, and personal and socio-demographic data were collected by questionnaires. A significant relationship between living near the SWI and exposure to non-carcinogenic PAHs, evaluated as urinary fluorene, naphthalene, fluoranthene, and pyrene, was found using multiple linear regression models taking in account all collected information and confirmed by various sensitivity analyses. On the contrary, no association was found between SWI exposure and urinary metals (Pb, Cd, Hg, Mn, Ni, Cu, Zn). The results obtained on PAH exposure confirmed those of the pilot study conducted in 2010 (Ranzi et al. 2013). This study, conducted with a rigorous methodology as regard sample size, recruitment criteria, exposure assessment, the use of specific and sensitive biomarkers, and statistical analysis, suggests a possible role of SWI in determining PAH exposure in the general population. However, the exposure to SWI emission was very low, with biomarker levels ranging within the reference values of the Italian general population (Table 4).

In 2005–2006, the exposure to PCDD/Fs and PCB was assessed in 74 subjects living in the proximity and far away of two MSWIs in the Tuscany region, in an area with the presence of other industrial plants. PCDD/Fs and selected PCB were assayed in eight pooled blood samples. No increase of PCDD/Fs and PCB associated with the incinerator plants was found. As expected, higher levels of total PCDD/Fs and PCB were detected in older subjects. The authors concluded that the PCB congener profiles in all samples suggested a possible impact on the area of interest of all the industrial activities, but the limited number of pooled samples does not allow taking into consideration confounders (De Felip et al. 2008).

## Portugal

### General population

In Portugal, three SWIs have been under investigation in recent years, the MSWI in Lisbon (VALORSUL), the HSWI in Madeira Island, and the MSWI serving the region of Oporto.

Two biomonitoring studies were carried out with similar methodologies in Lisbon and in Madeira Island and for this reason, they are presented here together. The first was conducted in the frame of the environmental health surveillance programs regarding the VALORSUL plant, a modern MSWI that has been operating in the Metropolitan Area of North Lisbon since 1999, while the second concerned the update of an old SWI operating in Madeira Island since 2002. In both studies, subjects were volunteers living at different distance from the facilities. The exposure to metals (Pb, Cd, and Hg) was studied in blood samples collected in two to four consecutive observations from adults (for 688 participants), primiparous parturients (or at least after breastfeeding their last child for at least 3 years) (417), and 1–6 years old children (497) (Reis et al. 2007a, 2007b, 2007c). Both in adults and in parturients, metal levels were not different between exposed and non-exposed individuals, decreased from the baseline onwards, they were higher in Lisbon than in Madeira, and they were higher than the reference values of the Portuguese population (Reis et al. 2007a, 2007c). In children, no clear pattern of Pb exposure was found, but about 3% of children had Pb levels higher than 10 μg/dl (Reis et al. 2007b). Although a large number of observations were collected in the different surveys, the results of these studies correspond actually to a relatively small number of individuals in the single surveys. The higher levels observed in Lisbon than in Madeira were attributed to alternative sources, such as higher traffic or industrial density, but no statistical control for confounding factors was implemented, and consequently, the actual contribution of SWIs to the metal exposure of the participants could not be evaluated (Table 4).

In addition, the exposure to PCDD/Fs and PCB was studied in a limited number of individual blood and breast milk samples observing no association between PCDD/Fs blood or milk levels and the area of residence, no dioxin body burden increase over time, and an association with age (Reis et al. 2002; Reis, Miguel, et al. 2004; Reis, Sampaio, et al. 2004; Sampaio, Murk et al. 2004; Sampaio, Reis, et al. 2004b; Reis et al. 2005). A multiple regression analysis, taking in account the residence area, age, the exposure status, and parity (only for parturients), highlighted higher blood or breast milk PCDD/Fs levels in Lisbon than in Madeira and the influence of age (Reis, Miguel, et al. 2007; Reis, Sampaio, et al. 2007).

In 2001, in the frame of the External Monitoring Plan for the LIPOR II plant, a MSWI operating since January 2000 in the region of Oporto, the exposure to PCDD/Fs was assessed in individual blood samples from 46 adults and in breast milk samples from 19 mothers residing in the surroundings of the plant. Exposure levels in the range of the non-exposed general population were found, but no statistical analysis of results was implemented and the number of the studied subjects is too small to draw any conclusion (Calheiros et al. 2002).

## Slovakia

### General population

In Slovakia, a small study was conducted in four areas where MSWIs and other industrial plants, known to cause dioxin contamination, are present. The study date was not reported. Eighty-one volunteers living in the suspected polluted areas (no further described) and 44 matched control subjects living in rural areas were investigated measuring PCDD/Fs, PCB, and PBDE in individual blood samples. PCDD/Fs and PCB levels were higher in subjects residing in the polluted areas. However, PBDE levels were higher in controls than in exposed subjects (Chovancová et al. 2012). The actual contribution of SWIs to dioxin levels was not investigated or compared with that of the other industrial plants present in the areas; moreover, no control for confounders was implemented.

## Spain

### General population

In Spain, three SWIs have been under investigation in recent years, namely the HSWI in Constantí (Terragona County, Catalonia), and the MSWIs in Bilbao (Basque Country) and in Mataró.

In Constantí, an HSWI started operating in 1999 in the same area where a MSWI was already operating, together with an important chemical complex and two oil refineries. A periodic monitoring program, including a baseline study, was designed to assess the health risks of the population living near the HSWI and of workers working in the plant. In particular, the exposure to metals was studied in hair samples from 96–196 children aged 12–14 years (Nadal et al. 2005; Ferré-Huguet et al. 2009; Martorell et al. 2015) and in blood samples from 144 adults living in the surroundings of the plant (Ferré-Huguet et al. 2009). Participants were included based on the residence area and, apparently, no control for confounding sources, such as the presence of other industrial facilities, was implemented in the statistical analysis of results. In children, the levels of most metals in hair decreased from 1998, at baseline, to the last survey in 2012, while Cr increased in all the investigated areas (urban area, near the chemical complex and closer to the HSWI) (Martorell et al. 2015). Higher levels of Pb were always found in children from the incinerator area (Nadal et al. 2005; Ferré-Huguet et al. 2009; Martorell et al. 2015), but the potential confounding effect of the high traffic near the school where the samples were collected was not considered. In adults living near the HSWI, blood Cd, Ni, and Pb significantly increased during the period 1998–2007, and As e Pb were higher than in controls, but similar or lower than those reported in other studies for general population (Ferré-Huguet et al. 2009; Martorell et al. 2015). Overall, the results of this study, based on a quite large number of subjects, suggest a low exposure to metals of the surrounding population. However, the lack of information regarding the possible confounders and of adequate statistical analysis make the results only partially informative of the actual contribution of the SWI to the total body burden of metals (Table 4). In the frame of the same study, also the exposure to PCDD/Fs was assessed in individual blood samples from a very limited number of individuals (20–40) (Schuhmacher et al. 1999; Bocio et al. 2004; Agramunt et al. 2005; Nadal et al. 2008, 2013) and in breast milk samples from 15–20 primiparae mothers (together with PCBs and PBDE) (Schuhmacher et al. 2004, 2007, 2009, 2013) finding a significant decreasing trend from 1996 to 2012.

In Bilbao (Basque Country), a modern MSWI was commissioned in 2005. The local government demanded, as a prerequisite to authorize the construction of the plant, to carry out a study to evaluate the exposure to pollutants from the SWI and changes over time. The exposure to PCDD/Fs and PCBs was assessed in 2006 and in 2008 in serum pooled samples, grouped by age and sex, from 163 adults living less than 2 km away from the plant, and from 163 controls living at 5 and 20 km away from the plant (Zubero et al. 2011). Subjects were recruited both by census selection and on voluntary base. No significant differences were found in PCDD/Fs exposure as a function of the area of residence or proximity to the plant over the time, while non-ortho PCBs decreased in the nearby areas, and mono-ortho PCBs significantly increased in both areas (Zubero et al. 2011). No control of diet and other confounding factors was implemented; moreover, the use of pooled serum samples prevented the study of the associations between dioxin levels and possible determinant of the exposure (Table 4). In 2013, a smaller survey was carried out in the same area investigating PCDD/Fs and PCBs levels in individual serum samples from exposed ($n = 61$) and not exposed ($n = 66$) subjects. A food frequency questionnaire was adopted to collect information about diet. A significant decrease of PCDD/Fs and PCBs levels was observed in comparison with the previous results. The implementation of a multiple regression analysis showed that levels in people living close to the plant were not different from those living far. No difference between sexes was shown, moreover PCBs, but not PCDD/Fs increased with age (Zubero et al. 2017). The exposure to metals was studied in 57 exposed and 50 controls, by measuring, Pb in blood and urinary Cd, Cr and Hg (Zubero et al. 2010). A multiple regression model, adjusted for several confounding variables, did not show increases over time of the levels of any metals in the exposed vs. the control subjects (Zubero et al. 2010). In summary, the study conducted in Bilbao, although characterized by differences in the study methodologies conducted along the years, shows no influence of the local MSWI for PCDD/Fs, PCBs, and metal exposure for the surrounding population.

In Mataró, a residential-industrial area with high traffic density 25 km north of Barcelona, the construction of a MSWI was initiated in 1995 and regular operations started in 1999. The plant was modernized in 2004 to comply with the limit of 0.1 ng-TEQ/m$^3$ for the PCDD/Fs. The PCDD/Fs and PCB plasma concentrations were measured repeatedly in pooled blood samples from a limited group of randomly selected adult individuals (68–104) living at different distances from this plant, and in breast milk pools from 46 women. No controls for dietary exposure or other confounding factors were implemented. No significant differences between the exposed and the non-exposed subjects were found (Parera et al. 2013). Similarly, the levels of blood Pb and Cd, and of urinary Cr and Hg, measured in 1995 and in 1997, showed no differences between exposed and controls and between surveys, but for blood Pb that decreased in both groups (Gonzalez et al. 2000). In 1997, the effect of exposure to PAHs and electrophilic compounds was assessed by the thioether assay in a small group of children aged 7–10 years living near or far from the plant. Urinary thioethers were not different between the two groups, while a strong influence of exposure to passive smoking was noted (Ardévol et al. 1999). In summary, the results of the Mataró study, based on a limited sample size, show no influence of the local MSWI for PCDD/Fs, PCBs, and metal exposure for the surrounding population. The pooled determination of dioxins, as recognized by the authors, did not allow an adequate statistical assessment of the associations between levels and suspected risk factors.

### *Workers*

The exposure to PCDD/Fs, PCB, HCB, PCP, metals (Mn, Hg, Pb, Cd, Cr, Ni, and V), and PAHs was assessed in 19–29 workers with different job titles at the HSWI plant in Constantí (Terragona County, Catalonia) in a series of studies performed from 1999 to 2011 (Agramunt et al. 2002, 2003; Schuhmacher et al. 2002; Mari et al. 2007, 2009, 2013). Results showed that the mean PCDD/Fs plasma concentrations decreased significantly since the baseline survey, metals were similar to those found in the baseline survey and in the same range than those found in the general population living in the same area, while blood Hg levels were slightly higher than at the baseline. Similarly, the mean levels of 1-OHPYR were very low, with no trend along the years. No difference between the different jobs (plant, laboratory, and administration workers) were reported for any of the investigated chemical.

As concerns the MSWI plant in Mataró, the mean PCDD/Fs plasma concentrations measured in 17 workers between 1995 and 2012 did not change over time, while the mean

PCB plasma concentrations slightly decreased over time (Gonzalez et al. 2000; Mari et al. 2007; Parera et al. 2013). Both PCDD/Fs and PCB values were not different from those measured in the population living near the plant. As for metals, the levels of blood Pb and Cd, and of urinary Hg were similar in 1997 and in 1995, while urinary Cr was lower in 1997 (Gonzalez et al. 2000).

Notwithstanding some evident limitations of the studies conducted at both plants such as the low number of investigated subjects and the use of pooled samples, the authors of these studies concluded that there was no evident sign of occupational exposure to the investigated pollutants for study workers (Mari et al. 2013; Parera et al. 2013).

### Sweden

#### Workers

Two small investigations were conducted on two limited groups of workers from the plant Sakab in Norrtorp (Kumla), a HSWI operating since 1983 (Rappe et al. 1992; Selden et al. 1997). In 1988, PCDD/Fs levels in blood from 10 workers that had been working for 5 years at this plant were found within the range expected for the Swedish general population (Rappe et al. 1992). Later, PCB and HCB exposure was investigated in blood from 29 workers and compared with that of 60 blue-collar workers from the same plant as controls: the mean PCB levels were not different between the two groups, but the levels of some specific congeners and HCB levels, were higher in workers (Selden et al. 1997). No information is given on the duration of exposure or on the time of the investigation. A significant decrease of several PCB congeners, but an increase of HCB levels over time was evident in historical samples from a subgroup of 20 workers, obtained prior to the start of employment at this plant (6–12 years before this investigation). Moreover, a correlation was found between some lower chlorinated PCB congeners in air samples and plasma, indicating a certain influence of the occupational exposure on the overall PCB load (Selden et al. 1997). No information is given on workers' activity, as well as, on collection, handling, and analysis of samples, and no statistical elaboration of data is presented for these limited investigations.

### The Netherlands

#### General population

A very small investigation involved five subjects living near the MSWI in the town of Duiven, to determine if the exposure to fly ash blown away from the storage site near the waste incinerator increased their level of blood PCDD/Fs. The comparison with five unexposed subjects from the general population showed no difference between the two groups (Van den Hazel and Frankort 1996). The year of the study is not reported.

#### Workers

In repeated urine samples ($n = 67$) from three chemical waste incinerator operators, collected before and after the work shift, an enhanced excretion of thioethers in end-shift samples was found, suggesting that incinerator workers inhale electrophilic compounds, successively metabolized to thioethers and finally excreted in urine (van Doorn et al. 1981). The study year, as well as information about the specific job task of the workers, was not reported. No conclusion can be drawn as to which compound caused the enhanced excretion of thioethers.

Four workers from the MSWI of Duiven were investigated to determine if occupational exposure to fly ash or slug at the waste plant increased their level of blood PCDD/Fs in comparison with a group of 10 workers of a water purifying plant situated near to the SWI. The comparison showed that some congeners were increased in SWI workers, so the authors concluded that this was probably due to occupational exposure to fly ash or slug (Van den Hazel and Frankort 1996). The very small number of the investigated subjects and the absence of any statistical evaluation should temper this conclusion.

## Northern and Southern American countries

### Brazil

#### General population

A small study was conducted in the year 2001 in the city of Capivari de Baixo (Santa Caterina State, Brasil), located downwind the local HSWI burning solid residues of health services (Possamai et al. 2009; Wilhelm Filho et al. 2010). The exposure to metals was measured in blood from 20 individuals living about 5 km from the plant and in 20 individuals living 130 km northeast from the plant. No control for confounding sources was implemented in the statistical analysis of results that showed higher mean levels of Pb, Cu, and Zn, and lower Mn levels in the near residents than in controls (Wilhelm Filho et al. 2010). Several enzymatic and non-enzymatic blood biomarkers of oxidative stress were measured too, showing a condition of severe oxidative stress in near residents that was attenuated after the supplementation of vitamin E and vitamin C for 6 months (Possamai et al. 2009; Wilhelm Filho et al. 2010). The small number of the investigated subjects and the absence of adequate statistical analysis do not make it possible to draw any conclusion about the role played by the SWI in determining or not an exposure to metals in residents.

#### Workers

The exposure to metals (Pb, Cu, Fe, Mn, and Zn) was measured in blood of 20 workers from the HSWI located in the city of Capivari de Baixo and compared with those measured in residents living near (within 5 km) or far (130 km away) from the plant (see above). The mean levels of Pb, Cu, Fe, and Zn were higher, while Mn levels were lower, in workers than in controls (Wilhelm Filho et al. 2010). The supplementation of vitamin E and vitamin C for 6 months attenuated the condition of oxidative stress that was altered in workers in comparison with controls (Possamai et al. 2009; Wilhelm Filho et al. 2010).

## USA

### General population

In 1992, the exposure to TCDD and dioxin-like compounds was investigated in individual samples from 67 subjects living near a HSWI burning material contaminated with dioxins in Times Beach (Missouri), and in 61 subjects living outside the incinerator area. Participants were randomly selected from an area that air-modeling projections indicated as a potentially high exposure area and compared to a randomly selected control group. TCDD serum levels and TEQ decreased from pre-incineration to four months into incineration and decreased further 11 months later, immediately after the end of the incineration; therefore incineration did not result in any measurable exposure to the population surrounding the plant (Evans et al. 2000). Although conducted on a limited number of samples, the exposure assessment modeling and the repeated measurement design support the lack of TCDD exposure from incineration of TCDD contaminated material.

### Workers

In 1988, 104 workers from seven MSWIs in six US states were investigated to ascertain whether occupational exposure to MSWI increased urinary mutagens in comparison with workers of water treatment plants, taken as controls. Only a small group of SWI out of 64 US SWI plants accepted to take part in the study. A careful collection of confounders and an appropriate statistical analysis were performed. An increased risk for those who were wearing protective clothing, defined as clothing other than mask and gloves, was found; this odd result may be perhaps associated with the major protection undertaken by workers who experienced the highest exposure (Scarlett et al. 1990). In 1990, a follow up study investigated urinary mutagenicity in 37 workers from four plants that were repetitively sampled and compared with 35 water treatment workers; while the first sample showed higher mutagens and pro-mutagens in MSWI workers than in controls, the same was not true in the following two samples, showing that the repeatability was poor. Authors suggested that exposure was variable or that workers modified their exposure (i.e. they wore mask) as a consequence of being studied (Ma et al. 1992). Due to inconsistency of obtained results and the lack of specificity of the applied biomarkers, the evidence that linked SWI exposure and biomarkers of mutagenicity is poor.

In 1988, exposure to metals was investigated in 86 out of 105 workers from the Philadelphia SWI by measuring blood Hg, and Pb, and urinary Hg, Pb, As, and Cd; also ZPP in blood was assessed. Workers were divided into low and high exposure groups by an industrial hygienist. Levels of biomarkers were in the normal range for all subjects; no difference was found between the groups with the exception of urinary As, that resulted higher in the low exposure group; this could be possibly associated with dietary intake, but no data on diet was collected (Bresnitz et al. 1992). It should, however, be highlighted that this study was mostly focused on workers morbidity and that results on biomarkers were only marginally reported.

In 1989, the exposure to metals of 56 maintenance workers from three SWIs of New York City was investigated by measuring blood Pb and EPP and compared with that of 15 maintenance workers at heating plants. Blood Pb was higher in SWI workers than in controls, but for both groups, levels were within the range of those measured in the US general population (Malkin et al. 1992). EPP, expected to increase following Pb exposure, was however lower in workers than in controls; this was without clinical relevance as levels were within the normal range for all subjects. Wearing a personal protective device decreased the level of blood Pb. The results of this study indicated additional exposure to Pb in incinerator workers without any health effects. The blood leftovers were pooled and analyzed for PCDD/F; the comparison with a pooled blood sample from 14 individuals with unknown exposure showed comparable levels between groups, but some congeners were higher in MSWI workers (Schecter et al. 1991). This very preliminary investigation did not take into account other sources of dioxins in the individuals.

Blood Pb, and ZPP were measured in an unspecified number of workers, probably submitted to periodical and repeated evaluations, from 10 different MSWIs to evaluate potential Pb exposure and its effect, while blood and urine Cd and urinary beta-2-microglobuline were tested to evaluate potential Cd exposure and its effect. Out of 1371 blood samples, 1010 had Pb below 10 μg/dL, and only 6 had Pb exceeding 30 μg/dL (the BEI of the American Conference of Governmental Industrial Hygienists, ACGIH). Similarly, out of 1404 samples tested for ZPP, only 1 exceeded 100 μg/dL, the ACGIH BEI at that time. Considering blood and urinary Cd, out of 753 and 209 samples, only 5 and 2, respectively, exceeded the ACGIH BEI; no criticism for beta-2-microglobulin was detected. The authors concluded that the use of personal protective equipment and hygienic work practices were effective in controlling exposure (Hoffman et al. 1997). The results indicated increased levels of Pb, and to a minor extent of Cd, in biological fluids of incinerator workers; such exposure was mostly within the biological limit values and was not associated with any alteration of effect biomarkers.

Benzene and toluene were assessed in exhaled air from six workers at an incinerator in Tennessee. Samples were collected before and after each specific job task, showing inconsistent variations between post- and pre-task levels (Thrall et al. 2001). These results were reported as a part of the validation of a breath-sampling device, so their relevance to investigate the relationship between exposure to SWI and biomarkers is poor.

Overall, studies performed in the US in the late eighties-early nineties indicated that workers, dealing with incinerator ashes enriched with metals during waste incinerator, experienced an increased body burden of metals, especially Pb; however, the exposure was kept within biological limit values by use of personal protective equipment and did not affect biomarkers of health effects.

## Asian countries

### China

#### General population

In recent years, the MSWI located in Shenzhen (South China) and operating since 2005 was the object of a biomonitoring study to investigate the potential exposure of the surrounding population to heavy metals and the main exposure pathways (Deng et al. 2016; Li et al. 2017). In 2012 the exposure to Hg was studied in 269 adults living within 5 km from the plant (residential exposure group) and in 143 adults living beyond 5 km from the plant (control group) (Deng et al. 2016). Participants in the study were recruited as volunteers. The influence distance of 5 km downwind was selected based on the environmental impact assessment of this plant, previously conducted, and on literature evidences for other SWIs. The presence of other potential pollution sources in the area is not reported. All participants had lived in the study area for more than three years. Information about diet (fish, meat, rice, eggs, and vegetable intake, mass per meal and meals per week) were collected through a questionnaire. The food origin (meat, fish, and vegetables) was mainly local. The measurement of total gaseous mercury and of particle-bound mercury, performed in a limited number of sites ($n = 6$), showed that the first was not different among sites, while the second was present at the highest concentration at the site closest to the MSWI. Biological monitoring results showed that total blood Hg was not different between exposed and controls, while the blood concentrations of methylmercury were higher in the exposed subjects. A multiple regression model, taking into account personal characteristics, the exposure indices (residence distance from the SWI, residence time, mercury in the air), and diet (fish intake) found that blood Hg and methylmercury were not correlated with the distance of the residence from the plant or the residential time, while they were significantly correlated with the fish intake. Blood methylmercury was also correlated with the total gaseous mercury concentration in air. The combination of internal and external exposure assessment showed that the direct contribution of the MSWI emissions (inhalation and soil ingestion) to the Hg exposure was minimal in comparison with the dietary contribution (Deng et al. 2016). A major weakness of this study is the lack of information (age and sex) about the study participants, although this information has been included in the statistical analysis.

In the following years (2013–2014) the exposure to Cr, Cd, Pb, and Mn was studied in 195 adults (24–45 years) living within 3 km from the same plant and in 230 adults living beyond 3 km from the plant (Li et al. 2017). No other potential heavy metal pollution sources beside the SWI was identified in the studied area. The selection criteria of the participants was not reported, moreover, it is not clear if the subjects were the same as the previous investigation. Food from local market resulted contaminated with Pb and Cr. The air concentration and the soil contamination was measured also in a limited number of sites ($n = 6$), observing a decreasing concentration trend of metals with increasing distance from the SWI. Biological monitoring results showed that that blood Pb and Cr were higher in those living within 3 km from the plant than in the reference group. The metal intake rates through ambient air, drinking water, and food and soil ingestion were calculated, observing that food ingestion played a major role in the total adsorbed daily dose. No statistical analysis of results was done to assess the actual contribution of the SWI in determining the metal exposure in the near residents (Table 4).

Overall, given the quite large number of involved subjects and the consideration of different exposure sources, the Shenzhen study, although conducted with different methodologies, underlines the role of food as a major source of exposure to heavy metals in the population residing near the local SWI.

#### Workers

The exposure to Hg was evaluated in 35 workers from the same MSWI plant of Shenzhen investigated for the general population. The worker job tasks or activities were not described. Mean blood methylmercury, but not mean blood Hg, was higher than those of the general population living both near and far from the plant (Deng et al. 2016). No association between job tasks and exposure to metals is shown.

### Japan

#### General population

In Japan, there is a large number of incinerators (around 2000), that represent the major source of dioxins of the country. In 1997, a national survey on PCDD/Fs in emission gases from MSWIs showed that 50 out of the 1500 investigated SWIs emitted more than the national allowable level of 80 $ng/Nm^3$. Following these results, the Ministry of Health and Welfare organized a research to evaluate the health effects of chronic exposure to dioxins and its accumulation in SWI workers and in the general population living around plants.

In 1999–2000, a study was conducted on 240 breastfeeding mothers residing in Tokyo, where many industrial and municipal SWIs are present (the exact number was not reported in the paper). The association between the level of PCDD/Fs and CO-PCBs in breast milk and the distance of women's domicile from the nearest waste incinerator was evaluated by multivariate analysis. Age, smoking habit, consumption of fish and of vegetables from the own garden were considered as confounding factors. No significant association between dioxins levels in breast milk and proximity of the domicile to an incinerator was found (Tajimi et al. 2005). Among the confounding factors, only age and history of delivery were significant predictors of dioxins levels. No influence of the diet was observed on PCDD/F and CO-PCB levels. Several other factors, including the wind direction, the level of dioxin emitted from each incinerator, the level of environmental pollution of dioxins in air, soil, dust and water, and the average time the mothers stayed at home each day were not considered (Table 4).

Kitamura et al. reported dioxins concentrations in blood samples from 95 subjects living in Osaka within 2 km from incinerators that emitted slightly higher levels of dioxins than the allowed levels of 80 ng/Nm$^3$, 50 subjects living within 2 km from incinerators that emitted very high levels of dioxins (not reported), and of 80 controls living at least 5 km away from any incinerator. Higher PCDD/Fs levels (1.5-fold higher) were found in the group of 50 subjects than in the other groups, but no inferential analysis were performed and no confounding factors were considered in this study (Kitamura et al. 2001)(Table 4).

Takei et al. have reported dioxin concentrations in blood samples collected in the years 1999–2000 from 73 exposed and 47 non-exposed subjects living in the region of Kansai, Kanto, and Hugoku. Only descriptive analysis (mean values and standard deviation) of dioxins concentrations and immunological parameters were reported, showing no differences between groups (Takei et al. 2001).

Other studies conducted in Japan have some important limitations, which make it extremely difficult to draw any conclusions. Aozasa et al. measured blood dioxin level from only 13 residents near an incineration facility and analyzed the monthly variation of blood dioxin level in the three subjects with the higher baseline level (Aozasa et al. 2003). Likewise, Miyata et al. found very high blood dioxin levels (81 pgTEQ/g in men and 149 pgTEQ/g in women) in 17 residents near a MSWI (Miyata et al. 1998). Results of these studies are inconclusive, given the extremely low sample size and the absence of statistical analysis taking into account the confounding factors.

### Workers

At the end of the 90 s, the Ministry of Labor required, together with the closure of some incinerators, a biomonitoring evaluation of incinerator workers, because of the high levels of dioxin found in the exhaust gas emitted from the chimney of several incinerators (higher than the Japanese legal limit of 80 ng TEQ/m3). Most of the biomonitoring studies were performed by the Department of Environmental Health of the Osaka Prefecture, where the public concern was particularly high due to the closure of two incinerators, a MSWI (Bika Center) in 1997 and a HSWI in 2000. Studies were all performed in the years 1995–2002.

In Osaka Prefecture, the highest dioxin levels in serum have been reported in two cross-sectional studies, the first one including workers at Bika Center (TEQ of PCDD/Fs in serum samples of 96 workers, one year after the closure of the plant (mean 99.7 ± 135.5 pg/g lipid) (Kitamura et al. 2000), and the second one including workers from a MSWI (Toyono-gun Clean Center) (TEQ of PCDD/Fs in serum samples of 92 workers: mean 84.8 ± 130.2 pg/g lipid) (Takata 2003). These values were definitely higher than those measured in blood samples from the general population living in the same area (total PCDD/Fs and PCB TEQ level, mean 24.8 ± 11.9 pg/g lipid) (Kitamura et al. 2001). In the study at the Bika Center, some blood biochemistry data were also evaluated, showing a statistically significant positive correlation between dioxin levels and GGT, total protein, uric acid, and calcium at the univariate analysis. However, the correlation disappeared after performing a multivariate analysis adjusted for age, smoking status, and alcohol drinking. A small group of 16 subjects underwent to repeated health survey and chemical examinations from 2000 to 2007, showing that serum dioxin levels gradually decreased after the plant shutdown (Yamamoto et al. 2015).

Workers at the HSWI in Osaka, closed in 2000, have been also evaluated through a biomonitoring case-control study (Kumagai and Koda 2005). This is the only study on a HSWI in Japan, but the sample size represents a great limitation of this study and does not allow drawing any conclusions. Blood samples from only five workers were collected 1 and 16 months after the end of the occupational exposure, and were compared with five subjects of the general population matched for age. TEQ value of PCDD/Fs were particularly high 1 month after the closure of the plant (mean 49.1 pg/g lipid), but they remained lower than serum levels found in Bika Center workers. In comparison with controls, mean TEQ levels in workers were 2.7 and 1.6 times higher than the controls at the first and second-time point, respectively.

The other studies in the same area were performed on workers of operating MSWI.

Two studies characterized by a case-control design included overall 50 incinerator workers (30 workers at a continuously burning MSWI and 20 at an intermittently burning MSWI) and 50 controls taken from municipal government employees not occupationally exposed to dioxins (Kumagai et al. 2000, 2002). Serum dioxin values were similar between the two groups, with mean total TEQ values around 20/ pg/g lipid, therefore much lower than the Japanese studies presented previously. Considering the different congeners, only the levels of 1,2,3,4,6,7,8-Hp-CDF were significantly higher in workers than in controls (in both continuously and intermitting burning MSWI), showing a possible occupational exposure via inhalation of contaminated dust. This conclusion was confirmed by multiple regression analysis adjusted for smoking status, BMI and age, suggesting that serum concentrations of HpCDF increased with the duration of employment.

A cross-sectional study on 57 subjects employed in four different MSWIs located in the same area was conducted in years 2000–2001 to evaluate the effect of dioxin on the metabolism of estrogens and on DNA damage (Yoshida et al. 2005, 2006). Mean total TEQ value was 38.9 pg/g lipid, but no inferential analysis was possible for the lack of a control group. No clear evidence was found as regards the influence of dioxin exposure on the metabolism of estrogens (Yoshida et al. 2005) as only the distribution of 2- and 4-hydroxy estrogens, but not the total level of estrogens, was impacted by dioxin exposure. In addition, results of serum and urinary 8-OH-dG were inconclusive as a negative association between serum 8-OH-dG and dioxin level was found, presumably attributable to other confounding factors not adequately considered (Yoshida et al. 2006). These results did not confirm previous findings by the same authors showing that the level of urinary 8-OH-dG, measured in 81 workers in the same MSWIs, rose with increased duration of engagement in jobs with exposure to MSWI fly ash (Yoshida et al. 2003).

Lastly, a case-control study was carried out in 1995 by collecting hair from 68 MSWI workers and 64 controls from the general population. The mean TEQ values in hairs resulted definitely lower if compared to serum levels previously presented. The mean values in workers were 2.5 fold higher than in the general population, but, given that no confounding factors were considered, the results are inconclusive (Nakao et al. 2005).

## South Korea

### General population

In South Korea 32 MSWIs and about 1000 small and medium scale incinerators are operating (Park et al. 2014). Studies were mainly conducted in Seoul, or in Pyeongtaek. As plant location and study years are not always indicated, it is difficult to understand whether the same plants were studied repeatedly.

In Seoul, a study was carried out on a large population sample of 841 individual, living between 2006 and 2009 within 0.3 km from three MSWIs, and 105 controls. However, the recruitment scheme was not detailed. Metal concentrations (Pb, Cd, and Hg) in blood were analyzed. Confounder data were collected by questionnaire (sex, age, marital status, education level, residence duration, smoking habit, economic status). Furthermore, a personal attitude survey was conducted about the perceived damage due to the plant. No significant difference of heavy metal concentrations between exposed and controls was observed. Multiple regression analyses indicated associations of metal concentration and personal factors, although trends were inconsistent. Pb and Hg concentrations were slightly higher in males, Cd and Pb levels were to some extent higher in those with longer residence duration. Although the study was conducted on a large sample, the study group was unbalanced, as 80% of exposed subjects were female; moreover, the diet exposure was not assessed by the study (Lee et al. 2012). (Table 4)

In Seoul, a survey of PCDD/Fs and PCBs serum levels was carried out over a 10-years period (2001–2011). Overall, 769 volunteers living within 3 km from MSWI plants (number not indicated) and 112 controls (living >10 Km away from any plants) were included. Recruitment procedure and population characteristics (age group and sex distribution) were not provided. PCDD/F and PCB levels were not different between exposed and controls. Overall, no clear reduction of PCDD/Fs or PCBs across the study period was observed when all subjects were considered together. A slight trend toward reduction was observed only for older subjects (>55 years) (Park et al. 2014). No statistical analysis was done to assess the actual contribution of the SWI in determining the PCDD/F and PCB exposure in the study subjects. Although this study was conducted on a large sample size over a 10-year period, the major confounders (diet, alternative sources of exposure, socio-demographic characteristics) were not collected, so the reported results cannot be properly evaluated (Table 4).

A study in Seoul conducted in the year 2000–2006 reported no difference when comparing individual serum PCDD/Fs and metal concentrations of 131 volunteers living within 0.3 km from a MSWI with those of 27 controls. A correlation between age and the levels of all considered pollutants was found (Yang et al. 2007). The authors postulate an influence of food on dioxin and metal levels, but actually, no control for the diet was implemented in this study.

Other smaller studies (including 22 to 75 subjects) mainly regarded MSWIs or HSWIs in Seoul and a HSWI in Pyongtack and assessed PCDD/F and PCB concentrations. Neither differences in PCB nor in PCDD/F concentrations were observed for residents near MSWs in Seoul (Leem et al. 2003; Park et al. 2007, 2009, 2013) or in other, not specified, large cities (Moon et al. 2005) in comparison with far residents. As regards HSWI plants, PCDD/Fs levels were found significantly higher in 10 residents near HSWIs than in 7 controls in Seoul (Park et al. 2009). In Pyongtack, PCDD/F concentrations and malondialdehyde (MDA) levels, measured as oxidative stress marker, were reported significantly higher in residents near the local HSWI in comparison to residents near two MSWIs in Seoul (Leem et al. 2003). These findings were not supported by other studies (Park et al. 2004; Leem et al. 2006). PBDE levels, measured in 22 residents near MSWIs in Seoul were higher than those reported for other countries (Kim, Ikonomou et al. 2005). Due to the small sample size, these papers are indicative for local research but do not allow firm conclusions.

### Workers

A study on 73 MSWI workers and residents (769 living near and 112 living far) was carried out in Seoul in the period 2001 to 2011 to assess the exposure to PCDD/Fs and dioxin-like PCB (Park et al. 2014). PCDD/Fs and PCB in workers were not different from those measured in residents. No clear reduction over the 10-year study period was observed. An association between PCDD/Fs and PCBs and age was found. Besides age and sex stratification, no further covariates were considered. Diet information was not collected, and job task was not described.

Smaller studies, conducted in Seoul in the period 2001–2003 on MSWI workers, obtained analogs results: no significant differences in PCDD/F or PCB concentrations were found in studies conducted on 10 to 25 MSWI workers in comparison to near residents (Leem et al. 2003; Kim, Ikonomou et al. 2005; Park et al. 2007, 2009). Similar findings were reported for 11–28 workers from different MSWIs in large Korean cities (not better identified) (Moon et al. 2005; Park et al. 2013). However, PBDEs concentrations were higher in 13 MSWI workers than in residents and suggested a correlation with working at an electronic dismantling facility in the MSWI (Kim, Ikonomou et al. 2005).

As regards HSWI plants, PCDD/Fs concentrations were twice as high in 10 HSWI workers in Seoul compared to 10 residents, while no difference was found for PCB levels (Park et al. 2009). Higher PCDD/F or PCB levels were found also in 15 HSWI workers than in 15 population controls (Kim et al. 2001), in a case study on 3 workers and 2 controls (Kim, Lee, et al. 2005), and in a study on 23 workers (combining incinerator and industrial workers) (Kim et al. 2002). A sound confounder control was not carried out by these studies, mainly due to sample size constraints.

PAH exposure was assessed by measuring 1-OHPYR glucuronide (1-OHPYRG) in workers from industrial HSWI plants (Lee, Kang, et al. 2002; Lee, Lee, et al. 2002; Lee et al. 2003).

Confounding variables were collected by questionnaire. No significant difference in 1-OHPYRG levels was found between 38 exposed and 21 control workers, while smoking was positively associated with 1-OHPYRG levels. Glycophorin A (GPA) variant frequency increased with 1-OHPYRG levels; this association was stronger in individuals with GSTM1 genotype status (Lee, Kang, et al. 2002; Lee, Lee, et al. 2002; Lee et al. 2003)). Conversely, significant higher 1-OHPYRG levels in 29 exposed workers than in the 21 administrative workers were reported in another study, presumably on the same plant (Lee, Kang, et al. 2002; Lee, Lee, et al. 2002; Lee et al. 2003). Linear regression analysis indicated that 1-OHPYRG was associated with smoking and with the GSTM1 phenotype but not with occupational exposure. DNA adducts were related to age and smoking, but not to work exposure (Lee, Kang, et al. 2002; Lee, Lee, et al. 2002; Lee et al. 2003). No association with work exposure is shown.

In 28 hospital incineration workers, 1-OHPYRG levels were analyzed in relation to the work shift and presence of genetic polymorphism (GSTM1 and GSTT1). A questionnaire collected personal information, job history, smoking, alcohol, and use of protective gear. Pre-shift (Monday morning) levels of 1-OHPYRG were not different from post-shift (Friday evening) levels. A significant association with the number of cigarettes was found. No further analysis on collected confounding factors was mentioned. GSTM1 genotype had a significant effect on 1-OHPYRG, not observed for the GSTT1 genotype (Lee, Kang, et al. 2002; Lee, Lee, et al. 2002; Lee et al. 2003).

In 2002, the impact of PAH exposure on DNA damage was assessed by measuring PAH metabolites (1-OHPYR, 2-NAPOH) and various effect markers in workers from an SWI plant in Ansan (plant type not indicated). Confounding factors (smoking, drinking, age, and medication) were collected by questionnaire. Differences between workers and population controls (automobile emission inspectors and general population subjects) were assessed by *t*-test or ANOVA, regression analysis was not applied. (Sul et al. 2003; Oh et al. 2005). Urinary 1-OHPYR and 2-NAPOH levels were higher in SWI workers than in controls and they were twice as high in workers as in automobile emission inspectors. Furthermore, significant amounts of single-strand DNA breakage in T- and B-lymphocytes and in granulocytes was observed in SWI workers in comparison with controls, with B-lymphocytes showing the most significant differences (Sul et al. 2003; Oh et al. 2005). As regards genotoxic effect markers, DNA damage in mono- and polynuclear blood cells and spermatozoa characteristics (number and mobility) were significantly different between SWI workers and controls, whereas smoking did not exert significant effects on DNA damage. Immunotoxicity assessed by leukocyte sub-populations, plasma immunoglobulins and cytokines did not show significant difference with the exceptions of IL-4 levels, and the activation of B-cells (Sul et al. 2003; Oh et al. 2005).

## Taiwan

### General population

In the period 1999–2004, the Taiwan Environmental Protection Agency conducted a surveillance program, including up to 19 MSWIs in North Taiwan and 1708 individuals, in order to monitor periodically serum PCDD/F levels in the nearby residents. Plants had been operating for up to 10 years at the time of the study. Three polluted zones and one background zone were defined for each plant, based on the concentration plot of the air pollutants as established by a dispersion model of stack emission validated by ambient air samples collected in the study areas (Huang et al. 2007). Subject selection was based on the population distribution of age and gender in each administrative district to achieve 100 subjects for each plant, evenly distributed in the four zones. However, no power calculation was mentioned. The inclusion criteria were age in the 18 to 65 years range, not being occupationally exposed to PCDD/Fs, residing in the study area for at least 5 years and within a 5-km radius from the plants. Subjects were included on a voluntary base (Table 4).

Considering almost the whole sample (1658 residents), no difference in PCDD/Fs serum levels were observed although PCDD/F air levels resulted different among the zones. Moreover, serum PCDD/F concentrations were not correlated with ambient air levels and residence duration. Higher serum PCDD/F levels were observed in older subjects. The data analysis shown did not take in account the information collected on confounders (Huang et al. 2007). The impact of diet (vegetarianism and consumption of locally grown or bought food) on serum PCDD/F levels was assessed during the period 2000–2004 in the total study group (1708 subjects), showing that eating poultry and vegetables locally grown near the MSWIs contributed significantly to serum concentration of PCDD/Fs. Multivariate regression models adjusted for sex, age, local food consumption, and BMI showed that a vegetarian regime is protective against PCDD/F accumulation, and that eating locally produced animal and vegetable food is associated with PCDD/F serum levels (Chen, Su, and Lee 2006). These two large investigations confirmed the results of the earlier smaller investigations, involving 95 to 372 residents, that reported no difference in serum and air PCDD/Fs levels among the four exposure zones and a weak but positive association between PCDD/F levels and seafood and sea fish intake (Chen et al. 2003, 2004; Lee et al. 2005). Significantly higher PCDD/F concentrations in females and older residents were also observed (Chen et al. 2003).

Biomarkers of effect and health outcome were also studied in 1034 individuals recruited between 2000 and 2001. Multivariate regression analysis (adjusting for age, sex, BMI) indicated that glucose and GGT values were positively correlated with serum PCDD/Fs levels, suggesting a potential modulation of the liver function and the glucose production. No differences were observed regarding the disease status when adjusting for age, sex smoking status and BMI. No association between these biochemistry parameters and exposure parameters was shown. Diet information was not included in this analysis (Chen, Su, et al. 2006). Overall, given the large number of investigated subjects, the use of dispersion models to assess the resident exposure, the careful consideration of confounding factors, including diet, and the statistical analysis, the results of this study are particularly reliable and suggest that dioxin intake from inhalation of

MSWI emissions is not large enough to affect the body burden from these chemicals.

A smaller study was carried out to investigate PCDD/F and metal (K, Al, Pb, Hg, Fe, Zn, Cd and Cu) exposure in 68 subjects living within a 4-Km radius of a MSWI and an electric arc furnace. The study year is not reported. Dioxin profiles in individual blood samples, studied by principal, component analysis, matched more closely to MSWI emission than to the electric arc furnace emissions. PCDD/F and metal levels were not associated with BMI, age, and sex; diet habits were not controlled for (Chen et al. 2010). The limited sample size and methodical issues hamper to draw a conclusion from this study.

### *Workers*

A study in Taipei investigated PCDD/F levels in indoor air and in blood sample from 133 randomly selected male workers employed for at least six months in three different MSWIs operating since 1991, 1994, and 1998, respectively. The study year is not reported. Occupational history, smoking, diet, and current workplace activity were collected by questionnaire. A detailed time activity profile of the job task was obtained. The median WHO-TEQ levels were lower than those reported in previous studies conducted in other countries and not different among the plants. Significant differences were observed only for some dioxin congeners, not attributable to differences in job task, employment duration and time activity as assessed by adjusted linear regression models taking in account age, BMI, smoking status, and frequency of milk/fish/meat consumption (Hu et al. 2004). In the same workers, the impact of PCDD/F exposure on blood lipids and hepatic function (GGT, ALT, AST, total bilirubin) was assessed. Cholesterol values were significantly increased in workers with PCDD/Fs levels higher than 15.3 pg/TEQ/g lipid as confirmed by regression analysis adjusted for incinerator plant, age, body mass index, smoking, and alcohol. Altered liver enzymes were more prevalent in the high exposure group workers, however, the results of the adjusted regression analyses were not statistically significant, nor was the hypothesized interaction between PCDD/F exposure and hepatitis B infection (Hu et al. 2003).

In 2004, As and Pb body burden was analyzed in 122 MSWI workers within 10 h after their work shift and in 122 residents living nearby (Chao and Hwang 2005). Subjects were asked to refrain from seafood consumption prior to sampling. Confounders were collected by questionnaire (home characteristics, diet, health status, past and present work exposure). Blood Pb levels of all workers were within the permitted range (0.7–13.6 μg/L); no comparison between exposed and controls was performed. According to their job tasks, workers were classified into three groups of As exposure: direct, indirect, and any contact with the combustion process. Blood and urinary As concentrations were significantly higher in workers than in control residents, but most samples were below the limit of detection. In workers, 6 and 16% of samples were higher than permitted level for As in urine (62 μg/g creatinine) and blood (7 μg/L), respectively. Inconsistent differences were found among the three groups of workers, with workers with direct exposure showing the lowest values of As. The study, although conducted on a large sample size, is affected by a poor data analysis.

A smaller study investigated the impact of the annual maintenance work on 35 contract workers at four MSWIs. The study year was not reported. Serum PCDD/Fs levels were measured before and one month after the maintenance work. A significant increase in PCDD/Fs was observed; increase was higher in workers at the first experience and in those exposed to fly ash (Shih et al. 2006).

## Summary for each group of biomarkers

### *Dioxins, PCBs and other POPs*

Among the selected studies/papers, 57 measured PCDD/Fs, 35 measured PCBs and 10 measured MCP, PCP, HCB DDE, HCB and other chlorobenzenes, and PBDE in plasma. Overall, 35 papers focused on the general population (Table 2) and 30 on workers (Table 3), some studied both groups; eight large studies investigating the general population were included in Table 4. Besides blood, seven studies investigated dioxins also in breast milk, mainly in Spain and Portugal, in both cases with repeated sampling over time.

All the studies conducted on a large sample size on apparently modern MSWIs did not highlight differences in serum levels of PCDDs/Fs (Kitamura et al. 2001; Huang et al. 2007; Frery et al. 2007a, 2007b; Zubero et al. 2011; Park et al. 2014), and PCB (Frery et al. 2007b; Schroijen et al. 2008; Park et al. 2014) between exposed and non-exposed subjects. Regarding adolescents, PCB, HCB, and DDE serum levels were not different between exposed and controls (Schroijen et al. 2008). PCB levels in children living near a HSWI were not different from those of controls (Osius et al. 1999). Furthermore, no association was observed between PCDD/Fs or PCB in breast milk samples and the residence proximity to SWIs (Tajimi et al. 2005).

Studies assessing thoroughly diet habits reported that dioxin levels were related to the consumption of locally produced food (Chen, Su, and Lee 2006; Fierens et al. 2007; Zeghnoun et al. 2007; Frery et al. 2007a, 2007b) and/or to specific dietary regime (Chen et al. 2003; Chen, Su, and Lee 2006). However, no influence of the consumption of fish or home garden vegetables was evidenced in a Japanese study (Tajimi et al. 2005).

Small studies investigating repeatedly PCCD/Fs, PCB and PBDE in blood or breast milk reported a decreasing trend in subjects living close to a HSWI (Nadal et al. 2013; Schuhmacher et al. 2013), and a MSWI in Spain (Parera et al. 2013; Zubero et al. 2017).

Increased levels of serum PCDD/Fs were reported in studies conducted on limited sample size (<50 subjects) in which confounders, especially diet, were not fully characterized or taken into account properly (Staessen et al. 2001; Pirard et al. 2005; Park et al. 2009; Viel et al. 2011).

In the occupational setting, most studies were characterized by a small sample size. Studies with a larger sample size (>50 individuals) were conducted in Germany in the early '90 s (Angerer et al. 1992; Wrbitzky et al. 1996), Japan from

1997 to 2002 (Kitamura et al. 2001; Takata 2003; Yoshida et al. 2003, 2005, 2006; Nakao et al. 2005), South Korea in 2001–2011 (Park et al. 2014), and in Taiwan in the early 2000s (Hu et al. 2004). Two follow up studies were conducted in Spain on workers of a MSWI and a HSWI, starting at the beginning of the plant activities (Mari et al. 2013; Parera et al. 2013).

The earliest studies reported small, but not always consistent, increments for some blood PCB and urinary PCP congeners (Angerer et al. 1992; Wrbitzky et al. 1996). Moreover, studies conducted on workers from old MSWIs that emitted high levels of dioxins found elevated levels of blood PCDD/Fs in comparison to the general population (Kitamura et al. 2000; Takata 2003); this was evidenced also using hair as a matrix for dioxin assessment (Nakao et al. 2005).

More recent studies showed no difference in serum PCDD/Fs and dioxin-like PCBs between MSWI workers and the general population living near or away from the plant (Park et al. 2014), as shown also in studies conducted in plants complying with emission standards (Kumagai et al. 2000, 2002; Yoshida et al. 2005); moreover, determinants of exposure based on job characteristics could not explain the PCDD/F level (Hu et al. 2004).

A decreasing trend of PCDD/Fs in blood and an overall decrease, although fluctuating across the years, for HCB and PCB-congeners were reported in HSWI workers (Mari et al. 2007, 2013), whereas no clear change in PCDD/F levels over time was reported for MSWI workers (Gonzalez et al. 2000; Parera et al. 2013).

In conclusion, the majority of studies conducted on the general population indicates that living near an incinerator had no significant effect on dioxin levels measured in blood or breast milk samples. However, the long-term ingestion of food produced under the plume of SWI may increase the dioxin internal dose in these populations. In the occupational setting, studies reporting increased PCDD/F and PCB levels in workers were carried out before the year 2000 or on declared old plants not complying with standard emissions.

### Metals

Twenty-eight studies/papers evaluated the associations between biomarkers of metals and exposure to SWI emissions. Among them, 15 studies investigated only the general population (Table 2) and 13 studies investigated only the occupational scenario (Table 3); four studies investigated both groups (Table 2 and 3); seven large studies investigating the general population were included in Table 4.

As regards the large studies concerning the general population, the most investigated metals were Pb and Cd in blood (all studies), followed by Hg in blood/urine/hair, and Mn, Ni, and Cr in urine or blood. Other investigated metals were Cu, Zn, Sn, Tl, Be, As, and V. Only 2 studies reported positive results (Lee et al. 2012; Deng et al. 2016; Li et al. 2017), while 5 studies reported no differences between residents and controls or no association between biomarker levels and SWI emissions (Osius et al. 1999; Nadal et al. 2005; Reis et al. 2007a, 2007b, 2007c; Schroijen et al. 2008; Ferré-Huguet et al. 2009; Martorell et al. 2015; Gatti et al. 2017).

Among the studies highlighting some significant association, the Chinese study in Shenzhen underlines the role of the diet as a major route of exposure to metals for resident eating food grown in the SWI area (Deng et al. 2016; Li et al. 2017), while the Korean study in the Seoul area reports an association between blood Pb and Cd and longer residence duration (Lee et al. 2012).

A trend toward lower values was reported when the levels of biomarkers, measured periodically after some years of SWI operations, were compared with baseline levels (Nadal et al. 2005; Reis et al. 2007a, 2007b, 2007c; Ferré-Huguet et al. 2009; Martorell et al. 2015). The downward trend is supported also by a smaller study (Gonzalez et al. 2000).

Among the 13 studies focused on workers, the most investigated metals were Pb in blood (9 studies), Hg in blood/urine/hair (6 studies), and Cd in blood/urine (6 studies). Other investigated metals were Mn, Cr, Ni, As, V, Cu, Fe, and Zn. Eight studies reported higher levels of metals in workers when compared to controls or with pre-exposure status (Malkin et al. 1992; Wrbitzky et al. 1996; Kurttio et al. 1998; Hours et al. 2003; Maître et al. 2003; Chao and Hwang 2005; Wilhelm Filho et al. 2010; Dame et al. 2015) . However, the biomarker levels were in most cases within the range of the general population and well below the existing biological limit values. Four studies showed an increase of blood Pb (Malkin et al. 1992; Wrbitzky et al. 1996; Hours et al. 2003; Wilhelm Filho et al. 2010), in some cases related to the maintenance of the plant or cleaning of the oven. In two studies, an increase in biomarkers of Hg was found (Kurttio et al. 1998; Deng et al. 2016). An increase of As was reported in a French study (Maître et al. 2003) and in a Taiwanese study (Chao and Hwang 2005), but these studies were affected by methodological issues. In contrast, for SWI plants built in the nineties in Spain, and for which there was an assessment of baseline exposure and several follow-up surveys, the levels of biomarkers showed a tendency toward lower levels (Mari et al. 2013; Parera et al. 2013). No differences in metal exposure between workers and controls were reported also in studies carried out in Austria (Wultsch et al. 2011) and in the USA (Bresnitz et al. 1992).

Overall, increased levels of biomarkers of metals in association to SWI were seldom reported in the general population. Conversely, the majority of the studies found no association between SWI exposure and biomarkers of metals or even showed a tendency toward lower levels when baseline levels were compared to results of follow-up studies. In SWI workers, some increase in biomarkers of metals was reported, mostly associated with Pb exposure and old plants (exposure before the year 2000). Among recent studies, some increase in biomarkers was reported in developing countries.

### Polycyclic aromatic hydrocarbons

Among the selected studies/papers, only 10 evaluated the associations between PAH biomarkers and exposure to SWI emissions: three investigated the general population

(Table 2) and seven an occupational scenario (Table 3). Two large studies regarding the general population were included in Table 4.

For the general population, the FLEHS II study conducted on adolescents showed no increased PAH exposure as measured by 1-OHPYR in the exposed vs. the control group (Schroijen et al. 2008; Croes et al. 2009). On the contrary, the use of specific and sensitive biomarkers, such as urinary PAHs, showed a significant relationship between living near a SWI and exposure to non-carcinogenic PAHs such as fluorene, naphthalene, fluoranthene and pyrene (Gatti et al. 2017), confirming the results obtained in a pilot study (Ranzi et al. 2013); however, exposure levels were low and in the range of those of the general population.

As regarding occupational exposure, most studies/papers reported no increase of 1-OHPYR excretion in comparison with the general population (Wrbitzky et al. 1996; Lee, Lee, et al. 2002; Lee et al. 2003; Maître et al. 2003). A series of successive surveys performed on HSWI workers in Spain showed that 1-OHPYR levels were always below the detection limit (Mari et al. 2013). A certain increase in 1-OHPYR or 2-NAPOH excretion in SWI workers in comparison with workers performing other jobs was reported in a few studies (Angerer et al. 1992; Lee, Kang, et al. 2002; Sul et al. 2003; Oh et al. 2005), however, the biomarker values were always in the range of the general population and the increase was small and comparable to that associated with tobacco smoking.

In conclusion, some studies showed a limited increase in PAH biomarkers in association with SWI emissions. However, as not many studies evaluated this exposure both in general population and in workers, further research is necessary to confirm these results.

### *Volatile organic compounds*

Among the reviewed studies/papers, only seven evaluated the associations between BTEX biomarkers and exposure to SWI: three studies investigated the general population (Table 2) and four the occupational scenario (Table 3). Only one large study regarding the general population was included in Table 4.

An increase of *t,t*-MA and o-cresol was first reported among 42 Flemish adolescents residing near two shut down waste incinerators (Staessen et al. 2001), however, in a later and larger study, including 207 adolescents living in proximity of six operating SWIs, this was not confirmed (Schroijen et al. 2008). No association between BTEX exposure, evaluated by urinary BTEX, and SWI emission was reported also by a small recent Italian study including 65 subjects living near the local modern MSWI (Ranzi et al. 2013).

In occupational settings, an increased level of toluene in blood, but not of benzene, ethylbenzene, and xylene, was reported in waste incinerator workers in comparison with periphery workers and managers. However, the levels of all analytes never exceeded the existing German biological limit values and were within the range of the general population (Wrbitzky et al. 1996). Other occupational studies did not report such an increase (Angerer et al. 1992; Maître et al. 2003).

Altogether, it appears that the exposure to BTEX was associated only with old plants and with a small increase of biomarkers, whose levels were in the range of those reported for the general population.

### *Biomarkers of effects*

Twenty-nine studies/papers evaluated biomarkers of effect, eight of which investigated the general population (Table 2) and 15 SWI workers (Table 3). Three large studies regarding the general population were included in Table 4.

The FLEHS II study on adolescents revealed alterations in sexual maturation and/or in the levels of hormones in those residing around MSWIs compared to controls, confirming previously limited evidences (Staessen et al. 2001; Den Hond et al. 2002; Croes et al. 2009). A study on German children showed no association between SWI and thyroid hormones (Osius et al. 1999).

The FLEHS II study on the adult population reported significant higher values of micronuclei, DNA-strand breaks and oxidative DNA damage in those living near SWIs in comparison with the average values of the total study population (De Coster et al. 2008), suggesting that residence near waste incinerators might be associated with an increase in cancer risk.

In a large group of Taiwanese subjects, PCDD/F levels were found positively correlated with glucose levels and marginally with GGT values, suggesting an effect of dioxins on liver functions (Chen, Su, et al. 2006), but no association between these biochemistry parameters and the residence near SWI was shown.

In occupational settings, hematological changes were considered in two large studies conducted in France and Japan, showing levels in the normal range (Kitamura et al. 2001; Hours et al. 2003). ZPP, EPP, and beta-2-microglobulin, investigated in early studies conducted in the US as markers of effect following the exposure to Pb and Cd, revealed no alteration of these parameters (Bresnitz et al. 1992; Malkin et al. 1992; Hoffman et al. 1997). Inconclusive results were reported as regards urinary mutagenicity studied in MSWI workers in the US and in Japan (Scarlett et al. 1990; Ma et al. 1992; Yoshida et al. 2006). Oxidative stress, evaluated mainly as 8-oxo-dG in urine and blood lymphocytes, and with other biomarkers, showed some spurious associations with fly ash exposure, not confirmed in a successive investigation (Yoshida et al. 2003, 2006). DNA damage was studied by measuring different biomarkers in small studies in South Korea and in Austria, that reported no effect of job exposure on the levels of DNA adducts (Lee, Kang, et al. 2002), DNA migration, and MN frequencies (Wultsch et al. 2011). However, another small Korean study reported increased levels of DNA damage in T- and B-lymphocytes and in the spermatozoa of SWI workers; moreover, the number of sperms was lower in the SWI workers than in controls (Sul et al. 2003; Oh et al. 2005).

In conclusion, some studies suggest that emissions of SWIs may cause measurable biological effects, especially as regards the general population. However, these effects could be associated only in part with SWI pollutants, as most of the biomarkers are not specific. Moreover, a plethora of different effect biomarkers has been investigated in a very limited number of studies, so the reported effects are not supported by independent studies.

## Conclusions

Several biological monitoring studies have been conducted in the last 30 years, both in the general population and in SWI workers, to investigate the exposure and the health effects associated with SWIs. In some cases, long-term studies, that began before the start of the SWI operations and went on with periodic monitoring programs, were performed.

The systematic review of peer-reviewed literature of biological monitoring studies led to finally select and include 132 papers in this work, corresponding to about 80 studies. The majority of them were performed in the decade 2001–2010, with a decreasing number in the following years.

The levels of the studied biomarkers in the general population living near modern SWI were, in most studies, in the range of the reference values, showing no or very scarce impact of SWI emissions on the internal dose of the considered pollutants and on their effects. Similarly, in SWI workers biomarkers of exposure and effect seldom exceeded the reference values and were always within the biological limit values for occupational settings. Overall, results suggest a low contribution, if any, from SWI to the internal dose/early-biological effects of the investigated toxicants.

However, it is necessary to highlight that several pitfalls affected many of the reviewed studies. Therefore, future investigations in the field need to address issues associated with a proper recruitment of study subjects, a careful collection of individual characteristics and a thoughtful personal exposure assessment. Moreover, in order to explain biomarkers variability, taking into consideration the relevant above-mentioned covariates, an adequate sample size and a suitable statistical analysis need to be implemented.

Attention must be deserved to the participant selection that should be achieved with a randomized design, in order to get a sample representative of the exposed population, rather than on a volunteer recruitment. The exposure assessment to SWI emissions should be based on dispersion models integrating the information on atmospheric dispersions of the SWI plume rather than on the distance of the study subject's residence from the incinerator. The duration of residence of the exposed individuals should be carefully assessed, especially for those pollutants that accumulate in the living organisms, such as PCDD/Fs and PCB. A full characterization of personal exposure, including diet, smoking and other personal habits, medication, characteristics of the residence, such as the heating system, rural/urban location, distance from the main roads, traffic near home, commuting means, time spent in traffic, occupational exposure, recreational use of chemicals, car fueling, exposure to open fires, and presence of industrial emissions in the residence/working area, should be performed.

Among possible limitations of this review, there is the exclusion of papers not published in the scientific journals, such as gray literature and/or agency reports. We privileged the choice of peer-reviewed publications that were retrieved in public databases with a reproducible and easy to update methodology; moreover, the analysis of these papers could be done using a standardized tool, that is the STROBE-ME list. Another limitation is associated with grouping papers according to studies. While this is very useful to reflect the initiatives taken in this field, the information suitable to perform such association was not always available even after a careful screening of papers; this might have led, in a few cases, to incomplete or even wrong, grouping. Finally, another limitation is that the general conclusion on the limited impact of SWI on biomarkers of exposure and early effect is based on studies mainly conducted in Western and high-income Eastern countries, and on a limited number of biomarkers. In these countries the developed legislation body and the advanced environmental protection policy, have progressively improved SWI technologies, with reduction of emissions and a consequent beneficial impact on the general and working environment. Different situations may be foreseen in low-income countries where biomonitoring studies are desirable.

Future studies in this field should consider new biomonitoring approaches to enlarge the panel of study pollutants, including mixtures, and to investigate new biological effects. New and powerful technologies give the opportunities to include the application of omics techniques, such as metabolomics and methylomics. Moreover, the experience done so far, and reviewed in this work, stresses the importance of a proper study design to achieve results useful to answer questions over the health sustainability of the incineration process and to offer stakeholders useful tools to address environmental policies.

## Acknowledgments

The authors wish to thank the Library staff for their valuable help in defining the research string; the kind support provided by Dr. Gianfranco Frigerio in imputing the EndNote references is also acknowledged. The authors also thank Dr Roger O. McClellan and the anonymous reviewers for the valuable feedback received, which helped the authors to improve this article.

## Declaration of interest

The employment affiliations of the authors are shown on the cover page. The institutions with which the authors are affiliated are public health bodies and traditional academies. All authors regularly conduct research with the local, regional, and national government, and with academia. None of the authors has appeared in any legal or regulatory proceedings within the past 5 years related to the contents of the paper nor have been engaged to make such appearances in the future. The paper has not been reviewed by either in-house or outside legal counsel. LC, PB, and SF conducted a biomonitoring study funded by the local public health service in the frame of the authorization for the upgrade of the local SWI (resolution no. 74, 02/02/2007). The review, synthesis, and conclusions reported in this paper are the exclusive professional work product of the four authors and may not necessarily represent the views of their employers.

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## References

ACGIH. 2017. TLVs and BEIs based on the documentation of the threshold limit values for chemical substances and physical agents and biological indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists (ACGIH).

Agramunt CM, Domingo JL, Domingo A, Corbella J. 2003. Monitoring internal exposure to metals and organic substances in workers at a hazardous waste incinerator after 3 years of operation. Toxicol Lett. 146:83–91.

Agramunt MC, Domingo JL, Schuhmacher M, Gomez M, Llobet JM, Mueller L. 2002. Biological monitoring of organic substances in workers at a hazardous waste incinerator of Catalonia, Spain. Organohalogen Compd. 55:263–266.

Agramunt MC, Schuhmacher M, Hernandez JM, Domingo JL. 2005. Levels of dioxins and furans in plasma of nonoccupationally exposed subjects living near a hazardous waste incinerator. J Expo Sci Environ Epidemiol. 15:29–34.

Angerer J, Heinzow B, Reimann DO, Knorz W, Lehnert G. 1992. Internal exposure to organic substances in a municipal waste incinerator. Int Arch Occup Environ Heath. 64:265–273.

Aozasa O, Ohta S, Nakao T, Miyata H, Mochizuki A, Fujimine Y, Nomura T. 2003. Monthly variation in blood dioxin level, characteristics of isomer composition, and isomer changes in residents near an incineration facility. Bull Environ Contam Toxicol. 70:660–667.

Ardévol E, Minguillón C, Garcia G, Serra ME, Gonzalez CA, Alvarez L, Eritja R, Lafuente A. 1999. Environmental tobacco smoke interference in the assessment of the health impact of a municipal waste incinerator on children through urinary thioether assay. Public Health. 113:295–298.

Ashworth DC, Elliott P, Toledano MB. 2014. Waste incineration and adverse birth and neonatal outcomes: a systematic review. Environ Int. 69:120–132.

Bocio A, Domingo JL, Garcia F, Schuhmacher M, Llobet JM. 2004. Monitoring dioxins and furans in subjects living in the vicinity of a hazardous waste incinerator after 4 years of operation. Organohalogen Compd. 66:2507–2512.

Bresnitz EA, Roseman J, Becker D, Gracely E. 1992. Morbidity among municipal waste incinerator workers. Am J Ind Med. 22:363–378.

Calheiros JM, Coutinho M, Borrego C, Santos R, Papke O. 2002. PCDD/PCDF levels in human blood and breast milk in the region of Oporto, Portugal. Organohalogen Compd. 55:279–282.

Campo L, Rossella F, Pavanello S, Mielzynska D, Siwinska E, Kapka L, Bertazzi PA, Fustinoni S. 2010. Urinary profiles to assess polycyclic aromatic hydrocarbons exposure in coke-oven workers. Toxicol Lett. 192:72–78.

Chao CL, Hwang KC. 2005. Arsenic burden survey among refuse incinerator workers. J Postgrad Med. 51:98–103.

Chen HL, Lee CC, Liao PC, Guo YL, Chen CH, Su HJ. 2003. Associations between dietary intake and serum polychlorinated dibenzo-p-dioxin and dibenzofuran (PCDD/F) levels in Taiwanese. Environ Res. 91:172–178.

Chen YM, Lin YC, Wu TY, Chang-Chien GP, Ma WF. 2010. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) and trace metals in the blood of nonoccupationally exposed residents living in the vicinity of a municipal solid waste incinerator and electric arc furnace. J Air Waste Manag Assoc. 60:731–740.

Chen HL, Su HJ, Lee CC. 2006. Patterns of serum PCDD/Fs affected by vegetarian regime and consumption of local food for residents living near municipal waste incinerators from Taiwan. Environ Int. 32:650.

Chen HL, Su HJ, Guo YL, Liao PC, Hung CF, Lee CC. 2006. Biochemistry examinations and health disorder evaluation of Taiwanese living near incinerators and with low serum PCDD/Fs levels. Sci Total Environ. 366:538–548.

Chen HL, Su HJ, Liao PC, Chen CH, Lee CC. 2004. Serum PCDD/F concentration distribution in residents living in the vicinity of an incinerator and its association with predicted ambient dioxin exposure. Chemosphere. 54:1421–1429.

Chovancová J, Čonka K, Fabišiková A, Sejáková ZS, Dömötörová M, Drobná B, Wimmerová S. 2012. PCDD/PCDF, dl-PCB and PBDE serum levels of Slovak general population. Chemosphere. 88:1383–1389.

Croes K, Baeyens W, Bruckers L, Den Hond E, Koppen G, Nelen V, Van de Mieroop E, Keune H, Dhooge W, Schoeters G, et al. 2009. Hormone levels and sexual development in Flemish adolescents residing in areas differing in pollution pressure. Int J Hyg Environ Health. 212:612–625.

Dame ZT, Aziat F, Mandal R, Krishnamurthy R, Bouatra S, Borzouie S, Guo AC, Sajed T, Deng L, Lin H, et al. 2015. The human saliva metabolome. Metabolomics. 11:1864–1883.

De Coster S, Koppen G, Bracke M, Schroijen C, Den Hond E, Nelen V, Van de Mieroop E, Bruckers L, Bilau M, Baeyens W, et al. 2008. Pollutant effects on genotoxic parameters and tumor-associated protein levels in adults: a cross sectional study. Environ Health. 7:26.

De Felip E, Abballe A, Casalino F, di Domenico A, Domenici P, Iacovella N, Ingelido AM, Pretolani E, Spagnesi M. 2008. Serum levels of PCDDs, PCDFs and PCBs in non-occupationally exposed population groups living near two incineration plants in Tuscany, Italy. Chemosphere. 72:25–33.

Deml E, Mangelsdorf I, Greim H. 1996. Chlorinated dibenzodioxins and dibenzofurans (PCDD/F) in blood and human milk of non occupationally exposed persons living in the vicinity of a municipal waste incinerator. Chemosphere. 33:1941–1950.

Den Hond E, Roels HA, Hoppenbrouwers K, Nawrot T, Thijs L, Vandermeulen C, Winneke G, Vanderschueren D, Staessen JA. 2002. Sexual maturation in relation to polychlorinated aromatic hydrocarbons: Sharpe and Skakkebaek's hypothesis revisited. Environ Health Perspect. 110:771–776.

Deng C, Xie H, Ye X, Zhang H, Liu M, Tong Y, Ou L, Yuan W, Zhang W, Wang X. 2016. Mercury risk assessment combining internal and external exposure methods for a population living near a municipal solid waste incinerator. Environ Pollut. 219:1060–1068.

Domingo JL. 2010. Influence of cooking processes on the concentrations of toxic metals and various organic environmental pollutants in food: a review of the published literature. Crit Rev Food Sci Nutr. 51:29–37.

European Commission. 2010. Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control). Brussels, Belgium: European Commission.

Evans RG, Shadel BN, Roberts DW, Clardy S, Jordan-Izaguirre D, Patterson DG, Needham LL. 2000. Dioxin incinerator emissions exposure study Times Beach, Missouri. Chemosphere. 40:1063–1074.

Ferré-Huguet N, Nadal M, Schuhmacher M, Domingo JL. 2009. Monitoring metals in blood and hair of the population living near a hazardous waste incinerator: temporal trend. Biol Trace Elem Res. 128:191–199.

Fierens S, Eppe G, Focant JF, Heilier JF, De Pauw E, Bernard A. 2006. Five year follow-up to dioxin and PCB body burden of residents living in the vicinity of a MSWI in Wallonia, Belgium. Organohalogen Compd. 68:468–471.

Fierens S, Mairesse H, Heilier JF, Focant JF, Eppe G, De Pauw E, Bernard A. 2007. Impact of iron and steel industry and waste incinerators on human exposure to dioxins, PCBs, and heavy metals: results of a cross-sectional study in Belgium. J Toxicol Environ Health A. 70:222–226.

Fierens S, Mairesse H, Hermans C, Bernard A, Eppe G, Focant JF, De Pauw E. 2003. Dioxin accumulation in residents around incinerators. J Toxicol Environ Health A. 66:1287–1293.

Franchini M, Rial, E. Buiatti M, Bianchi F. 2004. Health effects of exposure to waste incinerator emissions:a review of epidemiological studies. Ann Ist Super Sanita. 40:101–115.

Frery N, Zeghnoun A, Sarter H, Volatier JL, Falq G, Pascal M, Grange D, Schmitt M, Berat B, Fabre P, et al. 2007a. Confounding factors influence serum dioxin concentrations in the French dioxin and incinerators study. Organohalogen Compd. 69:278/1–278/4.

Frery N, Zeghnoun A, Sarter H, Volatier JL, Falq G, Pascal M, Grange D, Schmitt M, Berat B, Fabre P, et al. 2007b. Exposure factors influencing serum dioxin concentrations in the French dioxin and incinerators study. Organohalogen Compd. 69:280/1–280/4.

Fustinoni S, Consonni D, Campo L, Buratti M, Colombi A, Pesatori AC, Bonzini M, Bertazzi PA, Foà V, Garte S, et al. 2005. Monitoring low benzene exposure: comparative evaluation of urinary biomarkers, influence of cigarette smoking, and genetic polymorphisms. Cancer Epidemiol Biomarkers Prev. 14:2237–2244.

Fustinoni S, Rossella F, Campo L, Mercadante R, Bertazzi PA. 2010. Urinary BTEX, MTBE and naphthalene as biomarkers to gain environmental exposure profiles of the general population. Sci Total Environ. 408:2840–2849.

Gallo V, Egger M, McCormack V, Farmer PB, Ioannidis JP, Kirsch-Volders M, Matullo G, Phillips DH, Schoket B, Stromberg U, et al. 2012. STrengthening the Reporting of OBservational studies in Epidemiology: Molecular Epidemiology STROBE-ME. An extension of the STROBE statement. J Epidemiol Community Health. 66:844–854.

Gatti MG, Bechtold P, Campo L, Barbieri G, Quattrini G, Ranzi A, Sucato S, Olgiati L, Polledri E, Romolo M, et al. 2017. Human biomonitoring of polycyclic aromatic hydrocarbonsand metals in the general population residing near the municipal solid waste incinerator of Modena, Italy. Chemosphere. 186:546–557.

Gonzalez CA, Kogevinas M, Gadea E, Huici A, Bosch A, Bleda MJ, Päpke O. 2000. Biomonitoring study of people living near or working at a municipal solid-waste incinerator before and after two years of operation. Arch Environ Health. 55:259–267.

González N, Marquès M, Nadal M, Domingo JL. 2019. Occurrence of environmental pollutants in foodstuffs: a review of organic vs. conventional food. Food Chem Toxicol. 125:370–375.

Grover PL. 1986. Pathways involved in the metabolism and activation of polycyclic hydrocarbons. Xenobiotica. 16:915–931.

Hoffman BH, Tuomanen B, Price R, Beaulieu HJ. 1997. Biological monitoring of employees with potential exposures to inorganic lead and cadmium at municipal solid waste resource recovery, or trash-to- energy, facilities. Appl Occup Environ Hyg.12:470–479.

Hours M, Anzivino-Viricel L, Maitre A, Perdrix A, Perrodin Y, Charbotel B, Bergeret A. 2003. Morbidity among municipal waste incinerator workers: a cross-sectional study. Int Arch Occup Environ Health. 76: 467–472.

Hu SW, Chang Chien GP, Chan CC. 2004. PCDD/Fs levels in indoor environments and blood of workers of three municipal waste incinerators in Taiwan. Chemosphere. 55:611–620.

Hu SW, Cheng TJ, Chang Chien GP, Chan CC. 2003. Association between dioxins/furans exposures and incinerator workers' hepatic function and blood lipids. J Occup Environ Med. 45:601–608.

Huang HY, Jeng TY, Lin YC, Ma YC, Kuo CP, Sung FC. 2007. Serum dioxin levels in residents living in the vicinity of municipal waste incinerators in Taiwan. Inhal Toxicol. 19:399–403.

IARC. 2004. Tobacco smoke and involuntary smoking. IARC Monographs on the evaluation of carcinogenic risks to humans. Lyon, France: International Agency for Research on Cancer (IARC).

IARC. 2010. Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol 92. Lyon, France: International Agency for Reaserch on Cancer (IARC).

IARC. 2012. A review of human carcinogens. Chemical agents and related occupations. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 100F. Lyon, France: International Agency for Research on Cancer (IARC).

IARC. 2014. Diesel and gasoline engine exhausts and some nitroarenes. IARC Monographs on the evaluation of carcinogenic risks to humans. Lyon, France: International Agency for Research on Cancer.

IARC. 2016. Polychlorinated biphenyls and polybrominated biphenyls. IARC Monographs on the evaluation of carcinogenic risks to humans, Vol 107. Lyon, France: International Agency for Research on Cancer (IARC).

Kim HS, Kim BH, Lee SJ, Chang YS. 2002. Levels of PCDD/Fs and dioxin-like PCBs in the blood of Korean workers and residents. Organohalogen Compd. 58:257–260.

Kim BH, Ikonomou MG, Lee SJ, Kim HS, Chang YS. 2005. Concentrations of polybrominated diphenyl ethers, polychlorinated dibenzo-p-dioxins and dibenzofurans, and polychlorinated biphenyls in human blood samples from Korea. Sci Total Environ. 336:45–56.

Kim BH, Lee SJ, Mun SJ, Chang YS. 2005. A case study of dioxin monitoring in and around an industrial waste incinerator in Korea. Chemosphere. 58:1589–1599.

Kim Y, Yang SH, Kim M, Shin DC. 2001. PCDD and PCDF exposures in workers and controls living near an industrial waste incinerator. Chemosphere. 43:985.

Kitamura K, Kikuchi Y, Watanabe S, Waechter G, Sakurai H, Takada T. 2000. Health effects of chronic exposure to polychlorinated dibenzo-P-dioxins (PCDD), dibenzofurans (PCDF) and coplanar PCB (Co-PCB) of municipal waste incinerator workers. J Epidemiol. 10:262–270.

Kitamura K, Yoshikawa K, Iwama M, Nagao M. 2001. Justification of measurement of eight congeners levels instead of twenty congeners of dioxins for mass screening of human exposure. J Toxicol Sci. 26: 163–168.

Kontsas H, Pekari K. 2003. Determination of polychlorinated biphenyls in serum using gas chromatography-mass spectrometry with negative chemical ionization for exposure estimation. J Chromatogr B Analyt Technol Biomed Life Sci. 791:117–125.

Kumagai S, Koda S. 2005. Polychlorinated dibenzo-p-dioxin and dibenzofuran concentrations in serum samples of workers at an infectious waste incineration plant in Japan. J Occup Environ Hyg. 2:120–125.

Kumagai S, Koda S, Miyakita T, Ueno M. 2002. Polychlorinated dibenzo-p-dioxin and dibenzofuran concentrations in serum samples of workers at intermittently burning municipal waste incinerators in Japan. Occup Environ Med. 59:362–368.

Kumagai S, Koda S, Miyakita T, Yamaguchi H, Katagi K, Yasuda N. 2000. Polychlorinated dibenzo-p-dioxin and dibenzofuran concentrations in the serum samples of workers at continuously burning municipal waste incinerators in Japan. Occup Environ Med. 57:204–210.

Kurttio P, Pekkanen J, Alfthan G, Paunio M, Jaakkola JJ, Heinonen OP. 1998. Increased mercury exposure in inhabitants living in the vicinity of a hazardous waste incinerator: a 10-year follow-up. Arch Environ Health. 53:129–137.

Lee CC, Chen HL, Su HJ, Guo YL, Liao PC. 2005. Evaluation of PCDD/Fs patterns emitted from incinerator via direct ambient sampling and indirect serum levels assessment of Taiwanese. Chemosphere. 59: 1465–1474.

Lee K-H, Cho S-H, Hong Y-C, Lee K-H, Kwan H-J, Choi I, Kang D. 2003. Urinary PAH metabolites influenced by genetic polymorphisms of GSTM1 in male hospital incinerator workers. J Occup Health. 45: 168–171.

Lee J, Kang D, Lee KH, Ichiba M, Zhang J, Tomokuni K, Hwang ES, Park CG, Ha M, Kim S, et al. 2002. Influence of GSTM1 genotype on association between aromatic DNA adducts and urinary PAH metabolites in incineration workers. Mutat Res. 514:213–221.

Lee KH, Lee J, Ha M, Choi JW, Cho SH, Hwang ES, Park CG, Strickland PT, Hirvonen A, Kang D. 2002. Influence of polymorphism of GSTM1 gene on association between glycophorin a mutant frequency and urinary PAH metabolites in incineration workers. J Toxicol Environ Health A. 65:355–363.

Lee CS, Lim YW, Kim HH, Yang JY, Shin DC. 2012. Exposure to heavy metals in blood and risk perception of the population living in the vicinity of municipal waste incinerators in Korea. Environ Sci Pollut Res. 19:1629–1639.

Leem JH, Hong YC, Lee KH, Kwon HJ, Chang YS, Jang JY. 2003. Health survey on workers and residents near the municipal waste and industrial waste incinerators in Korea. Ind Health. 41:181–188.

Leem JH, Lee DS, Kim J. 2006. Risk factors affecting blood PCDDs and PCDFs in residents living near an industrial incinerator in Korea. Arch Environ Contam Toxicol. 51:478–484.

Li T, Wan Y, Ben Y, Fan S, Hu J. 2017. Relative importance of different exposure routes of heavy metals for humans living near a municipal solid waste incinerator. Environ Pollut. 226:385–393.

Liu A, Ren WY, Lin F, Wang J-Y. 2015. A review of municipal solid waste environmental standards with a focus on incinerator residues. Int J Sustain Built Environ. 4:165–188.

Luotamo M, Patterson DG, Jr, Needham LL, Aitio A. 1993a. Concentrations of PCB congeners in sera from workers with past and present exposure. Chemosphere. 27:171–177.

Luotamo M, Patterson DG, Jr., Needham LL, Aitio A. 1993b. Concentrations of PCDDs, PCDFs and PCBs in sera from workers with past and present exposure. Organohalogen Compd. 13:9–12.

Ma XF, Babish JG, Scarlett JM, Gutenmann WH, Lisk DJ. 1992. Mutagens in urine sampled repetitively from municipal refuse incinerator workers and water treatment workers. J Toxicol Environ Health. 37:483–494.

Maître A, Collot-Fertey D, Anzivino L, Marques M, Hours M, Stoklov M. 2003. Municipal waste incinerators: air and biological monitoring of workers for exposure to particles, metals, and organic compounds. Occup Environ Med. 60:563–569.

Malkin R, Brandt-Rauf P, Graziano J, Parides M. 1992. Blood lead levels in incinerator workers. Environ Res. 59:265–270.

Mari M, Borrajo MA, Schuhmacher M, Domingo JL. 2007. Monitoring PCDD/Fs and other organic substances in workers of a hazardous waste incinerator: a case study. Chemosphere. 67:574–581.

Mari M, Nadal M, Schuhmacher M, Domingo JL. 2013. Body burden monitoring of dioxins and other organic substances in workers at a hazardous waste incinerator. Int J Hyg Environ Health. 216:728–734.

Mari M, Schuhmacher M, Domingo JL. 2009. Levels of metals and organic substances in workers at a hazardous waste incinerator: a follow-up study. Int Arch Occup Environ Health. 82:519–528.

Martorell I, Nadal M, Vilavert L, Garcia F, Schuhmacher M, Domingo JL. 2015. Concentrations of trace elements in the hair of children living near a hazardous waste incinerator in Catalonia, Spain. TE Electrolytes. 32:43–51.

Miyata H, Kuriyama S, Nakao T, Aozasa O, Ohta S. 1998. Contamination levels of PCDDs, PCDFs, and non-ortho coplanar PCBs in blood samples collected from residents in high cancer-causing area close to batch-type municipal solid waste incinerator in Japan. Organohalogen Compd. 38:143–146.

Moon CS, Chang YS, Kim BH, Shin D, Ikeda M. 2005. Evaluation of serum dioxin congeners among residents near continuously burning municipal solid waste incinerators in Korea. Int Arch Occup Environ Health. 78:205–210.

Nadal M, Bocio A, Schuhmacher M, Domingo JL. 2005. Monitoring metals in the population living in the vicinity of a hazardous waste incinerator: levels in hair of school children. Biol Trace Elem. 104:203–213.

Nadal M, Fàbrega F, Schuhmacher M, Domingo JL. 2013. PCDD/Fs in plasma of individuals living near a hazardous waste incinerator. A comparison of measured levels and estimated concentrations by PBPK modeling. Environ Sci Technol. 47:5971–5978.

Nadal M, Perelló G, Schuhmacher M, Cid J, Domingo JL. 2008. Concentrations of PCDD/PCDFs in plasma of subjects living in the vicinity of a hazardous waste incinerator: follow-up and modeling validation. Chemosphere. 73:901.

Nakao T, Aozasa O, Ohta S, Miyata H. 2005. Survey of human exposure to PCDDs, PCDFs, and coplanar PCBs using hair as an indicator. Arch Environ Contam Toxicol. 49:124–130.

National Research Council. 2010. Waste incineration and public health. Committee on Health Effects of Waste Incineration, Board on Environmental Studies and Toxicology, Commission on Life Sciences. Washington, D.C: National Academy Press.

Nawrot TS, Staessen JA, Den Hond EM, Koppen G, Schoeters G, Fagard R, Thijs L, Winneke G, Roels HA. 2002. Host and environmental determinants of polychlorinated aromatic hydrocarbons in serum of adolescents. Environ Health Perspect. 110:583–589.

Nordberg GF, Fowler BA, Nordberg M. 2014. Handbook on the toxicology of metals. 4th ed. Cambridge, MA, USA: Academic Press.

Oh E, Lee E, Im H, Kang HS, Jung WW, Won NH, Kim EM, Sul D. 2005. Evaluation of immuno- and reproductive toxicities and association between immunotoxicological and genotoxicological parameters in waste incineration workers. Toxicology. 210:65–80.

Osius N, Karmaus W, Kruse H, Witten J. 1999. Exposure to polychlorinated biphenyls and levels of thyroid hormones in children. Environ Health Perspect. 107:843–849.

Päpke O, Ball M, Lis A. 1993. Potential occupational exposure of municipal waste incinerator workers with PCDD/PCDF. Chemosphere. 27:203–209.

Päpke O, Ball M, Lis A, Menzel HM, Murzen R, Turcer E, Bolm-Audorff U. 1994. Occupational exposure of chemical waste incinerators workers to PCDD/PCDF. Organohalogen Compd. 21:105–110.

Parera J, Serra-Prat M, Palomera E, Mattioli L, Abalos M, Rivera J, Abad E. 2013. Biological monitoring of PCDD/Fs and PCBs in the City of Mataró. A population-based cohort study (1995-2012). Sci Total Environ. 461–462:612–617.

Park H, Ikonomou MG, Kim HS, Choi JW, Chang YS. 2009. Dioxin and dioxin-like PCB profiles in the serum of industrial and municipal waste incinerator workers in Korea. Environ Int. 35:580–587.

Park H, Kim J, Chang YS. 2013. Prevalence of low chlorinated dibenzo-p-dioxin/dibenzofurans in human serum. Chemosphere. 90:1658–1663.

Park S, Kim SJ, Kim KS, Lee DS, Kim JG. 2004. Influence of an industrial waste incinerator as assessed by the levels and congener patterns of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans. Environ Sci Technol. 38:3820–3826.

Park H, Lee SJ, Kang JH, Chang YS. 2007. Congener-specific approach to human PCB concentrations by serum analysis. Chemosphere. 68: 1699–1706.

Park H, Park E, Chang YS. 2014. Ten-year time trend of dioxins in human serum obtained from metropolitan populations in Seoul, Korea. Sci Total Environ. 470–471:1338–1345.

Pirard C, Eppe G, Massart AC, Fierens S, De Pauw E, Focant JF. 2005. Environmental and human impact of an old-timer incinerator in terms of dioxin and PCB level: a case study. Environ Sci Technol. 39: 4721–4728.

Porta D, Milani S, Lazzarino AI, Perucci CA, Forastiere F. 2009. Systematic review of epidemiological studies on health effects associated with management of solid waste. Environ Health. 8:60.

Possamai FP, Avila S, Budni P, Backes P, Parisotto EB, Rizelio VM, Torres MA, Colepicolo P, Wilhelm Filho D. 2009. Occupational airborne contamination in South Brazil: 2. Oxidative stress detected in the blood of workers of incineration of hospital residues. Ecotoxicology. 18:1158–1164.

Raemdonck A, Koppen G, Bilau M, Willems JL. 2006. Exposure of maintenance workers to dioxin-like contaminants during the temporary shutdown of a municipal domestic solid waste incinerator: a case series. Arch Environ Occup Health. 61:115–121.

Ranzi A, Fustinoni S, Erspamer L, Campo L, Gatti MG, Bechtold P, Bonassi S, Trenti T, Goldoni CA, Bertazzi PA, et al. 2013. Biomonitoring of the general population living near a modern solid waste incinerator: a pilot study in Modena, Italy. Environ Int. 61:88–97.

Rappe C, Lindström G, Hansson M, Andersson K. 1992. Levels of PCDDs and PCDFs in cow's milk and in worker's blood collected in connection with a hazardous waste incinerator in Sweden. Organohalogen Compd. 9:199–202.

Reis MF, Miguel JP, Pissarra MI, Sampaio C, Calheiros J. 2002. Infant exposure to PCDD/Fs in Portugal: first results from an environmental health survey program near Lisbon. Organohalogen Compd. 55:247–250.

Reis MF, Miguel JP, Sampaio C, Aguiar P, Melim JM, Päpke O. 2007. Determinants of dioxins and furans in blood of non-occupationally exposed populations living near Portuguese solid waste incinerators. Chemosphere. 67:S224–S30.

Reis MF, Miguel JP, Sampaio C, Melim JM, Aguiar P. 2004. First results from dioxins and dioxin-like compounds in the population from Madeira Island, Portugal. Part 1 - biomonitoring in blood of the general population living near to a solid waste incinerator. Organohalogen Compd. 66:2702–2708.

Reis MF, Sampaio C, Aguiar P, Matos P, Paepke P, Pereira MJ. 2005. Dioxin contamination status in people living near a Portuguese Municipal Solid Waste. Organohalogen Compd. 67:1552–1555.

Reis MF, Sampaio C, Aguiar P, Maurício Melim J, Pereira Miguel J, Päpke O. 2007. Biomonitoring of PCDD/Fs in populations living near portuguese solid waste incinerators: levels in human milk. Chemosphere. 67:S231–S7.

Reis MF, Sampaio C, Brantes A, Aniceto P, Melim M, Cardoso L, Gabriel C, Simão F, Miguel JP. 2007a. Human exposure to heavy metals in the vicinity of Portuguese solid waste incinerators–Part 1: biomonitoring of Pb, Cd and Hg in blood of the general population. Int J Hyg Environ Health. 210:439–446.

Reis MF, Sampaio C, Brantes A, Aniceto P, Melim M, Cardoso L, Gabriel C, Simão F, Miguel JP. 2007b. Human exposure to heavy metals in the vicinity of Portuguese solid waste incinerators–Part 3: biomonitoring of Pb in blood of children under the age of 6 years. Int J Hyg Environ Health. 210:455–459.

Reis MF, Sampaio C, Brantes A, Aniceto P, Melim M, Cardoso L, Gabriel C, Simão F, Segurado S, Miguel JP. 2007c. Human exposure to heavy metals in the vicinity of Portuguese solid waste incinerators–Part 2: biomonitoring of lead in maternal and umbilical cord blood. Int J Hyg Environ Health. 210:447–454.

Reis MF, Sampaio C, Melim JM, Miguel JP. 2004. First results from dioxins and dioxin-like compounds in the population from Madeira Island, Portugal. Part 2 - biomonitoring in breast milk of women living near to a solid waste incinerator. Organohalogen Compd. 66:2709–2715.

Sampaio C, Murk A, Reis MF, Miguel JP. 2004. Possible additional exposure to dioxin and dioxin-like compounds from waste incineration. Biomonitoring using human milk and animal samples. Organohalogen Compd. 66:2773–2778.

Sampaio C, Reis MF, Miguel JP, Aguiar P. 2004. Levels and trends of PCDD/Fs in human blood and milk of residents in the vicinity of a modern municipal solid waste incinerator near to Lisbon. Organohalogen Compd. 66:2779–2783.

Scarlett JM, Babish JG, Blue JT, Voekler SE, Lisk DJ. 1990. Urinary mutagens in municipal refuse incinerator workers and water treatment workers. J Toxicol Environ Health. 31:11–27.

Schecter AJ, Malkin R, Papke O, Ball M, Brandt-Rauf PW. 1991. Dioxin levels in blood of municipal incinerator workers. Med Sci Res. 19:331–332.

Schecter A, Päpke O, Ball M, Lis A, Brandt-Rauf P. 1995. Dioxin concentrations in the blood of workers at municipal waste incinerators. Occup Environ Med. 52:385–387.

Schroijen C, Baeyens W, Schoeters G, Den Hond E, Koppen G, Bruckers L, Nelen V, Van De Mieroop E, Bilau M, Covaci A, et al. 2008. Internal exposure to pollutants measured in blood and urine of Flemish adolescents in function of area of residence. Chemosphere. 71:1317–1325.

Schuhmacher M, Domingo JL, Agramunt MC, Bocio A, Müller L. 2002. Biological monitoring of metals and organic substances in hazardous-waste incineration workers. Int Arch Occup Environ Health. 75:500–506.

Schuhmacher M, Domingo JL, Kiviranta H, Vartiainen T. 2004. Monitoring dioxins and furans in a population living near a hazardous waste incinerator: levels in breast milk. Chemosphere. 57:43–49.

Schuhmacher M, Domingo JL, Llobet JM, Lindström G, Wingfors H. 1999. Dioxin and dibenzofuran concentrations in blood of a general population from Tarragona, Spain. Chemosphere. 38:1123–1133.

Schuhmacher M, Kiviranta H, Ruokojärvi P, Nadal M, Domingo JL. 2009. Concentrations of PCDD/Fs, PCBs and PBDEs in breast milk of women from Catalonia, Spain: a follow-up study. Environ Int. 35:607–613.

Schuhmacher M, Kiviranta H, Ruokojärvi P, Nadal M, Domingo JL. 2013. Levels of PCDD/Fs, PCBs and PBDEs in breast milk of women living in the vicinity of a hazardous waste incinerator: assessment of the temporal trend. Chemosphere. 93:1533–1540.

Schuhmacher M, Kiviranta H, Vartiainen T, Domingo JL. 2007. Concentrations of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in milk of women from Catalonia, Spain. Chemosphere. 67:S295–S300.

Selden AS, Westberg B, Hanberg AH, Nygren Y. 1997. Congener-specific monitoring of PCB and hexachlorobenzene in hazardous waste incineration workers. Organohalogen Compd. 33:398–401.

Shih TS, Chen HL, Wu YL, Lin YC, Lee CC. 2006. Exposure assessment of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) in temporary municipal-waste-incinerator maintenance workers before and after annual maintenance. Chemosphere. 64:1444.

Staessen JA, Nawrot T, Hond ED, Thijs L, Fagard R, Hoppenbrouwers K, Koppen G, Nelen V, Schoeters G, Vanderschueren D, et al. 2001. Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers. Lancet. 357:1660–1669.

Stockholm Convention on Persistent Organic Pollutants (POPs). Geneva, Suisse. [accessed 2019 Jun 14]. Available from: http://chm.pops.int.

Sul D, Oh E, Im H, Yang M, Kim CW, Lee E. 2003. DNA damage in T- and B-lymphocytes and granulocytes in emission inspection and incineration workers exposed to polycyclic aromatic hydrocarbons. Mutat Res. 538:109–119.

Tajimi M, Uehara R, Watanabe M, Oki I, Ojima T, Nakamura Y. 2005. Correlation coefficients between the dioxin levels in mother's milk and the distances to the nearest waste incinerator which was the largest source of dioxins from each mother's place of residence in Tokyo, Japan. Chemosphere. 61:1256–1262.

Takata T. 2003. Survey on the health effects of chronic exposure to dioxins and its accumulation on workers of a municipal solid waste incinerator, rural part of Osaka Prefecture, and the results of extended survey afterwards. Ind Health. 41:189–196.

Takei T, Yamazaki M, Kanai K, Tohyama C. 2001. Exposure assessment for PCDD/Fs and coplanar PCBs in Japan: findings of the 1999 survey. Organohalogen Compd. 52:192–196.

Thrall KD, Callahan PJ, Weitz KK, Edwards JA, Brinkman MC, Kenny DV. 2001. Design and evaluation of a breath-analysis system for biological monitoring of volatile compound. AIHAJ. 62:28–35.

Van den Berg M, Birnbaum LS, Denison M, De Vito M, Farland W, Feeley M, Fiedler H, Hakansson H, Hanberg A, Haws L, et al. 2006. The 2005 World Health Organization reevaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds. Toxicol Sci. 93:223–241.

Van den Hazel P, Frankort P. 1996. Dioxin concentrations in the blood of residents and workers at a municipal waste incinerator. Organohalogen Compd. 30:119–122.

van Doorn R, Leijdekkers CM, Bos RP, Brouns RM, Henderson PT. 1981. Enhanced excretion of thioethers in urine of operators of chemical waste incinerators. Br J Ind Med. 38:187–190.

van Larebeke NA, Bracke ME, Nelen V, Koppen G, Schoeters G, Van Loon H, Vlietinck R. 2006. Differences in tumor-associated protein levels among middle-age Flemish women in association with area of residence and exposure to pollutants. Environ Health Perspect. 114:887–892.

Viel JF, Floret N, Deconinck E, Focant JF, De Pauw E, Cahn JY. 2011. Increased risk of non-Hodgkin lymphoma and serum organochlorine concentrations among neighbors of a municipal solid waste incinerator. Environ Int. 37:449–453.

Waidyanatha S, Zheng Y, Rappaport SM. 2003. Determination of polycyclic aromatic hydrocarbons in urine of coke oven workers by headspace solid phase microextraction and gas chromatography-mass spectrometry. Chem Biol Interact. 145:165–174.

Wilhelm Filho D, Avila S, Possamai FP, Parisotto EB, Moratelli AM, Garlet TR, Inácio DB, Torres MA, Colepicolo P, Dal-Pizzol F. 2010. Antioxidant therapy attenuates oxidative stress in the blood of subjects exposed to occupational airborne contamination from coal mining extraction and incineration of hospital residues. Ecotoxicology. 19:1193–1200.

World Health Organization. 2007. Population health and waste management: scientific data and policy options. Report of a WHO workshop, Rome, Italy. Copenhagen, Denmark: Regional Office for Europe: World Health Organization.

Wrbitzky R, Göen T, Letzel S, Frank F, Angerer J. 1996. Internal exposure of waste incineration workers to organic and inorganic substances. Int Arch Occup Environ Heath. 68:13–21.

Wultsch G, Mišík M, Nersesyan A, Knasmueller S. 2011. Genotoxic effects of occupational exposure measured in lymphocytes of waste-incinerator workers. Mutat Res. 720:3–7.

Yamamoto K, Kudo M, Arito H, Ogawa Y, Takata T. 2015. Isomer pattern and elimination of dioxins in workers exposed at a municipal waste incineration plant. Ind Health. 53:454–464.

Yang J, Shin D, Kim H, Lee Y, Kim C, Lim Y. 2007. Biomonitoring dioxins and heavy metals in blood for the residents living in the vicinity of

the municipal waste incinerators in Seoul, Korea. Organohalogen Compd. 69:688/1–688/4.
Yoshida J, Kumagai S, Tabuchi T, Kosaka H, Akasaka S, Oda H. 2005. Effects of dioxin on metabolism of estrogens in waste incinerator workers. Arch Environ Occup Health. 60:215–222.
Yoshida J, Kumagai S, Tabuchi T, Kosaka H, Akasaka S, Kasai H, Oda H. 2006. Negative association between serum dioxin level and oxidative DNA damage markers in municipal waste incinerator workers. Int Arch Occup Environ Health. 79:115–122.
Yoshida R, Ogawa Y, Mori I, Nakata A, Wang R, Ueno S, Shioji I, Hisanaga N. 2003. Associations between oxidative stress levels and total duration of engagement in jobs with exposure to fly ash among workers at municipal solid waste incinerators. Mutagenesis. 18:533–537.
Zeghnoun A, Frery N, Volatier JL, Falq G, Pascal M, Sarter H, Focant JF, Eppe G. 2007. Factors explaining variation in serum dioxin concentrations for the specific congeners in the French dioxin and incinerators study. Organohalogen Compd. 69:262/1–262/4.
Zubero MB, Aurrekoetxea JJ, Ibarluzea JM, Arenaza MJ, Rodríguez C, Sáenz JR. 2010. Heavy metal levels (Pb, Cd, Cr and Hg) in the adult general population near an urban solid waste incinerator. Sci Total Environ. 408:4468–4474.
Zubero MB, Aurrekoetxea JJ, Ibarluzea JM, Rivera J, Parera J, Abad E, Rodríguez C, Sáenz JR. 2011. Evolution of PCDD/Fs and dioxin-like PCBs in the general adult population living close to a MSW incinerator. Sci Total Environ. 410–411:241–247.
Zubero MB, Eguiraun E, Aurrekoetxea JJ, Lertxundi A, Abad E, Parera J, Goñi-Irigoyen F, Ibarluzea J. 2017. Changes in serum dioxin and PCB levels in residents around a municipal waste incinerator in Bilbao, Spain. Environ Res. 156:738–746.

## Appendix

**Table A1.** Study quality assessment: modified version of the STROBE-ME checklist used to assess the reporting and general standard of each paper.*

| Item | Item number | Item description | Item maximum score |
|---|---|---|---|
| **Title and abstract** | 1.1 | State the use of specific biomarker(s) in the title and/or in the abstract | 1 |
| | 1.2 | Provide an informative summary of methods and results | 1 |
| **Introduction** | 2.1 Background rationale | Explain how/why the specific biomarker(s) have been chosen | 1 |
| | 2.2 Aim | State specific objectives, with inclusion of biomonitoring | 1 |
| **Methods** | 3.1 Study design | Describe the special study designs (nested case/control, case/cohort) and how they were implemented | 1 |
| | 3.2 Ethics | Describe informed consent and approval from ethical committee(s) | 1 |
| | 3.3 Setting | Describe the setting, locations, and relevant dates, including periods of recruitments, exposure, follow-up and data collection | 1 |
| | 3.4 Participants | Give the eligibility criteria and the sources and methods of selection of participants. Report any habit, clinical condition, physiological factor or working or living condition that might affect the characteristics or concentrations of the biomarker(s) | 1 |
| | 3.5 Study size | Explain how the study size was arrived at | 1 |
| | 3.6 Questionnaires | Describe data collection | 1 |
| | 3.7 Bias | Describe how potential sources of bias (confounders) were addressed. Describe how information of potential confounders was collected | 1 |
| | 3.8 Biological sample collection | Report on the setting of the biological sample collection: amount of sample, collecting procedures, time and setting of sample collection | 1 |
| | 3.9 Biological sample storage | Describe sample processing (centrifugation, timing, additives, etc.) before storage and timing/condition of sample storage | 1 |
| | 3.10 Biological sample processing | Describe sample processing (quantity of biological sample used, manipulation, etc.) until biomarker analysis | 1 |
| | 3.11 Laboratory methods | Describe type of assay used and instrumental parameters | 1 |
| | 3.12 Quality control of measurement | Report the validity and reliability of biomarker measurement (detection limit, calibration procedures, internal or external validation) | 1 |
| | 3.13 Statistical methods 1 | Describe how biomarkers were introduced into statistical methods and how missing data or outliers were addressed | 1 |
| | 3.14 Statistical methods 2 | Describe all statistical methods, including those used to control for confounding, and any methods used to examine subgroups and interactions | 1 |
| **Results** | 4.1 Participants | Reports the number of individuals at each stage of the study and give reason for loss of biological samples at each stage | 1 |
| | 4.2 Descriptive data | Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders | 1 |
| | 4.3 Distribution of biomarker measurement | Give the distribution of the biomarker measurement (including mean, median, range and variance) | 1 |
| | 4.4 Other analysis | Report any other analysis done (e.g. analysis of subgroups, interaction analysis) | 1 |
| | 4.5 Confounders | Report results taking in account potential confounders (e.g. confounder-adjusted estimates, sensitivity analyses, multiple regression analyses) | 1 |
| **Discussion** | 5.1 Key results | Summarize key results with reference to study objectives | 1 |
| | 5.2 Validity | Discuss the validity of results considering also results from similar studies and discuss the generalizability (external validity) of the study results | 1 |
| | 5.3 Interpretation | Give an overall interpretation of results considering objectives, limitations, biological plausibility, effect of potential confounders | 1 |
| | 5.4 Limitations | Describe main limitations of the study (e.g. laboratory procedures, data collection, etc.) | 1 |
| **Other information** | 6.1 Founding and conflict of interest | Give the source of founding and the role of the funders, and report potential conflict of interest | 1 |

* Adapted from Gallo et al. (2012).

**Table A2.** Results of the general quality and reporting assessment for each paper included in this review. The mean value of the quality score assigned by two reviewers is reported. Each reviewer assigned to each item a score of 0 (not reported or not fulfilled), 0.5 (partially fulfilled), 1 (completely fulfilled).

| Reference | Title and abstract | | Introduction | | Methods | | | | | | | | | | | | | | Results | | | | | Discussion | | | | Other information | Total Score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **1.1** | **1.2** | **2.1** | **2.2** | **3.1** | **3.2** | **3.3** | **3.4** | **3.5** | **3.6** | **3.7** | **3.8** | **3.9** | **3.10** | **3.11** | **3.12** | **3.13** | **3.14** | **4.1** | **4.2** | **4.3** | **4.4** | **4.5** | **5.1** | **5.2** | **5.3** | **5.4** | **6.1** | |
| Agramunt et al. 2003 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,8 | 1,0 | 0,5 | 0,3 | 1,0 | 0,3 | 0,0 | 1,0 | 0,8 | 0,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | **19,5** |
| Agramunt et al. 2002 | 0,3 | 0,0 | 0,5 | 1,0 | 1,0 | 0,0 | 0,3 | 0,8 | 1,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,5 | 0,8 | 0,3 | 0,3 | 1,0 | 0,8 | 0,8 | 0,8 | 0,8 | 0,0 | 0,3 | 0,0 | 0,3 | 0,0 | 0,0 | **12,8** |
| Agramunt et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 1,0 | 0,8 | 0,8 | 0,0 | 0,0 | 0,8 | 0,5 | 1,0 | 0,8 | 0,0 | 0,3 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,8 | 0,0 | 0,8 | **18,8** |
| Angerer et al. 1992 | 0,5 | 1,0 | 0,5 | 0,0 | 1,0 | 0,0 | 0,3 | 0,8 | 1,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 0,3 | 1,0 | 0,3 | 0,5 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 0,3 | 0,0 | **12,8** |
| Aozasa et al. 2003 | 1,0 | 0,0 | 1,0 | 0,8 | 1,0 | 0,0 | 0,5 | 0,3 | 0,8 | 0,3 | 0,0 | 0,0 | 1,0 | 0,8 | 0,8 | 0,5 | 0,0 | 0,0 | 0,3 | 0,3 | 0,5 | 0,5 | 0,0 | 0,0 | 0,8 | 0,0 | 0,0 | 0,0 | **10,8** |
| Ardevol et al. 1999 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | 1,0 | 1,0 | 0,0 | 0,0 | 1,0 | 0,3 | 0,8 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 0,8 | 0,5 | 0,8 | **21,3** |
| Bocio et al. 2004 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,8 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,5 | 0,0 | 0,5 | 0,0 | 0,5 | 0,0 | 0,5 | 0,3 | 0,0 | 0,3 | 0,0 | 0,5 | 0,0 | 0,5 | **8,5** |
| Bresnitz et al. 1992 | 0,0 | 0,5 | 0,0 | 0,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,8 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | **17,0** |
| Calheiros et al. 2002 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 0,0 | 1,0 | 0,5 | 0,5 | 0,3 | 0,0 | 0,5 | 0,8 | 0,5 | 0,8 | 0,3 | 0,0 | 0,0 | 0,8 | 0,5 | 1,0 | 0,0 | 0,0 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | **12,3** |
| Chao et al. 2005 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 0,8 | 0,3 | 0,3 | 1,0 | 0,8 | 0,3 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,3 | 0,3 | 0,0 | **21,0** |
| Chen et al. 2004 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,3 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,5 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,3 | 0,0 | 0,0 | **20,3** |
| Chen et al. 2006a | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,5 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,8 | 1,0 | 1,0 | 0,0 | 0,8 | **22,0** |
| Chen et al. 2006b | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,8 | 1,0 | 1,0 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | **24,3** |
| Chen. et al. 2003 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,5 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 0,5 | 1,0 | 0,8 | 1,0 | 1,0 | 0,0 | 0,0 | **21,0** |
| Chen et al. 2010 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,8 | 1,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,5 | 0,8 | 0,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 0,5 | 0,3 | 0,0 | **16,0** |
| Chovancova et al. 2012 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,8 | 0,0 | 0,0 | 0,5 | **24,0** |
| Croes et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | **25,3** |
| De Coster et al. 2008 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | **23,0** |
| De Felip et al. 2008 | 1,0 | 0,8 | 1,0 | 0,8 | 0,8 | 0,5 | 1,0 | 1,0 | 0,3 | 0,8 | 0,8 | 0,5 | 0,0 | 0,5 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,0 | 0,0 | 0,5 | **15,3** |
| Deml et al. 1996 | 1,0 | 0,5 | 0,5 | 0,8 | 1,0 | 0,0 | 1,0 | 0,5 | 0,3 | 0,8 | 0,8 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | 0,3 | 0,0 | 0,5 | 0,8 | 1,0 | 1,0 | 0,8 | 1,0 | 0,5 | 0,0 | 0,0 | 0,0 | **15,5** |
| Den Hond et al. 2002 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,8 | 0,8 | 0,8 | 0,8 | 0,0 | 0,0 | 0,0 | 0,3 | 0,0 | 0,3 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,0 | **17,8** |
| Deng et al. 2016 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 0,3 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | **23,8** |
| Evans et al. 2000 | 0,5 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 0,3 | 0,5 | 0,5 | 0,8 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | **22,0** |
| Ferre-Huguet et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 1,0 | 0,0 | 0,0 | 0,5 | 0,5 | 0,5 | 0,3 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,8 | 1,0 | 0,0 | 0,8 | 1,0 | 0,0 | 0,0 | 0,8 | **17,3** |
| Fierens et al. 2003 | 0,5 | 1,0 | 0,8 | 0,0 | 1,0 | 0,0 | 0,8 | 0,8 | 1,0 | 0,8 | 0,8 | 0,3 | 0,0 | 0,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,5 | **17,3** |
| Fierens et al. 2006 | 1,0 | 0,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,5 | 1,0 | 0,0 | 0,5 | 0,5 | 0,5 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | **14,0** |
| Fierens et al. 2007 | 0,8 | 1,0 | 1,0 | 0,8 | 1,0 | 0,8 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | **20,8** |
| Fréry et al. 2007a | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | 0,5 | 0,5 | 1,0 | 0,3 | 0,3 | 0,3 | 0,5 | 1,0 | 0,8 | 0,5 | 0,8 | 0,0 | 0,8 | **19,0** |
| Fréry et al. 2007b | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,8 | 0,5 | 0,5 | 1,0 | 0,3 | 0,3 | 0,5 | 0,0 | 0,5 | 0,8 | 0,8 | 0,5 | 0,0 | 0,8 | **18,5** |
| Gatti et al. 2017 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | **27,8** |
| Gonzalez et al. 2000 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 0,5 | 1,0 | 1,0 | 0,5 | 0,3 | 0,0 | **23,8** |
| Hoffman et al. 1997 | 0,8 | 0,3 | 0,8 | 0,0 | 0,5 | 0,0 | 0,0 | 0,3 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 1,0 | 1,0 | 0,0 | 0,0 | 0,3 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | **6,3** |
| Hours et al. 2003 | 0,3 | 0,8 | 0,0 | 0,3 | 1,0 | 0,3 | 0,5 | 0,8 | 1,0 | 0,8 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,5 | 1,0 | 0,8 | 0,5 | 0,0 | 0,5 | 1,0 | 0,5 | 0,0 | 0,8 | **12,3** |
| Hu et al. 2003 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | **21,8** |
| Hu et al. 2004 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,3 | 1,0 | 0,8 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,3 | 0,8 | 0,5 | **20,8** |
| Huang et al. 2007 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 0,3 | 1,0 | 1,0 | 0,8 | 1,0 | 0,3 | 0,8 | 0,8 | 0,5 | 1,0 | 0,5 | 0,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,0 | 0,8 | 0,8 | 0,3 | 0,0 | 0,0 | **17,5** |
| Kim et al. 2005a | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 1,0 | 0,5 | 0,0 | 0,8 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | 0,8 | 0,5 | 1,0 | 1,0 | 0,3 | 0,8 | 1,0 | 0,3 | 0,0 | 0,5 | **18,3** |
| Kim et al. 2005b | 1,0 | 0,5 | 1,0 | 0,5 | 0,5 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,3 | 0,8 | 0,8 | 0,0 | 0,0 | 0,8 | 0,5 | 0,3 | 1,0 | 0,0 | 0,0 | 0,8 | 0,3 | 0,0 | 0,3 | 0,5 | **10,3** |
| Kim et al. 2002 | 1,0 | 0,0 | 0,8 | 0,8 | 0,3 | 0,0 | 0,5 | 0,3 | 1,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,8 | 0,5 | 0,0 | 0,0 | 1,0 | 0,5 | 0,3 | 1,0 | 1,0 | 0,3 | 0,5 | 0,0 | 0,0 | 0,0 | 0,8 | **12,0** |
| Kim et al. 2001 | 1,0 | 0,3 | 1,0 | 0,8 | 0,5 | 0,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,8 | 1,0 | 0,8 | 0,0 | 0,0 | 0,0 | 0,5 | 0,3 | 0,5 | 0,0 | 0,0 | 0,3 | 0,3 | 0,0 | 0,5 | 0,0 | **9,3** |
| Kitamura et al. 2000 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | 0,5 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 0,3 | 0,8 | 1,0 | 1,0 | 0,8 | 0,0 | 0,5 | **21,5** |
| Kitamura et al. 2001 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,0 | 0,5 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **11,5** |
| Kontsas et al. 2003 | 1,0 | 0,8 | 1,0 | 1,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | **12,3** |
| Kumagai et al. 2000 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | **25,0** |
| Kumagai et al. 2002 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | **24,8** |
| Kumagai et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,3 | 0,0 | 0,0 | **21,0** |
| Kurttio et al. 1998 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | **25,5** |
| Lee et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,8 | 1,0 | 0,3 | 0,5 | 1,0 | 0,8 | 1,0 | 1,0 | 0,5 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | 1,0 | 0,5 | 0,8 | 0,5 | **21,0** |
| Lee et al. 2012 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 0,8 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,5 | 0,0 | **21,8** |
| Lee et al. 2002a | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | 0,3 | 1,0 | 0,3 | 0,5 | 1,0 | 1,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 0,8 | 0,5 | 0,5 | 0,5 | **18,5** |

*(continued)*

**Table A2.** Continued.

| Reference | Title and abstract | | Introduction | | | | | | | | | Methods | | | | | | | | | Results | | | | Discussion | | | Other information | Total Score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lee et al. 2002b | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,5 | 0,3 | 0,3 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,3 | 0,0 | 0,0 | 0,0 | **16,5** |
| Lee et al. 2003 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,5 | 0,0 | 0,3 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **18,0** |
| Leem et al. 2003 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 0,0 | 0,5 | 1,0 | 0,5 | 1,0 | 0,5 | 0,8 | 0,5 | 0,0 | 0,5 | 0,5 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 0,3 | 0,5 | 0,8 | 0,8 | 0,3 | 0,0 | 0,0 | **15,0** |
| Leem et al. 2006 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,8 | 0,5 | 1,0 | 0,5 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,3 | 0,3 | **21,3** |
| Li et al. 2017 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 0,0 | 0,8 | 1,0 | 0,3 | 0,0 | 0,5 | **20,3** |
| Luotamo et al. 1993a | 1,0 | 0,0 | 0,5 | 0,8 | 0,5 | 0,0 | 0,0 | 0,3 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,0 | 0,0 | 0,8 | **6,0** |
| Luotamo et al. 1993b | 1,0 | 0,5 | 0,5 | 0,5 | 0,5 | 0,0 | 0,3 | 0,5 | 0,3 | 0,0 | 0,0 | 0,3 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,8 | 0,0 | 0,3 | 0,8 | 0,0 | 0,0 | 0,8 | **8,3** |
| Ma et al. 1992 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,5 | 0,8 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,8 | 0,5 | 0,0 | **23,0** |
| Maître et al. 2003 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 1,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 0,5 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **13,5** |
| Malkin et al. 1992 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | **15,8** |
| Mari et al. 2007 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,8 | 0,8 | 1,0 | 0,5 | 0,5 | 0,5 | 0,8 | 1,0 | 1,0 | 0,3 | 0,3 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 0,0 | 0,0 | 0,8 | **17,8** |
| Mari et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 1,0 | 0,3 | 0,0 | 0,3 | 0,5 | 0,5 | 0,5 | 0,8 | 0,8 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,8 | 1,0 | 0,0 | 0,0 | 0,8 | **16,3** |
| Mari et al. 2013 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | 0,5 | 0,5 | 0,5 | 0,0 | 0,5 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | **17,0** |
| Martorell et al. 2015 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,3 | 0,0 | 0,0 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **19,5** |
| Miyata et al. 1998 | 1,0 | 0,0 | 1,0 | 0,8 | 0,8 | 0,0 | 0,8 | 0,3 | 1,0 | 0,3 | 0,0 | 0,5 | 0,5 | 0,8 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,5 | 0,0 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 0,8 | **10,5** |
| Moon et al. 2005 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | 0,8 | 0,5 | 0,3 | 0,3 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,5 | 0,3 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,3 | 0,0 | 0,5 | **19,5** |
| Nadal et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,5 | 0,8 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,3 | 1,0 | 1,0 | 0,3 | 0,3 | 1,0 | 0,5 | 0,0 | 0,0 | **16,5** |
| Nadal et al. 2008 | 1,0 | 0,6 | 1,0 | 1,0 | 0,4 | 0,0 | 1,0 | 0,9 | 0,8 | 0,0 | 0,0 | 0,5 | 0,6 | 1,0 | 0,9 | 0,8 | 1,0 | 1,0 | 0,9 | 0,9 | 1,0 | 1,0 | 0,3 | 0,6 | 1,0 | 0,3 | 0,0 | 0,5 | **18,8** |
| Nadal et al. 2013 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,0 | 1,0 | 0,8 | 0,5 | 0,3 | 0,3 | 0,5 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,5 | 0,3 | 1,0 | 0,8 | 0,5 | 0,8 | 1,0 | 0,5 | 0,0 | 0,8 | **19,0** |
| Nakao et al. 2005 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,3 | 0,3 | 0,8 | 0,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 0,0 | 0,0 | 0,5 | **14,8** |
| Nawrot et al. 2002 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | **25,3** |
| Oh et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,3 | 0,3 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,3 | 0,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **18,3** |
| Osius et al. 1999 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | **25,3** |
| Päpke et al. 1993 | 1,0 | 0,5 | 1,0 | 0,5 | 0,5 | 0,0 | 0,5 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,8 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | **6,8** |
| Päpke et al. 1994 | 1,0 | 0,8 | 0,8 | 0,8 | 0,3 | 0,0 | 0,0 | 0,3 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | **8,0** |
| Parera et al. 2013 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,0 | 1,0 | 1,0 | 0,3 | 1,0 | 0,5 | **22,0** |
| Park et al. 2007 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **19,0** |
| Park et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,3 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | **18,3** |
| Park et al. 2014 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 0,3 | 0,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,3 | 0,8 | 0,8 | 0,3 | 0,0 | 0,5 | **18,8** |
| Park  et al. 2013 | 1,0 | 0,5 | 1,0 | 1,0 | 0,8 | 0,0 | 0,3 | 0,8 | 0,5 | 0,8 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | **18,5** |
| Park et al. 2004 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 0,8 | 0,3 | 0,0 | 0,8 | 1,0 | 1,0 | 0,3 | 0,0 | 0,0 | 0,3 | 0,0 | 0,8 | 0,5 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 0,0 | **13,3** |
| Pirard et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,8 | 0,5 | 1,0 | 0,5 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | 1,0 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 0,8 | 1,0 | 0,3 | 0,8 | 0,5 | **18,5** |
| Possamai et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,8 | 1,0 | 0,5 | 0,5 | 0,8 | 0,0 | 0,0 | 0,3 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,8 | 0,8 | 0,0 | 0,5 | 1,0 | 0,3 | 0,0 | 0,8 | **14,3** |
| Raemdonck et al. 2006 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,8 | 0,3 | 0,5 | **17,8** |
| Ranzi et al. 2013 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,8 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | **26,0** |
| Rappe et al. 1992 | 0,5 | 0,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,8 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,8 | 0,0 | 0,0 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | **5,3** |
| Reis et al. 2002 | 0,8 | 0,0 | 1,0 | 1,0 | 0,5 | 0,8 | 0,5 | 1,0 | 0,5 | 1,0 | 0,8 | 0,8 | 0,0 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | 0,0 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | 0,5 | 0,3 | 0,0 | 0,0 | **12,8** |
| Reis et al. 2004a | 1,0 | 0,0 | 0,5 | 1,0 | 0,8 | 1,0 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,0 | 0,5 | 0,5 | 0,8 | 1,0 | 0,5 | 1,0 | 1,0 | 0,8 | 0,5 | **18,8** |
| Reis et al. 2004b | 1,0 | 0,0 | 0,8 | 1,0 | 0,8 | 1,0 | 0,5 | 1,0 | 0,8 | 1,0 | 0,5 | 0,8 | 0,0 | 0,5 | 0,5 | 0,0 | 0,3 | 0,5 | 0,0 | 0,3 | 0,5 | 0,0 | 0,3 | 0,5 | 0,8 | 0,0 | 0,0 | 0,3 | **13,3** |
| Reis et al. 2005 | 0,8 | 0,0 | 0,8 | 0,8 | 0,8 | 0,0 | 0,8 | 0,8 | 0,0 | 0,0 | 0,0 | 0,3 | 0,3 | 0,3 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 0,8 | 0,8 | 0,8 | 0,3 | 0,5 | 0,8 | 0,0 | 0,0 | 0,3 | **10,8** |
| Reis et al. 2007a | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,0 | 1,0 | 0,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,8 | 0,5 | 0,5 | **22,0** |
| Reis et al. 2007b | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,3 | 0,5 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 0,3 | **21,5** |
| Reis et al. 2007c | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 0,8 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,0 | 0,3 | 1,0 | 0,3 | 0,5 | 1,0 | 1,0 | 0,3 | 1,0 | 0,3 | 0,3 | 0,0 | 0,3 | **18,8** |
| Reis et al. 2007d | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,3 | 0,0 | 0,0 | 1,0 | 0,0 | 0,8 | 1,0 | 1,0 | 0,0 | 0,5 | 0,3 | 0,5 | 0,3 | 0,3 | **17,0** |
| Reis et al. 2007e | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,3 | 0,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 0,5 | 0,3 | 0,3 | **17,8** |
| Sampaio et al. 2004a | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,3 | 1,0 | 0,8 | 0,8 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 0,5 | 0,8 | 0,8 | 0,3 | 0,5 | 0,5 | 0,0 | 0,0 | 0,3 | **14,3** |
| Sampaio et al. 2004b | 1,0 | 0,0 | 0,8 | 0,8 | 0,8 | 0,5 | 0,8 | 1,0 | 0,3 | 1,0 | 0,5 | 0,8 | 0,3 | 0,0 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 0,5 | 1,0 | 1,0 | 0,5 | 0,5 | 0,8 | 0,0 | 0,0 | 0,5 | **14,5** |
| Scarlett et al. 1990 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,8 | 0,8 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 0,8 | 0,3 | **23,0** |
| Schecter et al. 1991 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,3 | 0,3 | 1,0 | 0,3 | 1,0 | 1,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,8 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 0,3 | 0,0 | 0,0 | 0,0 | **11,5** |
| Schecter et al. 1995 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,5 | 0,3 | 0,5 | 0,3 | 0,8 | 1,0 | 0,0 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 0,5 | 0,0 | 0,8 | 0,3 | 0,0 | 0,3 | 0,0 | **12,3** |
| Schroijen et al. 2008 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,8 | **25,8** |
| Schuhmacher et al. 1999 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 1,0 | 0,3 | 0,0 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,5 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,5 | **18,5** |
| Schuhmacher et al. 2002 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,5 | 0,8 | 0,5 | 1,0 | 0,8 | 0,0 | 0,0 | 0,5 | 0,5 | 0,5 | 0,0 | 1,0 | 0,3 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **15,8** |

(*continued*)

**Table A2.** Continued.

| Reference | Title and abstract | | Introduction | | Methods | | | | | | | | | | | | | Results | | | | | | Discussion | | | | Other information | Total Score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Schuhmacher et al. 2004 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,0 | 0,5 | 0,0 | 1,0 | 0,8 | 0,0 | 0,5 | 1,0 | 0,5 | 0,0 | 0,5 | **18,5** |
| Schuhmacher et al. 2007 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,5 | 0,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 0,0 | 0,5 | **21,0** |
| Schuhmacher et al. 2009 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,8 | 0,8 | 0,8 | 0,0 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 0,8 | 0,0 | 0,5 | **22,8** |
| Schuhmacher et al. 2013 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | 1,0 | 0,5 | 0,5 | 1,0 | 0,5 | 0,0 | 0,5 | **22,5** |
| Selden et al. 1997 | 1,0 | 0,8 | 0,5 | 0,8 | 0,0 | 1,0 | 0,0 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 0,3 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 0,0 | **7,8** |
| Shih et al. 2006 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,3 | 0,3 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,3 | 0,5 | 0,5 | **19,8** |
| Staessen et al. 2001 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,3 | 0,8 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | **22,8** |
| Sul et al. 2003 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,0 | 0,5 | 1,0 | 0,3 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,8 | 1,0 | 0,3 | 0,0 | 0,5 | **17,5** |
| Tajimi et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 0,5 | 0,5 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,5 | 1,0 | 1,0 | 0,0 | **21,3** |
| Takata 2003 | 1,0 | 0,5 | 0,5 | 0,5 | 1,0 | 0,5 | 0,8 | 0,0 | 0,3 | 1,0 | 0,0 | 0,8 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,8 | 1,0 | 1,0 | 0,8 | 0,3 | 0,8 | 0,0 | 0,0 | 0,0 | 0,3 | **12,0** |
| Takei et al. 2001 | 1,0 | 0,0 | 0,5 | 0,8 | 0,8 | 0,5 | 0,8 | 0,5 | 0,3 | 1,0 | 0,3 | 0,3 | 0,0 | 0,8 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,8 | 0,3 | 0,0 | 0,5 | 0,3 | 0,3 | 0,0 | 0,0 | **9,8** |
| Thrall et al. 2001 | 1,0 | 1,0 | 1,0 | 0,3 | 0,5 | 0,8 | 0,5 | 0,3 | 0,0 | 0,3 | 0,0 | 0,5 | 0,0 | 0,8 | 1,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,3 | 0,0 | **10,0** |
| Van den Hazel et al. 1996 | 0,8 | 0,0 | 1,0 | 1,0 | 0,5 | 0,0 | 0,5 | 0,5 | 0,3 | 0,5 | 0,8 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,8 | 0,0 | 0,0 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | **8,5** |
| Van Doorn et al. 1981 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,3 | 0,3 | 0,0 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,3 | 0,0 | 0,8 | 0,0 | 0,0 | 0,0 | 0,0 | **10,3** |
| van Larebeke et al. 2006 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 0,3 | 0,0 | **20,5** |
| Viel et al. 2011 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,5 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 0,3 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | **24,3** |
| Wilhelm Filho et al. 2010 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,3 | 0,0 | 0,3 | 0,0 | 0,5 | 0,5 | 0,3 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,0 | 0,0 | 0,5 | **13,5** |
| Wrbitzky et al. 1995 | 1,0 | 1,0 | 0,0 | 1,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,5 | 0,0 | 0,0 | 0,0 | 0,0 | 0,5 | 0,5 | 0,5 | 0,8 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,3 | 0,0 | **13,5** |
| Wultsch et al. 2011 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 0,5 | 1,0 | 0,0 | 0,5 | 1,0 | 0,5 | 0,5 | 0,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 0,5 | 0,8 | **19,0** |
| Yamamoto et al. 2015b | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,5 | **20,5** |
| Yamamoto et al. 2015a | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 0,8 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 0,25 | **25,0** |
| Yang et al. 2007 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,8 | 0,5 | 0,5 | 1,0 | 0,8 | 1,0 | 0,8 | 0,8 | 0,8 | 1,0 | 0,0 | 0,0 | 0,0 | 0,5 | 1,0 | 0,8 | 0,5 | 0,5 | 0,3 | 0,0 | 0,0 | 0,0 | **16,3** |
| Yoshida et al. 2005 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,5 | 0,5 | **24,5** |
| Yoshida et al. 2006 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 0,5 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,8 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,0 | **22,8** |
| Yoshida et al. 2003 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,8 | 0,0 | 0,5 | 0,5 | 0,5 | 0,5 | 0,5 | 1,0 | 0,0 | 0,5 | 0,0 | 0,0 | 0,5 | 0,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,0 | 0,3 | 0,0 | **15,3** |
| Zeghnoun et al. 2007 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 0,3 | 0,8 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 0,0 | 0,0 | 0,0 | 0,0 | 1,0 | 1,0 | 0,8 | 0,0 | 0,3 | 0,5 | 1,0 | 0,8 | 0,0 | 0,8 | 0,0 | 0,0 | **15,8** |
| Zubero et al. 2010 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 0,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,8 | 0,3 | 0,0 | **23,5** |
| Zubero et al. 2011 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,3 | 1,0 | 1,0 | 0,8 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,8 | 1,0 | 0,3 | **25,0** |
| Zubero et al. 2017 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 0,5 | 1,0 | 1,0 | 0,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | 1,0 | **26,5** |