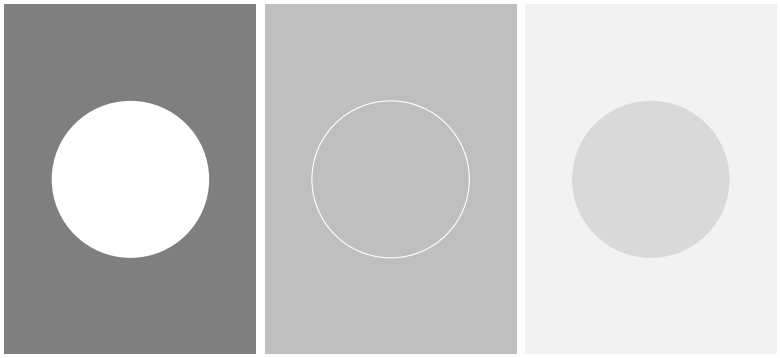

Biological monitoring of persistent organic pollutants (POPs) in New Zealand

A thesis by publications presented in partial fulfilment of the requirements

for the degree of Doctor of Philosophy in Public Health.

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Abstract

This thesis reports the results of a national research program investigating persistent organic pollutants (POPs) in New Zealanders. The research investigated human body burdens, and exposure sources, of the following POPs:

- Polychlorinated dibenzo-p-dioxins (PCDDs) and furans (PCDFs)
- Polychlorinated biphenyls (PCBs)
- Organochlorine pesticides (OCPs) such as dichlorodiphenyltrichloroethane (DDT)
- Brominated flame retardants (BFRs) such as polybrominated diphenyl ethers (PBDEs)
- Perfluoroalkyl substances (PFAS) such as perfluorooctanosulfonic acid (PFOS)

Previous research has shown that POPs are toxic, and that they are found in the bodies of all humans and wildlife. This thesis builds on previous research by describing the results of recent studies of New Zealand human body burdens of POPs and comparing these results to previous New Zealand research and international studies.

The research includes the second national survey of POPs in the serum of adult New Zealanders, and a related study of the importance of household dust as an exposure source for BFRs in breast-feeding infants. The POPs serum survey methodology was assessed, showing that younger adults, and those of Māori ethnicity, are less likely to participate in human biological monitoring surveys. The research found that the body burdens for the chlorinated POPs were higher for the older age groups. In contrast, the majority of BFRs showed higher serum concentrations in younger age groups. The observed positive association with age for the chlorinated POPs may be

attributed primarily to a cohort effect (i.e. more recent cohorts having been exposed to lower levels of chlorinated POPs). The research also provides evidence that within the same cohort, chlorinated POPs body burdens have reduced over time, though some POPs appeared to have reached steady-state concentrations in individuals. In addition, burdens of BFRs and PFASs were found to be higher in men compared to women, possibly due to sex-related differences in human elimination of these POPs. In comparison to international results, New Zealand adults have (a) relatively low body burdens of PCDDs, PCDFs, and PCBs, and (b) similar body burdens of BFRs, PFASs, and OCPs (especially DDT compounds) to the rest of the world. Household dust is an important exposure source of BFRs in human milk. Over the past 15 years, human body burdens (measured in serum and breast milk) of chlorinated POPs have decreased in New Zealand and internationally, illustrating the effectiveness of measures to control POPs (e.g. the Stockholm Convention). The research provides the first reference point for human body burdens of BFRs and PFASs in the New Zealand adult population.

In summary, the research outlined in this thesis provides insights into the distribution and dynamics of POPs in humans. The findings from the research, particularly the influence of age on the dynamics of POPs over time, and the exposure of children to POPs at a very early age, provide incentive for further research and public health initiatives. The research provides a resource to inform future biological monitoring programmes, and to aid in the assessment of human health risks from exposure to POPs.

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List of Abbreviations

WHO – World Health Organisation

UNEP – United Nations Environment Programme

MEA – multi-lateral environmental agreement

HBM – human biological monitoring

TEF – toxic equivalency factors

TEQ – toxic equivalency

POP – persistent organic pollutant

PCDD – polychlorinated dibenzo-*p*-dioxin

PCDF – polychlorinated dibenzo-*p*-furan

PCB – polychlorinated biphenyl

OCP – organochlorine pesticide

DDT – dichlorodiphenyltrichloroethane

DDD – dichlorodiphenyldichloroethane

DDE – dichlorodiphenyltrichloroethylene

BFR – brominated flame retardant

PBDE – polybrominated diphenyl ether

HBCD – hexabromocyclododecane

PBB – polybrominated biphenyl

PFAS – perfluorinated alkyl substance

PFC – perfluorinated compound

CBAT – cross-sectional body-burden-age trend

Chapter 1. Introduction

For the first time in the history of the world, every human being is now subjected to contact with dangerous chemicals, from the moment of conception until death.

- Rachel Carson, Silent Spring (1962)

Image credit: https://en.wikipedia.org/wiki/Rachel_Carson

Humans are exposed to a range of toxic anthropogenic chemicals through our entire lifetimes. These toxic chemicals silently build up in our bodies and can be unwittingly passed on to our children. Rachel Carson's seminal work, *Silent Spring* [1], was a wake-up call to the public on the dangers arising from rampant use of organochlorine pesticides, particularly dichlorodiphenyltrichloroethane (DDT). As a result of the courage and leadership of people like Rachel Carson, we now have a better understanding of the dangers associated with exposure to toxic anthropogenic chemicals. This understanding largely stems from improved scientific methods to investigate these chemicals in humans and the environment. The findings from the catalogue of data produced by investigators in the fields of analytical chemistry, environmental health, and epidemiology have spurred government authorities to take global action to reduce the risks posed by these chemicals in our bodies and the environment. This thesis plays a part in the global

response to the risks of toxic chemicals through its investigation into the distribution of a class of highly toxic anthropogenic chemicals in New Zealand adults.

Persistent organic pollutants (POPs) are a class of highly toxic chemicals that are the subject of international attention [2]. POPs are a diverse group of chemicals with certain characteristics in common, and the chemical nature and toxic effects of POPs are described in detail in Chapter 2. However, it is informative to note that one class of POPs, dioxins and furans, has been called "the most toxic chemicals known to man [*sic*]" [3] and that levels in humans are "at or near the point where adverse health effects may be occurring" [4]. The universal and long-lasting presence of POPs in humans is as a public health issue worthy of ongoing investigation and action.

POPs have been used by humans, or inadvertently produced by humans, for over a century. For example, DDT was developed in 1874 by the Austrian chemist Othmar Zielder and introduced as a pesticide to the market in 1942 [5]. Polychlorinated biphenyls (PCBs) were discovered in 1865 as a by-product of coal tar processing, and industrial production of PCBs started in 1910 [6]. Dioxins and furans have a much longer global history as they are produced naturally during high-temperature events involving organic materials, for example forest fires and volcanic eruptions, and also result from anthropogenic thermal processes, such as incineration of municipal waste [7]. Brominated flame retardants (BFRs) are more recent players in the POPs story. In fact, prior to the development and commercialisation of BFRs, PCBs were used as flame retardants in a number of industrial and commercial applications until global bans on PCBs in the 1970's and 1980's [6]. BFRs were developed in the 1970's as a replacement for PCBs and were employed in a wide range of uses, particularly as

additives to plastics in electronic goods (e.g. computers and televisions), foams, and textiles to reduce fire hazards [8]. Many BFRs have been phased out internationally, however many are still in use around the world today. Finally, R. J. Plunkett, a chemist at DuPont, patented polytetrafluoroethylene (PTFE) in 1939 [9] . Plunkett's formulation was commercialised by DuPont and 3M in the 1940's and 1950's in their Teflon® and Scotchgard® products. Perfluorinated alkyl substances (PFASs) such as perfluorooctanoic acid (PFOA) are used in PTFE production and end up in manufactured articles containing PTFE [10]. Some of the common PFAS formulations have been phased out internationally; however other PFASs continue to be used as surface-active ingredients in the production of textiles and other materials that are found in many common household and commercial products [11].

Awareness of the global distribution and potential risks from POPs started to emerge from the scientific community in the 1970s. POPs were found in humans and wildlife, and in many environmental media around the planet including sediment, trees, dust, and soil [12]. There is clear evidence that the relatively high levels of POPs in the environment are a result of human activity, as shown by POPs contamination in locations far removed from industrial areas, such as remote lake sediments in the Pyrenees Mountains [13] and ice fields in Svalbard, Norway [14]. POPs accumulate in the food chain to negatively affect top predators. For example, DDT was shown to cause eggshell thinning [15], PCBs cause birth deformities (twisted beaks) in top predator bird species[16], and high levels of dioxins and PCBs have been measured in arctic-dwelling fish that live well away from sources of industrial pollution [17]. The effects of POPs on humans and wildlife were a

controversial topic for many years, until enough evidence was gathered to convince government and industry to reduce the production and use of these toxic chemicals. Humans are top predators, so it should come as no surprise that we are primarily exposed to POPs from our diet [18]. However, some may be surprised to learn that high levels of POPs can be found in the most important human food source, breast milk [19].

POPs are found in every environment on Earth. Atmospheric processes mobilise POPs around our planet through long-range transport of atmospheric particulates, volatilisation and condensation of POPs (the so-called global "distillation" effect where POPs used in the tropics migrate to the North and South polar regions), and through the migratory movements of contaminated wildlife across great distances [20, 21]. The global migration of POPs is not entirely without obstacles, as scientists have discovered a "chemical equator" which restricts movement of POPs from the "polluted North" to the "cleaner Southern Hemisphere", related to latitude-dependent atmospheric wind patterns [22]. However, this "chemical equator" is by no means protective and may result in greater exposure of residents of the Northern Hemisphere who do not benefit from a dilution effect.

POPs are toxic to humans and wildlife. Exposure to POPs can result in serious health effects, including effects on the reproductive, developmental, behavioural, neurologic, endocrine, and immunological systems [23, 24]. Numerous studies have shown an increase in the incidence of diseases related to endocrine disruption since the 1950's, and this has been partially attributed to increased global levels of POPs from industrial and agricultural activities [24]. There is emerging evidence that POPs

alter epigenetic markers that are related to disease, and these epigenetic changes may be transmitted to the next generation [25]. Our understanding of the toxic effects of POPs is enough to warrant action to minimize our exposure to these toxic chemicals, but this understanding is by no means complete. The more we learn about POPs, the more we realise how their effects on humans and wildlife are wide-ranging and worthy of further study.

The amount of POPs in a person's body is called the "body burden" – defined in the Oxford Dictionary as "the total amount of a particular chemical present in a human's or animal's body, typically a … toxic substance". Every human lives and grows with their personal body burden of POPs throughout their entire life, and each individual has very little control over their personal body burden. A person's body burden can be estimated by measuring POPs in specific parts of the body such as blood or breast milk [26, 27]. The body burden is a dynamic quantity that changes according to environmental concentrations of POPs, and an individual's life-stage of growth and development [28]. As children grow, their body burden changes with growth – increasing during the toddler years when nursing mothers pass some of their POPs body burden to their children in breast milk and decreasing during the period of rapid growth in adolescence (referred to as growth dilution) [29]. As adults, people are continuously exposed to POPs through food, dust, and direct exposure to POPs-containing materials [30]. The body burden changes because of other natural human biological processes such as menstruation and metabolism, and artificial procedures that result in loss of POPs-containing body fluids (e.g. venesection) [31, 32]. Most POPs are lipophilic and accumulate in human adipose tissue. Weight loss

may release and mobilise POPs into the human circulatory system with an increase in concentrations of POPs in blood, but no overall change to the body burden [33]. POPs may also be stored in other body compartments, for example PFASs are associated with blood proteins rather than lipids [34].

Human biological monitoring (HBM) is an epidemiologically-based technique employed in this thesis to assess concentrations of POPs in a representative sample of the New Zealand adult population. The information from national surveys is particularly valuable when the surveys are periodically repeated using a standardised methodology. Researchers can assess temporal trends, and this trend data can be used to monitor changes in human exposure to POPs. The results of HBM can be used to monitor the effectiveness of public health intervention strategies; for example, bans on the import and use of POPs. Despite the value of the data realised in HBM surveys of POPs in the general population, such surveys are often expensive and time-consuming, and therefore are scarce internationally [30].

Differences in exposure to POPs based on demographic determinants [30], particularly age and sex, but also ethnicity and geographic region, suggest that the burden of disease associated with POPs exposure is higher in some members of the population. Exposure of children to POPs in their environment, including through human milk, is a key area of research [35]. An understanding of POPs concentrations in adult populations provides valuable information in determining children's exposure; it takes fewer resources to recruit and collect biological samples (e.g. blood, urine, milk) from adult participants in biological monitoring studies. The use of national registers such as the Electoral Roll provides a study population that can

be reduced to a survey sample, allowing for detailed assessment of demographic determinants of POPs body burdens.

Analytical methods and technology to quantify POPs in biological samples were developed in the 1940's. Since that time the methods have improved to the point where POPs can be detected at ultra-trace, or parts-per-billion, levels in biological samples. These technological advances, along with better access to high-quality commercial laboratories with recognised accreditation systems, provide the vehicle to assess background concentrations of POPs in general populations, as long as resources permit this expensive testing.

Countries have signed up to multi-lateral environmental agreements (MEAs) to control POPs. *The Stockholm Convention on Persistent Organic Pollutants* (2001) is the key MEA to control effects of POPs on human health and the environment. It is supported by the *Basel Convention on Transboundary Movement of Hazardous Wastes and Their Disposal* (1989) and the *Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade* (1998).

New Zealand has ratified the Stockholm Convention and has a National Implementation Plan to achieve the aims of the convention [2]. However, as new POPs are added to the Stockholm Convention, and "old" POPs continue to be detected in New Zealanders, there is a need for ongoing work. We need reliable data to support actions to eliminate these toxic chemicals from our own bodies, the bodies of our mokopuna (children), and in other taonga (treasures, including the natural environment).

In New Zealand, a land considered by many to be "clean and green", the spectre of contamination, pollution, and related disease causes sufficient public concern that a range of agencies study POPs or use research evidence to develop strategies to control the negative effects of POPs. Government agencies, including the Ministry of Health and the Ministry for the Environment, have had policy programs in place since the early 1990's to monitor and control the adverse effects of POPs in humans and the environment [2]. One of the main reasons that government puts such an emphasis on POPs is their persistence – they may last for decades in humans and the environment before breaking down, suggesting that the effects of POPs will continue to be observed for generations.

Therefore, it is important to study the spatial distribution of POPs in the environment, in communities, and in people. Through an iterative process of study and practical control measures, we can gain a better understanding of the distribution of toxic chemicals in the environment and in people, and we can evaluate our actions to mitigate risks to human health.

The research described in this thesis is a key element of New Zealand's commitment to reducing the health effects of POPs, by providing current and nationally-representative data on the levels of POPs in the bodies of New Zealand adults. This thesis applies a robust methodology to answer the following questions:

1. Are human body burdens of POPs changing over time?
2. What are the key exposure pathways for POPs (specifically BFRs in human milk)?

3. Are there differences in the body burden of POPs between demographic groups?
4. How does the average New Zealand body burden of POPs compare to the rest of the world?

The thesis is divided into the following Chapters:

Chapter 1: Introduction

The scientific question that underpins the research is discussed in the context of the scientific literature. The position of New Zealand internationally in this field of research is reviewed. The relationship of this research to other domestic and international research is described. The policy initiatives that support the biological monitoring programme are outlined. The benefits of the research to New Zealand are outlined.

Chapter 2: Literature review

This chapter provides background and historical data on POPs in New Zealand and internationally. The global distribution of POPs is reviewed. The international initiatives to monitor and manage POPs are reviewed, including New Zealand's commitments under the Stockholm Convention. New Zealand data on POPs emissions and environmental concentrations are described. Key exposure pathways and human health effects of POPs are described. The scope and purpose of human biological monitoring in assessing exposure to toxic chemicals, including current methods for laboratory analysis of POPs in serum. We describe previous New

Zealand studies of human body burdens of POPs, along with an overview of temporal trends of POPs in humans over the past 50 years.

Chapter 3: Comparison of New Zealand and international temporal trends of chlorinated POPs in human milk, 1985 to 2008. (submitted for publication in the Australian and New Zealand Journal of Public Health)

This chapter provides the result of a comparison of temporal trends of chlorinated POPs in New Zealand and international human milk results. International results are determined by review and interpolation of results from tables and graphs in published reports. Temporal trends for chlorinated POPs in New Zealand are adopted from published literature.

Chapter 4: Recruitment methodology of a national survey of adult New Zealanders' serum concentrations POPs and determinants of response.

This chapter provides an assessment and discussion of the effectiveness of the human biological monitoring methodology of the national POPs serum study. In particular, the response rate of the serum survey is described and discussed to determine differences in response and participation rates between demographic groups.

Chapter 5: Chlorinated persistent organic pollutants in serum of New Zealand adults, 2011-2013 (published in Science of the Total Environment [36])

This chapter provides the results of a national survey of serum concentrations of chlorinated POPs in adult New Zealanders. The survey assesses the concentrations

of dioxins, PCBs, and OCPs in a representative sample of the New Zealand adult population. The associations between age, gender, ethnicity, and geographic region and serum POPs concentrations are assessed. Temporal trends for POPs (1997 to 2012) are presented and discussed. The New Zealand results are compared to results from international monitoring programs.

Chapter 6: Polybrominated diphenyl ethers and perfluorinated alkyl substances in blood serum of New Zealand adults, 2011-2013. (Published in Chemosphere [37])

This chapter describes serum concentrations of polybrominated diphenyl ethers (PBDE) and perfluoroalkyl substances (PFAS) in a representative sample of the New Zealand adult population. The associations between age, gender, ethnicity, and geographic region and serum PBDE and PFAS concentrations are assessed. Temporal trends of PBDEs in serum are estimated using previous New Zealand data. An international comparison of PBDE and PFAS serum concentrations is presented and discussed.

Chapter 7: Concentrations of PBDEs in matched samples of indoor dust and human milk in New Zealand (published in Environment International [38])

This chapter provides the results of an investigation into concentrations of PBDEs in matched samples of indoor dust and human milk in New Zealand. The results of laboratory analysis of dust samples are presented and assessed. Statistical correlation of dust and human milk PBDE results is described and assessed. The influence of socio-demographic determinants on PBDE concentrations in human milk

and household dust is assessed. An estimated daily PBDE intake for children through ingestion of human milk and dust is calculated and discussed.

Chapter 8: Discussion and Conclusions

This chapter provides an over-arching summary of the major findings of the research, and a discussion of the relevance of these findings to our current understanding of the distribution and dynamics of POPs in the New Zealand adult general population. The study strengths and limitations are discussed. Recommendations for ongoing biological monitoring programmes in New Zealand (e.g. timeframes, key challenges that need to be addressed) are provided.

Chapter 2. Literature Review

Persistent Organic Pollutants (POPs)

Persistent organic pollutants (POPs) are a group of environmental pollutants that are found throughout the environment, in wildlife, and in humans. These highly-toxic contaminants are widely spread in the global environment, and humans are exposed to them mainly through food [39]. The majority of POPs result from anthropogenic activity – polychlorinated biphenyls (PCBs) were widely used in industry and organochlorine pesticides (OCPs) were widely used in agriculture. Polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzo-*p*-furans (PCDFs) are released to the environment as unintentional by-products of industrial thermal processes, and in fires (natural and accidental). Brominated flame retardants (BFRs), including the common pentabrominated diphenyl ethers (PBDEs), are still in common use as treatments to reduce fire risk in a broad range of manufactured articles such as computers and textiles. Perfluorinated alkyl substances (PFASs) such as perfluorooctanesulfonate (PFOS) are also used in a wide range of consumer goods such as cookware, textiles, and food packaging.

In some cases, POPs are intentionally released for control of public health threats, for example the release of dichlorodiphenyltrichloroethane (DDT) for the control of pathogen-bearing pests. Environmental contamination by DDT was brought to worldwide public attention with the publication of Rachel Carson's (1907 – 1964) *Silent Spring* [1], a pivotal publication that gave voice to the concerns of many scientists and conservationists at the time concerned with the environmental effects of widespread pesticide use. Rachel Carson's work spearheaded public debate about the effects of POPs on wildlife and human health and earns credit as a foundation for

international action to control the release of POPs to the environment. Since the 1960's, POPs have remained among the most highly studied, and controversial, of environmental contaminants.

The chemical structure of POPs confers on them a number of defining characteristics, making them of high importance for local and global environmental management [40]:

- Toxicity to wildlife, including humans, over short periods (acute toxicity) and long periods (chronic toxicity)
- Persistence in the environment for long periods of time because of their resistance to chemical and biological degradation
- Tendency to bio-accumulate in organisms by building up in body fats, particularly in animals higher up the food chain (e.g. top predators)
- Mobility and tendency for long-range transport in the environment through air, water, and in migratory animals

POPs have been found throughout the environment and biota everywhere on Earth. The ubiquitous presence of POPs in the environment has been identified in studies of regions that are far-removed from anthropogenic industrial and agricultural activity, for example lake sediments in a remote polar lake in Svalbard, Norway [41] and glacier-fed lakes in Switzerland [42]. These and other studies [43] show a clear temporal pattern for global background environmental concentrations of a wide range of POPs over the past 100 years.

The rise and fall of chlorinated POPs

Chlorinated POPs are a group of synthetic compounds that has played an important role in global economic development. The prominence of chlorinated POPs in industrial and agricultural activities rose significantly after the second World War [44]. Global production and use of the PCBs and OCPs increased markedly in the third quarter of the twentieth century. PCBs comprise 209 congeners of a chlorinated biphenyl structure and were widely used since the 1930's as dielectrics in large electrical equipment, in heat transfer and hydraulic systems, as part of lubricating and cutting oils, and as paint plasticisers and ink solvents [44].

Organochlorine pesticides (OCPs) are a diverse group of chlorinated POPs that were used in a broad range of agricultural, industrial, and domestic pest-control applications. OCPs include the insecticides dichlorodiphenyltrichloroethane (DDT), lindane (hexachlorocyclohexane, HCH, where lindane is the γ-HCH isomer), and the cyclodiene insecticides dieldrin, aldrin, endrin, heptachlor, and endosulfan.

Unintentional by-products of the manufacture and use of chlorinated POPs are the PCDDs and PCDFs, collectively called dioxins. Many OCPs contain, as impurities, dioxins formed during the heating of chlorophenols during their manufacture. For example, pentachlorophenol (PCP) is a timber preservative that was commonly used in New Zealand for antisapstain timber treatment and contained dioxins as a contaminant [45]. PCDDs and PCDFs are also released to the environment during industrial accidents, production of bleached pulp and paper, combustion of organochlorine materials such as PCB waste, and incineration of municipal solid waste [44].

Restrictions on the production and use of chlorinated POPs were established in the 1960's because of public concern over the harmful effects of POPs on individual organisms, populations of organisms, and on communities and ecosystems of organisms [44]. Currently, the majority of commonly used chlorinated POPs are banned worldwide, with the notable exception of DDT that is still used as part of anti-malaria control strategies for disease-carrying mosquitoes in tropical areas [46, 47].

Dioxins and furans

Polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are a group of organic compounds whose chemical structure is characterised by two chlorine-substituted aromatic rings connected by either one or two oxygen atoms (Figure 1). PCDD and PCDF congeners are differentiated by the degree of chlorine substitution on the aromatic rings, with 75 and 135 possible congeners for PCDD and PCDF, respectively [48]. PCDDs and PCDFs are unintentional by-products of industrial processes such as chemical manufacture, pulp and paper bleaching, and high-temperature of industrial, medical, and municipal waste [48]. The most toxic dioxin congener (2,3,7,8-TCDD) was a well-documented contaminant of Agent Orange used as a military defoliant during the Vietnam war [49]. Other high-profile releases of dioxins to the environment include an industrial accident in Seveso, Italy in 1976 [50] and in food-poisoning incidents in rice in Yusho, Japan in 1968 [51, 52], pork in Ireland in 2008 [53], and poultry and eggs in Belgium in 1999 [54]. In 2004, dioxins made international headlines from their use in the attempted murder poisoning of the Ukrainian President Viktor Yuschenko [49]. Dioxins and furans are

also produced naturally through volcanic activity and forest fires, however the contribution of natural dioxin and furan sources is negligible compared to anthropogenic sources [55]. Studies of sediments in remote areas of North America and Europe show that atmospheric transport and deposition of dioxins increased from low levels in the 1920's to peak levels in the 1970's as a direct result of anthropogenic industrial and combustion sources [7, 56].

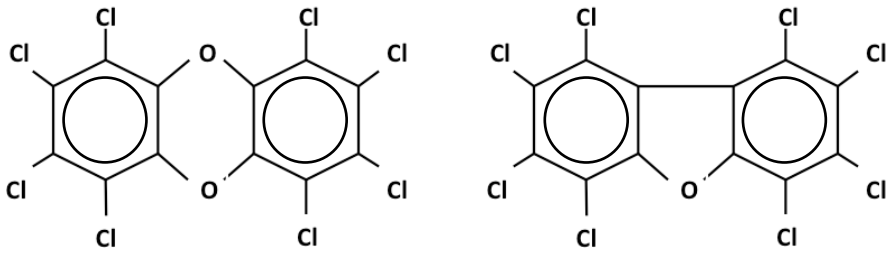


Figure 1. Chemical structure of 1,2,3,4,6,7,8,9-Octachlorodibenzo-p-dioxin and 1,2,3,4,6,7,8,9-Octachlorodibenzofuran

Toxic effects associated with dioxin and furan exposure in vertebrate species are related to their interaction with the aryl-hydrocarbon receptor [57] and include cardiovascular disease, diabetes, cancer, endocrine disruption, and altered thyroid homeostasis [4, 24]. The World Health Organisation [57] has developed a toxicity ranking scheme for dioxins and furans called Toxic Equivalents (TEQ) based on a set of published toxic equivalence factors (TEFs). TEFs, established in 1998 and updated in 2005, represent the toxicity of PCDD and PCDF congeners relative to the most toxic congener 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). TEQ is calculated by multiplication of congener-specific PCDD and PCDF concentrations by the appropriate TEF (Table 1).

Table 1. Dioxins and furans including WHO TEF values [27]

Congener	WHO 1998 TEF	WHO 2005 TEF
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD)	1	1
1,2,3,7,8-Pentachlorodibenzo-*p*-dioxin (1,2,3,7,8-PCDD)	1	1
1,2,3,4,7,8-Hexachlorodibenzo-*p*-dioxin (1,2,3,4,7,8-HxCDD)	0.1	0.1
1,2,3,6,7,8-Hexachlorodibenzo-*p*-dioxin (1,2,3,6,7,8-HxCDD)	0.1	0.1
1,2,3,7,8,9-Hexachlorodibenzo-*p*-dioxin (1,2,3,7,8,9-HxCDD)	0.1	0.1
1,2,3,4,6,7,8-Heptachlorodibenzo-*p*-dioxin (1,2,3,4,6,7,8-HpCDD)	0.01	0.01
1,2,3,4,6,7,8,9-Octachlorodibenzo-*p*-dioxin (OCDD)	0.0001	0.0003
2,3,7,8-Tetrachlorodibenzofuran (2,3,7,8-TCDF)	0.1	0.1
1,2,3,7,8-Pentachlorodibenzofuran (1,2,3,7,8-PeCDF)	0.05	0.03
2,3,4,7,8-Pentachlorodibenzofuran (2,3,4,7,8-PeCDF)	0.5	0.3
1,2,3,4,7,8-Hexachlorodibenzofuran (1,2,3,4,7,8-HxCDF)	0.1	0.1
1,2,3,6,7,8-Hexachlorodibenzofuran (1,2,3,6,7,8-HxCDF)	0.1	0.1
1,2,3,7,8,9-Hexachlorodibenzofuran (1,2,3,7,8,9-HxCDF)	0.1	0.1
2,3,4,6,7,8-Hexachlorodibenzofuran (2,3,4,6,7,8-HxCDF)	0.1	0.1
1,2,3,4,6,7,8-Heptachlorodibenzofuran (1,2,3,4,6,7,8-HpCDF)	0.01	0.01
1,2,3,4,7,8,9-Heptachlorodibenzofuran (1,2,3,4,7,8,9-HpCDF)	0.01	0.01
1,2,3,4,6,7,8,9-Octachlorodibenzofuran (OCDF)	0.0001	0.0003

Internationally there is evidence of an overall decreasing temporal trend of PCDDs and PCDFs in the general global population between 1992 and 2010 [39]. In addition there is consistent evidence that serum PCDD, PCDF, and some PCB concentrations are positively associated with age [39].

In New Zealand there have been a number of reports investigating dioxins and furans in humans (adult serum and breast milk) and the environment [19, 48, 58-64]. In 2001 the Ministry for the Environment published a health risk assessment for dioxins and furans [65] that estimated over 90% of New Zealanders' exposure coming from dietary sources, and this dietary intake was lower than any other country with comparable biological monitoring data. Nevertheless, the 2001 report

concluded that there was an “insufficient margin of safety” for background exposures to dioxins and furans in the New Zealand population, and recommended ongoing biological monitoring surveys every 5 to 10 years.

Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) are a range of industrial chemicals that were used in a wide range of commercial and industrial applications. The chemical properties and high thermal stability of PCBs made them ideally suited for use as heat transfer fluids, hydraulic fluids, dielectric fluids, and flame retardants [48, 66]. Similar to PCDD and PCDF, PCBs are characterized by 2 chlorine-substituted aromatic rings connected by a single carbon-carbon bond, with 209 congeners possible (Figure 2).

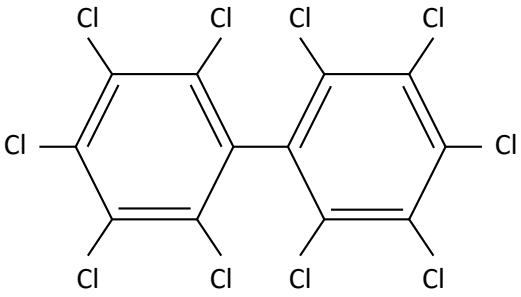


Figure 2. PCB209 with fully chlorine-substituted biphenyl structure.

Twelve PCB congeners have been classified as “dioxin-like”, that is they exhibit toxic effects similar to PCDD and PCDF and have had TEFs assigned by WHO (Table 2). Studies have shown the toxic effects of PCBs including neurodevelopmental effects in children [67], non-Hodgkin lymphoma [68], alteration of thyroid and reproductive function, cardiovascular disease, liver disease, and diabetes [69].

Table 2. Dioxin-like PCBs including WHO TEF values [27]

Congener	WHO 1998 TEF	WHO 2005 TEF
Non-*ortho*-substituted PCBs		
3,3',4,4'-Tetrachlorobiphenyl (PCB 77)	0.0001	0.0001
3,4,4',5- Tetrachlorobiphenyl (PCB 81)	0.0001	0.0003
3,3',4,4',5-Pentachlorobiphenyl (PCB 126)	0.1	0.1
3,3',4,4',5,5'-Hexachlorobiphenyl (PCB 169)	0.01	0.03
Mono-*ortho*-substituted PCBs		
2,3,3',4,4'-Pentachlorobiphenyl (PCB 105)	0.0001	0.00003
2,3,4,4',5-Pentachlorobiphenyl (PCB 114)	0.0005	0.00003
2,3',4,4',5-Pentachlorobiphenyl (PCB 118)	0.0001	0.00003
2',3,4,4',5-Pentachlorobiphenyl (PCB 123)	0.0001	0.00003
2,3,3',4,4',5-Hexachlorobiphenyl (PCB 156)	0.0005	0.00003
2,3,3',4,4',5'-Hexachlorobiphenyl (PCB 157)	0.0005	0.00003
2,3',4,4',5,5'-Hexachlorobiphenyl (PCB 167)	0.00001	0.00003
2,3,3',4,4',5,5'-Heptachlorobiphenyl (PCB 189)	0.0001	0.00003

PCBs have been studied extensively and are known to be ubiquitous in humans and the environment [39, 70]. In New Zealand PCBs are not permitted for any use and there is guidance for managing the storage and disposal of disused PCB stockpiles [71]. Levels of PCBs in New Zealand adult biological samples (breast milk and serum) have been shown to be low by international comparison [19, 62].

Organochlorine pesticides

Organochlorine pesticides (OCPs) were widely used in New Zealand agriculture and horticulture. OCPs include a wide range of pesticides, herbicides, fungicides, and other biocidal chemicals, legally used in New Zealand from the 1940's to the 1970's. A list of common OCPs is included in Table 3.

Table 3. Organochlorine pesticides (adapted from [58])

Hexacyclochloro-hexane (HCH)	Technical HCH is a mixture of five isomers α-HCH, β-HCH, γ-HCH, δ-HCH, and ε-HCH. Virtually all the insecticidal properties are resided in γ-HCH, commonly called lindane. Lindane is used to control lice, keds and blowflies on cattle and sheep, and grass grub in pasture and for household control of winged insects. Lindane is still approved in New Zealand as a treatment for scabies and lice in humans.
Pentachloro-benzene (PeCB)	PeCB was used as a component of a chlorobenzene mixture incorporated into PCB products to reduce viscosity, as a fungicide, flame retardant, and to combat oyster drills. PeCB has been found as an impurity in dyestuff carriers, as well as in herbicides, pesticides, and fungicides, including hexachlorobenzene. PeCB was used as a chemical intermediate for the production of pentachloronitrobenzene (quintozene) and is also produced unintentionally during thermal industrial processes.
Hexachloro-benzene (HCB)	HCB was used between 1970 and 1972 in New Zealand as an experimental seed dressing fungicide for cereal grains. HCB was also an impurity in the manufacture of chlorinated solvents and other chlorinated compounds including certain pesticides (e.g. pentachlorophenol).
Chlorinated cyclodienes	Aldrin and dieldrin are chlorinated cyclodiene insecticides used to control ectoparasites in sheep and to control horticultural and household pests. Dieldrin was also used as a timber preservative and in carpet treatment. The use of aldrin and dieldrin in New Zealand ceased around 1989. Aldrin breaks down into dieldrin in humans and the environment.
Endrin	Used as an insecticide, rodenticide, and avicide to control a range of pests on crops. Endrin is a stereoisomer of dieldrin. Very little endrin was used in New Zealand. Endrin aldehyde and endrin ketone occur as impurities or degradation products of endrin.
Heptachlor	Used as a soil and seed treatment for the protection of corn and grains, and to control ants, cutworms, maggots, termites, thrips, weevils, wireworms, termites, and household insects. Heptachlor is a component of chlordane (10% by weight). Heptachlor epoxide is an unintentional breakdown product of heptachlor and chlordane. Very little heptachlor was used in New Zealand.
Chlordane	Used to control a broad range of agricultural pests as well as controlling termites and borer for timber preservation, including as an additive in glues used for the manufacture of plywood, finger-jointed and laminated timber. Chlordane is a mixture of a number of chemicals including *trans*-chlordane (gamma-chlordane), *cis*-chlordane (alpha-chlordane), heptachlor, and *trans*- and *cis*-nonachlor. Oxychlordane is a metabolic degradation product of chlordane. The use of chlordane in New Zealand timber treatment ceased around 1989.

Dichlorodiphenyl-trichloroethane (DDT)	Used to control grass grub and porina caterpillars in pasture, lawns, market gardens and parks. DDT is listed as a POP under the Stockholm Convention, with specific exemptions for use and production in certain countries. Use of DDT in New Zealand to control grass grub (Costelytra zealandica) larvae in pasture was widespread. Thus, New Zealanders were historically exposed to DDT and continue to be exposed to DDT and its metabolites in ever-decreasing amounts through environmental sources. DDT breaks down to dichlorodiphenyltrichloroethylene (DDE) and dichlorodiphenyldichloroethane (DDD) in humans and the environment, of which DDE is the dominant metabolite because of its stability and persistence (Salihovic et al., 2016).
Mirex	Used as a pesticide to control fire ants in the southeastern USA, and as a flame retardant in plastics, rubber, paint, paper, and electrical goods. Mirex was never registered for use in New Zealand.
Endosulfan	Used on a range of vegetable, fruit and ornamental plants, and also used on turf at golf courses, bowling clubs, parks, sports grounds, and airports. Technical grade endosulfan contains 94% α-endosulfan and β-endosulfan with a ratio of 7:3 for α and β isomers. Endosulfan sulfate is a reaction impurity found in technical-grade endosulfan. Endosulfan was not used in aerial application or domestic use in New Zealand and was prohibited for import or use in 2008. Endosulfan is listed as a POP under the Stockholm Convention, with specific exemptions for use and production in certain countries.
Toxaphene	Used for control of insect pests on cotton and other crops in the southern USA, and for controlling other crop pests and pest fish. Toxaphene is a mixture of hundreds of different chlorinated camphene congeners and related chemicals. Congeners are named according to the Parlar system (after Dr. H. Parlar) according to their order of analytical detection. Toxaphene became a popular insecticide after worldwide bans on DDT. Very little toxaphene was used in New Zealand, where it was never registered for use.
Chlordecone	Chlordecone, also known by its trade name Kepone®, was introduced to New Zealand in 1958 as an experimental insecticide to control DDT-resistant apple leaf roller. Chlordecone could not be assessed in the current POPs survey because of analytical difficulties.
Methoxychlor	Used as an insecticide for a range of pests (e.g houseflies, mosquitoes, cockroaches) in crops, stored grain, livestock and domestic pets. Methoxychlor was developed as a replacement for DDT and the USEPA decided not to re-register it in 2004. Methoxychlor is not listed as a POP under the Stockholm Convention but is listed as persistent, bioaccumulative, and toxic chemical under the USEPA's Toxics Release Inventory (TRI) program. There is little information on the use of methoxychlor in New Zealand, though it was apparently used in sheep dipping and its use was banned in 1961 along with DDT, dieldrin, aldrin, and lindane.

Reported health effects from exposure to OCPs include cancer [72-76], endocrine disruption [77], metabolic syndrome [24], and adverse effects on reproductive health [78].

Levels of OCPs have previously been assessed in New Zealand breast milk [19] and adult serum [58]. These studies show relatively low levels of OCPs in New Zealand with the exception of DDE, which was comparable to international levels.

The rise of brominated and fluorinated POPs

Brominated POPs include the polybrominated biphenyls (PBBs) and polybrominated diphenyl ethers (PBDEs), commonly referred to as brominated flame retardants (BFRs). PBBs and PBDEs have been widely used since the early 1970's as flame retardants in a range of industrial applications and in plastic consumer goods, such as electronics and plastic foams (e.g. polystyrene). The use of PBBs was at a peak in the 1970's as the major component of the Firemaster™ flame retardant mixture, with production ceasing in 1974 after a major pollution incident in Michigan, USA [44].

PBDEs comprise 209 congeners of a brominated biphenyl structure, similar to PCBs, which are used in commercial flame retardant mixtures – the primary mixtures being the penta-, octa-, and deca-BDE formulations. Restrictions on the production of the penta-BDE formulation were established in the early 21st century. There is evidence that PBDEs, even the phased-out penta- formulation, are still present in consumer products and indoor environments [79, 80]. PBDE exposure is associated with adverse neurodevelopmental effects on young individuals of a range of organisms, including human children [81, 82]. Likely future restrictions on the production and use of the octa-, and deca-BDE formulations have prompted the manufacturers of flame retardants to produce and sell alternatives such

as tetrabromobisphenol A (TBBPA), decabromodiphenyl ethane (DBDPE), and hexacyclobromododecane (HBCD).

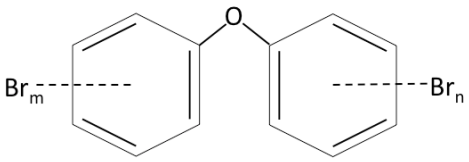
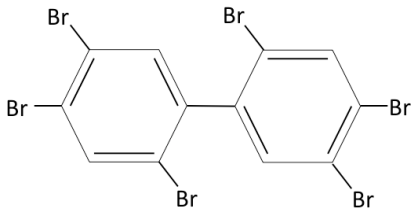
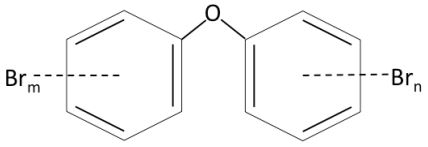
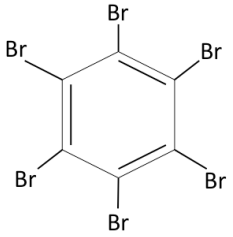
The 1950's saw the large-scale development of the industrial production of perfluorinated alkyl substances (PFASs) for use in many commercial applications, ranging from oil and water repellant coatings on fabrics to fire-fighting foams [11, 83]. PFASs are not naturally occurring and they persist for decades in the environment [84] and for years in humans that are exposed to them through water, food, air, and contact with consumer and industrial products [11]. There is emerging evidence, mostly from animal studies, that adverse effects on organisms from PFAS exposure and accumulation include hepatoxicity, developmental toxicity, immunotoxicity, hormonal effects, and carcinogenicity [11]. In 2004, the largest global manufacturer of PFASs voluntarily restricted the production of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), two of the most commonly studied PFASs.

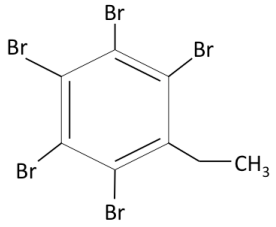
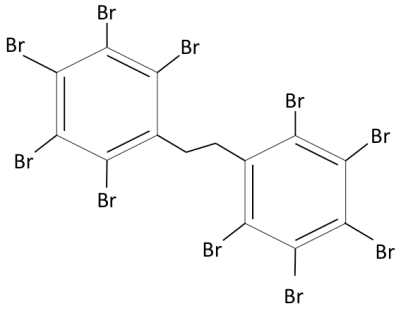
Brominated flame retardants

Brominated flame retardants (BFRs) are a broad class of synthetic organic chemicals that were incorporated into a wide range of manufactured articles to improve fire resistance [8]. Common flame retardants that have been used since the 1970's include polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane (HBCD), tetrabromobisphenol A (TBBPA), and polybrominated biphenyls (PBBs) (Table 4). BFRs are incorporated into manufactured goods as an additive component of raw plastics, however many BFRs are simply added after manufacture and are therefore not chemically bonded to the articles. BFRs were added to a wide range of consumer articles including computers, televisions, fabrics, and carpet underlay. During use of these articles, BFRs are released from these

articles during their use, and they have been shown to be ubiquitous indoor and outdoor environmental contaminants [85]. BFRs have been shown to accumulate in household dust and in food, key exposure pathways for humans [86-90]. Accumulation of BFRs in human breast milk is an area of global concern and the World Health Organisation has coordinated 4 rounds of an international survey of BFRs in breast milk between 1988 and 2009 [91].

Table 4. Selected brominated flame retardants (BFRs)

Chemical Name	Chemical Structure
BFRs listed under the Stockholm Convention	
<u>Commercial pentabromodiphenyl ether (C-PentaBDE):</u> C-PentaBDE is a mixture of tetrabromodiphenyl ethers (BDE40 to BDE81, m=2, n=2) and pentabromodiphenyl ethers (BDE82 to BDE127, m=2, n=3). BDE47 and BDE99 are the two main components of C-PentaBDE.	
<u>Commercial octabromodiphenyl ether (C-OctaBDE):</u> C-OctaBDE is a mixture of nonabromodiphenyl ethers (BDE206 to BDE 208, m=4, n=5), octabromodiphenyl ethers (BDE194 to BDE205, m=4, n=4), heptabromodiphenyl ethers (BDE170 to BDE193, m=4, n=3) and hexabromodiphenyl ethers (BDE128 to BDE169, m=3, n=3). Different C-OctaBDE formulations include varying percentages of these components, typically with the highest proportion from heptaBDEs and octaBDEs.	
Hexabromobiphenyl (HBB) has 42 isomeric forms and belongs to the wider group of polybromobiphenyls (PBBs). The common commercial formulation (Firemaster®) contains several PBBs with HBB as the principal component.	
BFRs determined in this study but not listed under the Stockholm Convention	
Monobrominated diphenyl ethers (BDE1 to BDE3, m=1, n=0) Dibrominated diphenyl ethers (BDE4 to 15, m=1, n=1) Tribrominated diphenyl ethers (BDE16 to BDE39, m=2, n=1) Decabromodiphenyl ether (BDE209, m=5, n=5)	
Hexabromobenzene	

Pentabromoethylbenzene (PBEB)	
Decabromodiphenylethane (DBDPE)	

Though the level of knowledge on health effects of BFR exposure is limited [92], BFRs are associated with neurological effects [93] and disruption of thyroid homeostasis [94, 95]. The exposure of general populations to BFRs is highly variable from country to country, and within countries [96].

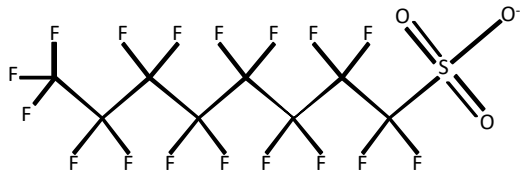
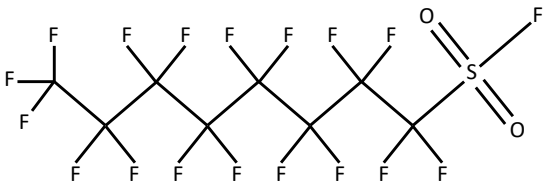
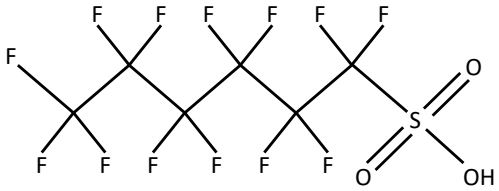
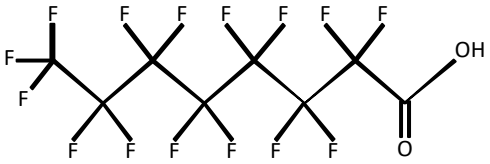
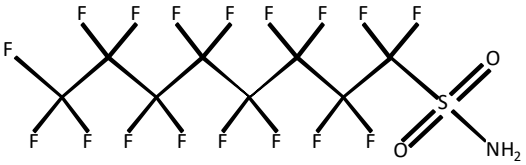
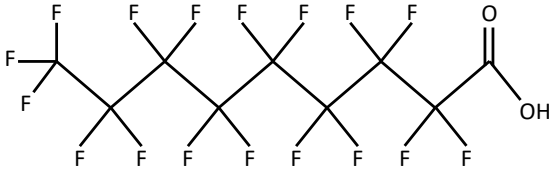
New Zealand has participated in 3 rounds of the WHO-coordinated survey of BFRs in breast milk [19] and the importance of dust as an exposure pathway for BFRs in breast milk has been investigated in several studies [38, 97, 98]. PBDEs have been previously assessed in human serum samples of Wellington adults in 2001 [99].

Perfluorinated alkyl substances

Perfluorinated alkyl substances (PFASs) are a class of synthetic chemicals with unique physico-chemical properties. Their chemical structure is comprised of a fully-fluorinated hydrophobic carbon chain connected to a hydrophilic functional group (Table 5). The chemical structure of PFASs means they repel water, grease, and oils, and they have high

chemical and thermal stability, and resistance to degradation [11]. The most commonly studied PFASs are perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA).

Table 5. Common perfluorinated alkyl substances (PFASs)

Perfluorooctane sulfonate (PFOS)	
Perfluorooctane sulfonyl fluoride (PFOSF)	
Perfluorohexanesulfonic acid (PFHxS)	
Perfluorooctanoic acid (PFOA)	
Perfluorooctanesulfonamide (PFOSA)	
Perfluorononanoic acid (PFNA)	

PFASs were developed in the 1950s and were used in a wide range of industrial applications and consumer goods, including fabric treatments, food packaging materials, electronic

devices, cleaning agents, cosmetics, and fire-fighting foams [11]. PFOS, its salts, and PFOSF are including in the Stockholm Convention, and their use has been controlled in Europe, the USA, and Canada. International restrictions on PFOS prompted the largest manufacturer to cease manufacture of all PFOS compounds in 2002.

The widespread use of PFASs has resulted in their ubiquitous presence in the environment and humans are exposed to PFASs through air, household dust, food, and drinking water [100]. There have been relatively few studies of the human health effects of PFAS exposure, with most studies showing inconclusive evidence of health effects [101]. Animal studies show associations with PFAS exposure and cancer as well as effects on the liver, immune, and endocrine systems; however there is limited epidemiological evidence of such effects in humans [102]. There have been no previous studies in New Zealand of PFAS exposure, however recently Auckland Council has included PFOS in their list of chemicals of concern when investigating organic contaminants in shellfish [103].

Mechanisms of toxicity

While it is outside the scope of this chapter to provide a full description of the mechanisms of toxicity associated with POPs, it is useful to include some general information on proposed models of toxicity arising from human and animal toxicity studies. The main toxicological end-points of POPs exposure in humans and animals can be grouped into three categories, namely endocrine disruption, cardiovascular disease, and neurotoxicity.

It can be argued that disruption of the biological endocrine system is the fundamental mechanism by which POPs cause human disease. Diseases associated with background (i.e. non-occupational) exposure to POPs are diverse, including breast cancer [104], prostate

cancer [105, 106], testicular cancer [107, 108], diabetes [109], metabolic disorders [110], and altered reproductive function [111, 112]. All these diseases are associated with endocrine disruption and their incidence and prevalence have increased markedly since the 1960's when global POPs use was at its peak [24]. Increased prevalence of many of the reported diseases may be the result of many factors, including increased diagnosis, however there is sufficient evidence and a plausible biological mechanism to explain the pathway by which POPs act upon the endocrine system.

Endocrine disrupting chemicals are a heterogeneous group including a wide range of ubiquitous synthetic industrial chemicals, displaying estrogenic, androgenic, antiestrogenic, and antiandrogenic properties. Endocrine-disrupting chemicals affect receptors in the hormonal and homeostatic systems (e.g. aryl hydrocarbon receptor AhR), pathways related to biosynthesis of steroids and metabolism, and many other biological systems comprising the nexus of the endocrine system including the human reproductive system [113-115]. Interaction of dioxins, furans, PCBs, and OCPs with the AhR receptor has been studied extensively in animal and human studies [4], and goes a long way in explaining observed effects on reproductive and neurological development, and cardiovascular health associated with these chemicals.

The timing of exposure is a critical variable in understanding the potential for an endocrine-disrupting chemical to elicit adverse health effects [116]. Therefore, the specific role of POPs in the apparent increase in endocrine system-related disease cannot be fully evaluated without a clear understanding of temporal variations in POPs exposure, within an individual's lifetime and over the decades in which humans and wildlife have been exposed to POPs.

POPs are concentrated in adipose tissue (AT) of living organisms, which has the benefit of protecting other body tissues from exposure to a POPs body burden [117]. However, the role of AT in physiological function, including endocrine and metabolic functions, has received considerable attention [118]. There is emerging evidence that POPs contribute to lipotoxicity, inflammation of AT, and dyslipidemia resulting in disruption of metabolic and endocrine systems [117]. The importance of AT as a reservoir of POPs is shown in studies of drastic weight loss and consequent releases POPs from AT [119-121] resulting in increased risk of metabolic disorders and liver toxicity [122].

The role of POPs in the etiology of cardiovascular disease (CVD) has been investigated, with inconclusive findings. Epidemiological studies have shown associations of CVD with POPs, for example in a large cohort study of people exposed to high concentrations of dioxins in the 1976 Seveso incident who suffered increased mortality from CVD in the years after the incident [123]. In a systematic review of available cohort studies (the majority of which were highly-exposed individuals in accidents or occupational settings) investigating the association of CVD and POPs exposure [124] the authors conclude that the available studies are limited by a lack of consideration of confounding from major CVD risk factors (i.e. smoking, physical exercise, diet, alcohol consumption).

There is evidence from *in vivo* and *in vitro* animal studies that serum POPs are associated with CVD through an increase in atherogenic (promoting fatty deposits in the arteries) serum lipids [125], and oxidative stress on endothelial cells [126]. However, evidence from population-based studies of background POPs exposure is insufficient to provide evidence of a role for POPs in the etiology of CVD and further study is needed in this area [127].

Over the past 10 years, a number of research programmes have investigated the adverse effects of POPs on mental and physical development. There is evidence that BFRs affect neurological development in young animals, including humans, and these deficits persist into later life as reduced intelligence and behavioural changes [128, 129], and altered sexual development [81, 130, 131]. Animal studies have shown effects of high BFR exposure on liver and thyroid gland function [132], as well as effects on the endocrine system [133]. It is hypothesized that BFRs, particularly polybrominated diphenyl ethers (PBDEs), bind to estrogen, progesterone, androgen, and glucocorticoid cellular receptors resulting in inhibition of enzymes for steroid production in animal studies [134]. In humans, there is evidence that BFRs cause neurotoxicity by disruption of thyroid hormone thyroxin homeostasis resulting in hypothyroidism [135], as well as affecting all levels of neurotransmission [136]. Similar neurotoxic effects in humans have been shown for PCBs, resulting from changes in neurotransmitter systems, altered intracellular signaling processes, and imbalance of thyroid hormones [137, 138].

The Stockholm Convention

The Stockholm Convention is an international treaty to protect human health and the environment from POPs. The convention entered into force for New Zealand in 2004, and an implementation plan was developed by the Ministry for the Environment [2]. The National Implementation Plan (NIP) includes strategies for minimising dioxin emissions, phasing PCBs out of existing uses, managing POPs-containing waste and contaminated sites, and monitoring POPs in humans and the environment. The New Zealand Environmental Protection Authority (EPA) sets controls on the import, export and management of POPs under the requirements of the Hazardous Substances and New Organisms (HSNO) Act 1996

and associated regulations. The Ministry of Health coordinates a number of programs to reduce the adverse effects of POPs on the New Zealand population, including surveys of occupational exposure [139], health support services, and provision of advice to medical practitioners and the public (www.health.govt.nz). The Ministry of Health is the key agency with responsibility for delivering national surveys of POPs in the general population, including the 2012 POPs serum survey and breast milk surveys that are the foci of this thesis.

Human biological monitoring

Fundamentally, human biological monitoring (HBM) is the systematic investigation of concentrations of chemical substances in human biological tissue (e.g. blood, urine, breast milk, feces) to assess potential human health risk [140]. Some of the earliest examples of systematic HBM surveys were assessment of blood lead concentrations in lead smelting workers [141, 142] and in non-occupationally exposed individuals [143]. Such studies paved the way for further research into the human health effects of lead, particularly on the developing brains of children, eventually leading to worldwide restrictions on environmental lead emissions in the 1970's [142]. With the increase of global awareness and concern of environmental chemicals in the 1960's and 1970's, and advances in analytical chemistry technology (e.g. atomic absorption spectroscopy) HBM developed into a reliable tool to measure human exposure to a wide range of anthropogenic chemicals. Modern HBM involves the standardised collection of human tissues including whole blood, urine, and breast milk from a representative sample of the population and analysis for a range of environmental chemicals.

The results of HBM are often combined with other demographic datasets collected through surveys or public registers (e.g. census demographic data) to identify determinants of exposure. This is a key strength of HBM in that it can identify populations that may be at higher risk from exposure to toxic chemicals, for example exposure of children to lead. Government and regulatory authorities use HBM results to guide policy decisions to reduce peoples' exposure to chemicals that may adversely affect their health and wellbeing [140]. For example, HBM results from the German Environmental Survey (GerES) are used by national authorities to establish reference values for characterising background exposure to environmental chemicals in the general population [144]. Considerable international attention has been focused on the use of HBM data in regulatory human health risk assessment, with a need for further research into the relationships between exposure and effect, validation of biomarkers, inter- and intra-individual variability in exposure, and the development of novel biomarkers of exposure [145, 146].

Currently, HBM employs sensitive laboratory analytical methods to quantify a wide range of chemicals in humans. Analytical techniques have advanced to the point that chemicals may be detected in human biological matrices at trace and ultra-trace concentrations (e.g. parts per billion), which are suitable for the determination of background concentrations of thousands of environmental chemicals in the general population [147]. The most effective analytical techniques for measuring POPs in human biological samples are atomic absorption spectroscopy (AAS), inductively coupled plasma–mass- spectrometry (ICP-MS), gas chromatography-mass spectrometry (GC-MS), gas chromatography-tandem mass spectrometry (GC-MS/MS), and liquid chromatography-tandem mass spectrometry (LC-MS/MS) [148]. In brief, these analytical techniques involve the following steps; sample

pretreatment, sample preparation and extraction, sample clean-up and fractionation, chromatographic separation, and instrumental analysis. Measured concentrations of POPs are often normalised to a physicochemical parameter, such as blood or breast milk lipid concentration, to account for differences in biological parameters between individuals [147, 150, 151].

As concentrations of POPs decrease in the general population there is a need for more sensitive techniques to monitor background concentrations, with resultant needs for specialised staff, ultra-clean laboratory spaces, and quality assurance/quality control (QA/QC) protocols. The availability of sub-ultra-trace analytical laboratory capability for large numbers of samples is confined to few large laboratories internationally, however smaller labs are able to analyse limited numbers of samples to a suitable detection limit [152].

HBM may be repeated at regular intervals to allow for the assessment of temporal changes in the population; however, the survey sample is not usually preserved between surveys so the surveys are generally cross-sectional in nature. For example, the US National Health and Nutrition Examination Survey (NHANES) uses a probability-based sampling design to select a representative sample of the civilian, non-institutionalised population for each of its bi-annual surveys of a wide range of environmental chemicals [153]. Ethical considerations such as prior informed consent for participants, secure handling and storage of biological samples, and participant confidentiality are key elements of HBM that must be addressed by HBM researchers [154].

International human biological monitoring of POPs

Internationally, there have been many published studies of POPs in humans, focusing on non-occupationally exposed adults. A review of PCDDs, PCDFs, and PCBs assessed in humans between 1989 and 2010 identified 187 studies from 26 countries [39]. Similarly, there have been at least 48 and 55 studies of PBDEs in serum and breast milk, respectively, in North America, Australasia, Asia/Africa, and Europe [96]. A global review of temporal trends of POPs in human breast milk identified 235 separate studies [155]. A review of PFASs in western countries included 35 separate studies of PFASs in non-occupationally exposed adults [11].

However, there have been relatively few studies conducted to estimate concentrations of POPs in the general population of countries, as opposed to specific regional, demographic, or occupational groups. An international review [30] suggests that "truly population-wide surveys" have only been conducted in the USA, Germany, Belgium, France, New Zealand, Japan, Australia, the Arctic region, and the Canary Islands. The key findings from surveys of POPs in general populations are:

1. Levels of PCDDs, PCDFs, OCPs and some PCBs in humans have decreased over the period 1989 to 2010.
2. There is a strong positive association with age for PCDDs, PCDFs, and PCBs; that is there are generally higher concentrations in older individuals.
3. Exposure to BFRs is highly variable between countries, and within countries.
4. There is evidence of reduced exposure to certain BFRs (i.e. PBDEs) after the year 2000.
5. Levels of PBDEs are consistently higher in children compared to adults.
6. Levels of PFASs do not show a consistent association with age.

7. Levels of PFASs are generally lower in women compared to men, however the influence of other socioeconomic and lifestyle predictors is not well-established.

While it is beyond the scope of this chapter to review all POPs biological monitoring studies, the next sections summarise published international studies that were designed to estimate central tendency concentrations of POPs in the general population, including studies from the USA, Canada, Australia, Sweden, Spain, and Germany. These surveys were selected because they provide results that are contemporary to the current New Zealand POPs survey and are frequently referenced in subsequent chapters of this thesis.

The results of international POPs surveys reveal key demographic trends of POPs, particularly related to age and sex. For the "traditional" POPs such as dioxins, furans, PCBs and OCPs there is a clear trend of higher concentrations in older age groups. For the newer POPs such as BFRs and PFASs, age trends are not as consistent, with some evidence of higher BFRs in younger age groups, and lower PFASs in females compared to males.

USA:

A comprehensive study of POPs in humans was completed as part of the USA's *National Health and Nutrition Examination Survey*, or NHANES [153]. NHANES includes a range of studies to assess health and nutritional status of American adults and children. Biological specimens, including blood serum, have been collected in NHANES since the 1970's from approximately 5,000 participants per year. Since 1999, NHANES has collected biological specimens and survey information from participants in bi-annual survey periods using a "complex, stratified, multistage, probability-cluster design to select a representative sample of the civilian, non-institutionalized population in the United States based on age, sex, and

race/ethnicity" [153]. Serum samples have been tested for PCDDs, PCDFs, PCBs, OCPs, BFRs, and PFASs in all the NHANES periods. The most recent NHANES results, including all previous results, are reported in the *Fourth Report on Human Exposure to Environmental Chemicals* [153]. PCDDs, PCDFs, PCBs, and OCPs were measured in a one-third sub-sample of participants aged 12 years and older in 1999-2000 and 2003-2004, and in participants aged 20 years and older in 2001-2002. Prior to the 2005-2006 survey individual samples were analysed for PCDDs, PCDFs, PCBs, OCPs, and BFRs, and in subsequent surveys a weighted-pool design was adopted to achieve better laboratory detection limits and reduce the cost of analysis for these analytes. PFASs continue to be analysed in individual samples.

Geometric mean concentrations of all PCDDs and PCDFs measured in NHANES decreased between study periods 1999/2000 and 2003/2004, when individual samples from participants over 20 years old were analysed [153]. Between 2005/2006 and 2007/2008, weighted arithmetic mean results for pooled samples from over 20-year olds similarly decreased in NHANES for all measured PCDDs and PCDFs [153]. Concentrations of PBDEs, PCBs, and OCPs in the NHANES surveys have decreased from 2003/2004 to 2007/2008 [156]. Data from NHANES during the period 1999 to 2008 showed a decrease in PFOS in adults [157]. Serum concentrations of PFHxS also decreased over the period 1999 to 2006, then increased in 2007/2008. Concentrations of PFOA remained steady during the period of the NHANES study, and PFNA increased during the study period. Demographic factors also contributed to PFAS concentrations in the US general population, with males having generally higher levels for all PFASs. However, there was no consistent age association for PFASs. The NHANES results show that predictors of PFAS concentrations in the general population are not well characterised.

Canada:

The *Canadian Health Measures Survey* (CHMS) established representative serum concentrations of POPs in Canadians aged 6 to 79 years [158]. There have been 3 cycles of the CHMS in 2007/09, 2009/11, and 2012/13. Data from Cycle 1 of the CHMS has been published for pooled serum concentrations of PCDDs, PCDFs, and PCBs [159], showing a positive association of these POPs with age. There were no associations with sex for PCDDs, PCDFs or PCBs. Concentrations of BFRs in Canadian pooled serum samples showed lower concentrations in the older participants [160]. In addition, PFAS concentrations were shown to be generally higher in males compared to females [161].

Analysis of PCDD/Fs and PCBs in Canadian breast milk shows a consistent decrease over the 20 year period, with TEQ_{05} concentrations in 2011 one-third those assessed in 1992 [162, 163].

Australia:

Australian researchers have completed a series of human biological monitoring surveys of POPs in human serum and breast milk, in adults as well as in children. PCDD, PCDF and PCB in pooled adult serum samples collected in 2003 from children and adults showed levels lower than international values, and similar to New Zealand results from the 1997 survey, though New Zealand samples compared were collected 6 years earlier [164]. There was a positive association with age in participants >25 years old, however there were no consistent differences in PCDD, PCDFs, or PCBs between males and females, or between regions.

Further pooled Australian adult serum samples were collected from pathology labs in 2010/11 and 2012/13 and tested for PCDD/Fs, PCBs, OCPs, BFRs, and PFASs [165]. These results showed a decrease in all POPs concentrations from the 2003 Australian survey, for example approximately 50% decrease in dioxin-like PCBs and BFRs over the 10-year period. Similar temporal reductions of POPs have been shown in Australian breast milk studies [165, 166]

OCPs have been assessed in pooled Australian serum samples collected over five time periods 2002/03, 2006/07, 2008/09, 2010/11, 2012/13 [167]. There was a significant decrease in most OCP levels between 2002/03 and 2012/13, with higher levels of OCPs in older age groups, and in females.

BFRs in Australian serum samples did not change between 2002/03 and 2008/09 [168, 169]. PBDEs in Australians were higher than in Europe, the United Kingdom, and Asia but lower than the USA. Levels of PBDEs were higher in children, with the lowest concentrations detected in adults >31 years old. The measured PBDEs did not show an association with sex, except for BDE153 that was higher in males. PBDEs in Australian human milk were at lower levels than North America, but higher than Europe and Asia [170].

PFASs were measured in Australian pooled serum samples taken in 2002 to 2013 in children and adults [171-174]. The majority of PFASs decreased between 2002 and 2013. Concentrations of most PFASs were higher in children compared to adults, but there was no clear association with age when only adults were considered. For some PFASs (e.g. PFOS) levels were higher in males.

Sweden:

Sweden has participated in the WHO global survey of POPs in breast milk, measuring POPs samples collected between 1972 and 2011 from Swedish mothers [175]. In these studies, concentrations of PCDDs, PCDFs, and PCBs in breast milk decreased over the 40-year period, and the rate of decrease of POPs in breast milk was higher in the last ten years than in the last 40 years.

Spain:

Participants in the *Catalonia Health Survey* and *Barcelona Health Survey* provided serum samples for testing of OCPs and PCBs in 2002 and 2006 [176, 177]. Concentrations of OCPs and PCBs decreased during the period 2002 to 2006. Age was positively associated with serum concentrations of these POPS, and for some POPs concentrations were higher in females. Between 2008 and 2013 the MCC-Spain study analysed POPs in serum from older adults in four Spanish regions; Barcelona, Madrid, Cantabria, and Navarra [178]. In the MCC-Spain study age was positively associated with serum concentrations of HCB, *p,p'*-DDE, and PCB180. Residence in an urban area was associated with PCB153 serum concentrations.

Germany:

Median concentrations of PCDD, PCDF, and PCBs in German adults living in Munich and the surrounding area (n=42 aged 20 to 68 years) were measured in samples collected in 2013 [179]. TEQ_{05} (PCDD+PCDF+PCB) was 11.6 pg TEQ_{05}/g lipid compared to New Zealand's 7.35 pg TEQ_{05}/g lipid. The German survey showed an increase of chlorinated POPs with age, but no association with sex.

Temporal trends of POPs in humans

The cross-sectional nature of most HBM surveys creates challenges for investigating temporal trends of POPs. Researchers infer temporal trends within specific groups by statistical comparison of results from sequential surveys with consistent demographic strata (e.g. females aged 19-34). To obtain a more detailed understanding of temporal trends of POPs in humans pharmacokinetic (PK) models have been used to clarify intake and elimination of POPs, taking into account temporal variation in POPs emissions scenarios [31, 180]. PK models provide helpful insight into temporal trends of POPs during periods of peak exposure, and in post-ban periods for those POPs that are prohibited worldwide. Mechanistic time-variant models of cross-sectional body burden-versus-age trends (CBATs) have been used to clarify apparent different age-related associations for POPs with different emissions scenarios and elimination half-lives [28]. For example, CBATs for PCBs show a consistent positive age-related increase, which is contrasted by BFRs that show a negative age-related association – this difference can be explained principally by differences in (a) the time since peak emissions and (b) the human metabolic elimination rates for these different chemical classes.

An example of the influence of time of sampling on CBATs for PCB153 is illustrated in Figure 3 [28]. These CBATs illustrate how the age-related association for PCB153 in females changes from a period of increasing emissions (1968), to a period where emissions have ceased for approximately 20 years (2000), and finally a future period (2030). Note that the average concentration for all ages increases during the period 1968 to 2000, reflecting an even higher body burden sometime between these 2 periods; that is, the period of peak exposure was likely in the 1980's shortly before global controls on PCBs were enacted. Also

of interest in these CBATs is a spike in PCB153 concentrations in the youngest age group (0-5 years) resulting from exposure to POPs in breast milk, which is matched by a small decrease in POPs in females approximately 30 years old (i.e. loss of POPs from breast-feeding).

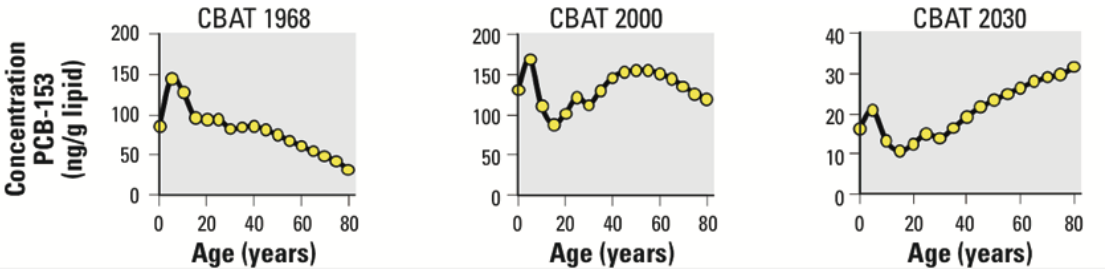


Figure 3. CBATs for PCB153 at different time periods

Image source: Environmental Health Perspectives, April 2012, Vol. 120 Issue 4, p554-559. Reproduced with permission from the author.

While PK and time-variant mechanistic models provide useful information on temporal changes of POPs in humans, these models are subject to certain limitations. In particular, emissions scenarios used as input parameters to the models are often based on imprecise historical estimates of POPs release from a multitude of sources [181]. Changing global phenomena such as the influence of climate change on the global distribution and fate of POPs may also influence current and future exposure and emissions scenarios [43, 182, 183]. In addition, there are no internationally accepted standardised methods for conducting studies to generate cross-sectional HBM data. Differences in study design (e.g. inconsistent categorisation of age groups) may introduce large uncertainties in the accuracy of the model estimates [180].

Chapter 3. Comparison of New Zealand and international temporal trends of chlorinated POPs in human milk, 1985 to 2008

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Abstract

There is global concern over the exposure of breast-feeding infants to toxic persistent organic pollutants (POPs) in human milk. A number of countries regularly monitor POPs in human milk, including New Zealand since 1988. In this research we used an internet search of published international results for POPs in human milk to compare the temporal trend of human milk concentrations in New Zealand with those reported for other countries. Since the 1980s, concentrations of chlorinated POPs in human milk have decreased in New Zealand and internationally. Current concentrations of chlorinated dioxins and furans, and polychlorinated biphenyls are lower in New Zealand than most other countries. However, dichlorodiphenyltrichloroethane (DDT) and its related compounds are in the middle of the international range. The research, along with recent estimates of infant exposure to chlorinated POPs in New Zealand, suggests a potential risk to infant health despite the declining trend of these chemicals in human milk. Ongoing monitoring of POPs and other chemicals of concern in human milk is recommended for assessing health risks for mothers and their children, particularly in countries for which contemporary breast milk concentrations of these compounds are known to be high.

Introduction

Persistent organic pollutants (POPs) are a group of toxic compounds, with chlorinated POPs including polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs), the most frequently studied because of high historic exposure and proven toxicity [4, 184]. While the production and use of chlorinated POPs has reduced significantly, most can still be detected in human tissue today, due to their long half-lives and persistence in the environment. Exposures to chlorinated POPs, while largely historical, thus continue to have potential impacts on human health, even for the youngest generations. For example, New Zealand infants' estimated daily intakes of DDT and dioxin-like compounds via human milk, although low compared to many other countries, still exceed the tolerable daily intake [185]. Continued reductions in human tissue levels of chlorinated POPs are desirable and may be predicted based on the temporal trends of chlorinated POPs observed over the past decades.

Human milk has been the matrix of choice in the biomonitoring of POPs due to its high lipid content and non-invasive collection. Since the 1980s most human milk monitoring of POPs has been conducted as part of a global WHO-UNEP initiative (United Nations Environment Programme, 2013). There have been five rounds of the WHO-UNEP initiative, with UN member countries participating on a voluntary basis. However, current knowledge on temporal changes of human milk concentrations of chlorinated POPs is based on only a very small number of countries, with a 2015 review [155] including temporal trends only for Japan and Sweden, which were the only countries that completed 5 surveys.

New Zealand participated in 3 rounds of the WHO-UNEP initiative in 1988, 1998, and 2008 [19, 61, 186], enabling the assessment of a temporal trend of chlorinated POPs in New Zealand [36]. How this compares to other countries has not previously been evaluated, nor were New Zealand's results of the WHO-UNEP initiative's 4th round included in a recent review of the results from the last rounds of the initiative [187].

In this paper we compare: (1) the temporal trend of human milk concentrations of chlorinated POPs in New Zealand with those reported for other countries; and (2) contemporary concentrations of chlorinated POPs (collected in 2008) in New Zealand to those reported for other countries that collected samples within a comparable time frame.

Methods

New Zealand results on human milk concentrations of chlorinated POPs, and estimated infant intakes during breast-feeding, have been previously reported [19, 185]. Other international studies with temporal trend data for chlorinated POPs were identified through a search of peer-reviewed journal articles on Scopus and PubMed. We included studies (Table 6) from countries that: (1) carried out at least 2 comparable surveys during the period 1985 to 2015; (2) included participants that were representative of breast-feeding mothers of the general population; and (3) published results in a format that allowed collection of information on individual POPs.

For most of the studies data for individual PCDD, PCDF, and PCB congener data and OCPs other than DDT were not consistently reported. We therefore focused on toxic equivalents (TEQ_{05}) for PCDD/Fs and PCBs [57], and the sum of DDT congeners (DDT+DDD+DDE). For countries that reported temporal trends for specific DDT compounds but not total DDT, the sum of all DDT compounds (DDT, DDD, and DDE) was calculated. While not all studies reported all DDT compounds, all of the included studies report at least DDT and DDE, the two DDT congeners typically found at the highest concentrations in human biological samples [188]. If studies reported multiple results for the same year, the mean was taken as the result for that year.

1

Table 6. Studies included in the review of temporal trends

Country	Reference	Year of sample collection	Number of participating mothers	Compounds analysed
New Zealand	[186]	1988*	38	PCDD, PCDF, PCB^
		1998*	53	PCDD, PCDF, PCB
		2008*	39	PCDD, PCDF, PCB
	[63]	1988*	37	DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
	[61]	1998*	53	DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
	[19]	2008*	39	DDT (p,p'-DDE, p,p'-DDD, o,p'-DDT, p,p'-DDT, o,p'-DDD, o,p'-DDE
Australia	[166]	1993	24 (3 pools)	PCDD, PCDF, PCB
		2002/2003*+	157 (17 pools)	PCDD, PCDF, PCB
	[189]	1993	24 (3 pools)	DDT (p,p'-DDE, p,p'-DDD, o,p'-DDT, p,p'-DDT)
		2002/2003*+	157 (17 pools)	DDT (p,p'-DDE, p,p'-DDD, o,p'-DDT, p,p'-DDT
	[165]	2008/2009*	Not specified	PCDD, PCDF, PCB, DDT (p,p'-DDE, p,p'-DDD, o,p'-DDT, p,p'-DDT)
		2012/2013*+	20 (2 pools)	PCDD, PCDF, PCB, DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
Czech Republic	[190]	1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2005, 2006, 2007, 2008, 2009	4,753 (approximately 300 individuals per year)	DDT (p,p'-DDE, p,p'-DDT)
Ireland	[53]	2001/2002*	37 (4 pools)	PCDD, PCDF, PCB
		2010*	109 (11 pools)	PCDD, PCDF, PCB
France	[191]	1999	244	PCDD, PCDF
		2007	44	PCDD, PCDF
Canada	[192]	1986/1987*	100 (10 pools)	PCDD (excluding 1,2,3,6,7,8-HxCDD), PCDF (excluding 1,2,3,7,8-PeCDF, 1,2,3,6,7,8-HxCDF, 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9-HpCDF, OCDF
	[163]	1992*	150	PCDD, PCDF, PCB

Country	Reference	Year of sample collection	Number of participating mothers	Compounds analysed
		2001/2002*	38 (18 for PCBs, 20 for PCDD/Fs)	PCDD, PCDF, PCB
		2005*	34	PCDD, PCDF (excluding 1,2,3,7,8,9-HxCDF), PCB
	[162]	2008/2011	298	PCDD, PCDF (excluding 1,2,3,7,8,9-HxCDF), PCB
	[193]	1986	412	DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
	[194]	1992	497	DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
USA	[195]	1986, 1987, 1993, 2005	942, 7 (1 pool), 98, 6	DDT (p,p'-DDE, o,p'-DDT, p,p'-DDT)
Sweden	[175]	1989, 1990, 1991, 1992, 1995, 1997, 1999, 2000, 2001, 2002, 2003, 2004, 2007, 2008, 2009, 2010, 2011	574 (18 to 140 samples per year)	PCDD, PCDF, PCB
	[196]	1985, 1989, 1990, 1991, 1992, 1994, 1996, 1997	422 (20 to 140 samples per year)	DDT (p,p'-DDE, p,p'-DDT)

^ Insufficient PCB congeners were measured to calculate TEQ

* Recruitment inclusion criteria and methodology are consistent with the WHO guidelines.

+ Age range of mothers is outside WHO guideline criteria

International data on the contemporary human milk concentrations of chlorinated POPs were identified from a recent review of the 4th/5th round of the WHO-UNEP initiative [187]. The 2017 global review included all the countries that submitted a pooled human milk sample during the period 2005 to 2015 to the WHO reference laboratory. To enable a direct comparison a New Zealand pooled milk sample was created from the 2008 individual human milk samples [19] and analysed for chlorinated POPs by the same WHO reference laboratory (State Laboratory for Chemical and Veterinary Analysis of Food, Freiburg, Germany).

Mean concentrations of chlorinated POPs were extracted from tables in the published reports. One report [190] only presented results in figures, so graphical interpolation methods and software were used to obtain mean concentrations (GetData Graph Digitizer [computer software] version 2.26, 2013, Russia).

Results

Figure 4 presents data for PCDDs and PCDFs (TEQ_{05}), with country-specific time trend data on the left hand line plot and the country-specific contemporary concentrations on the right hand bar plot. The figure indicates that for all 6 countries that had trend data available, the human milk concentrations of PCDDs/PCDFs have decreased substantially over time, with New Zealand's time trend similar to those reported for Australia and Sweden. Comparing New Zealand's current PCDDs/PCDFs human milk concentrations to those reported for other countries places New Zealand among the countries in the world with the lowest current human milk concentrations for PCDDs/PCDFs.

Figure 5 presents the data for PCBs (TEQ_{05}). Time trend data were available for only 5 countries. A clear decrease in PCB human milk concentrations over time was apparent for Sweden, Canada and New Zealand, with New Zealand's time trend showing particular similarity to that of Canada. As for the PCDDs/PCDFs, New Zealand's current PCB human milk concentrations are low compared to most other countries that participated in the most recent WHO human milk surveys.

Figure 6 presents the data for the sum of DDT and its metabolites. Of the 6 countries with time trend data available, New Zealand had the highest historic human milk concentrations and also showed the steepest decrease in DDT human milk concentrations over time. Decreases over time are also apparent for the USA, Sweden, Canada and the Czech Republic, while for Australia no clear time trend is observed. Comparing New Zealand's current DDT human milk concentrations with those reported for other countries places New Zealand in the middle of the range.

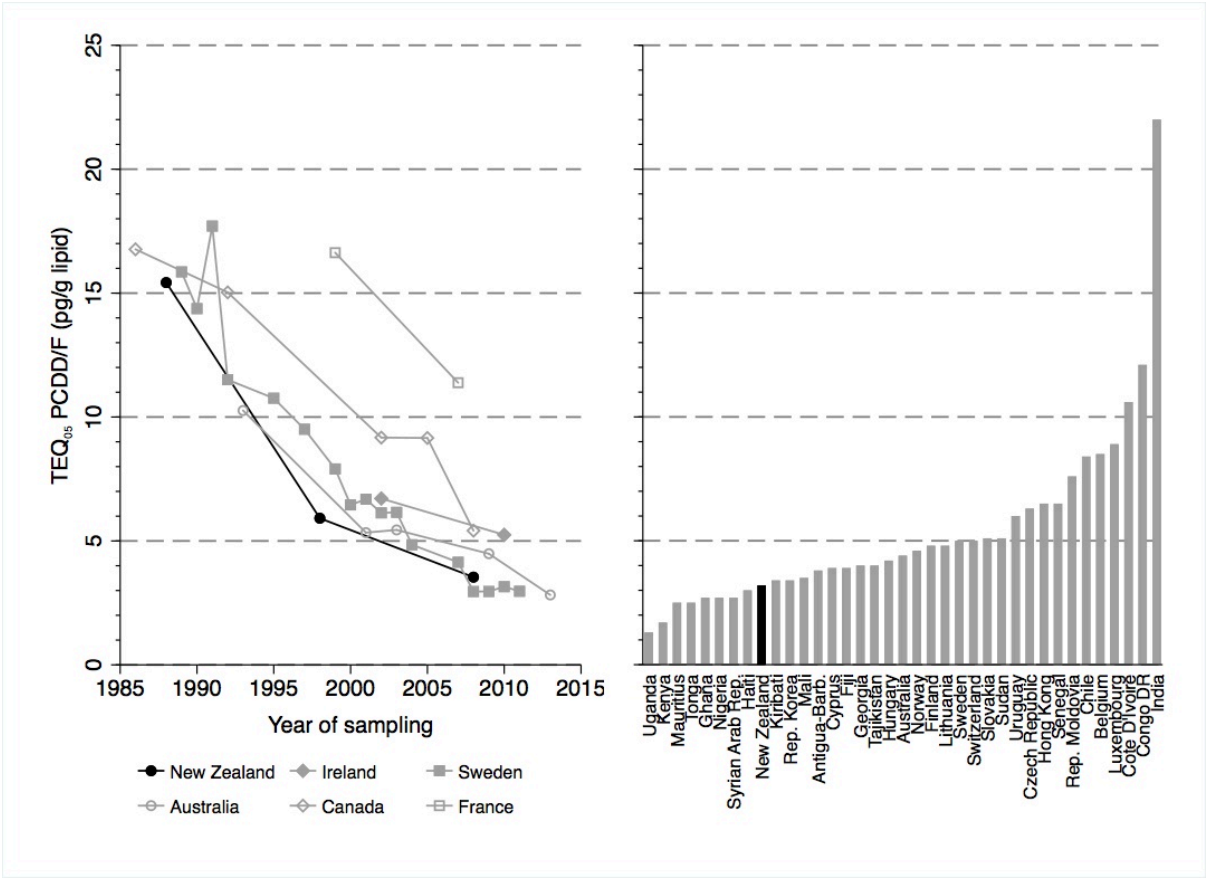

Figure 4. Temporal trend comparison (left side) and most recent country-specific WHO global survey comparison (right side) of TEQ_{05} (PCDD+PCDF) in human milk

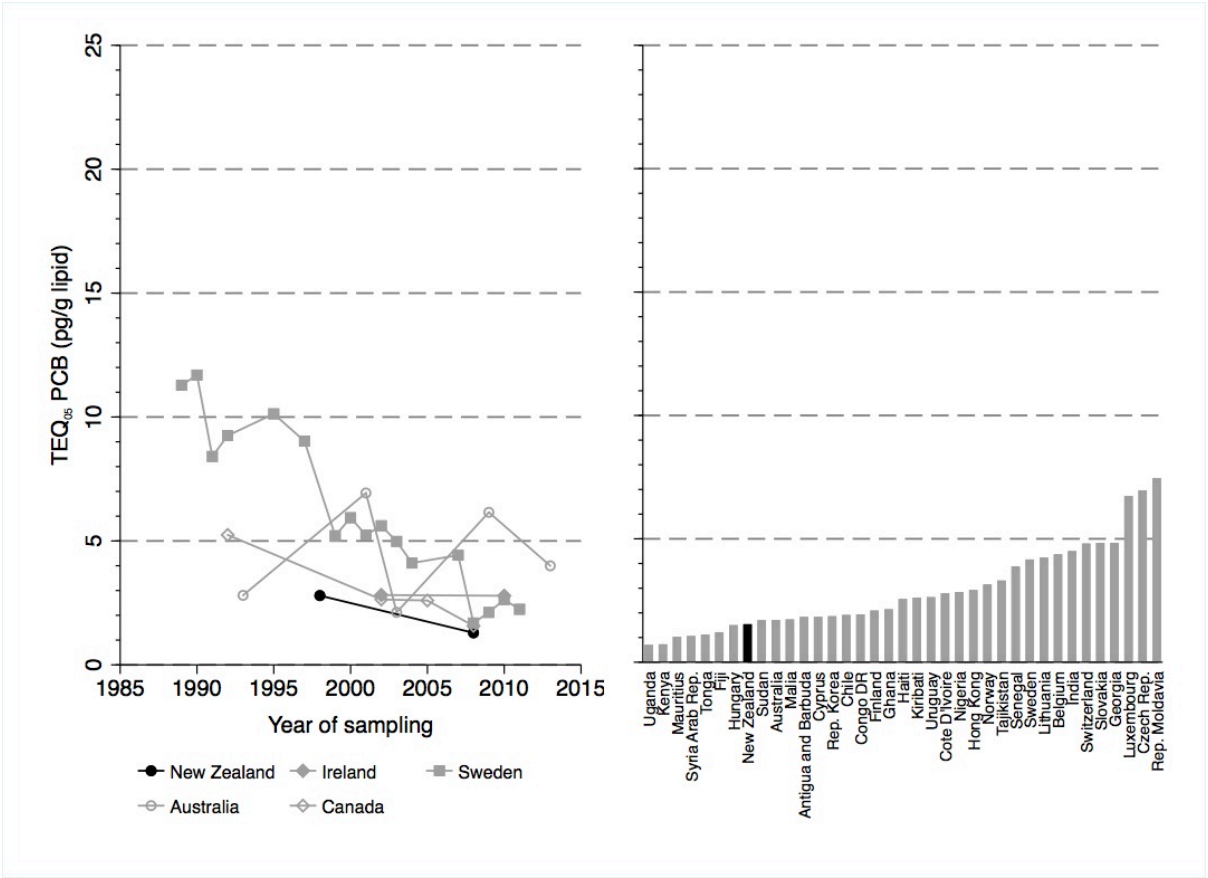

Figure 5. Temporal trend comparison (left side) and most recent country-specific WHO global survey comparison (right side) of TEQ_{05} (PCB) in human milk.

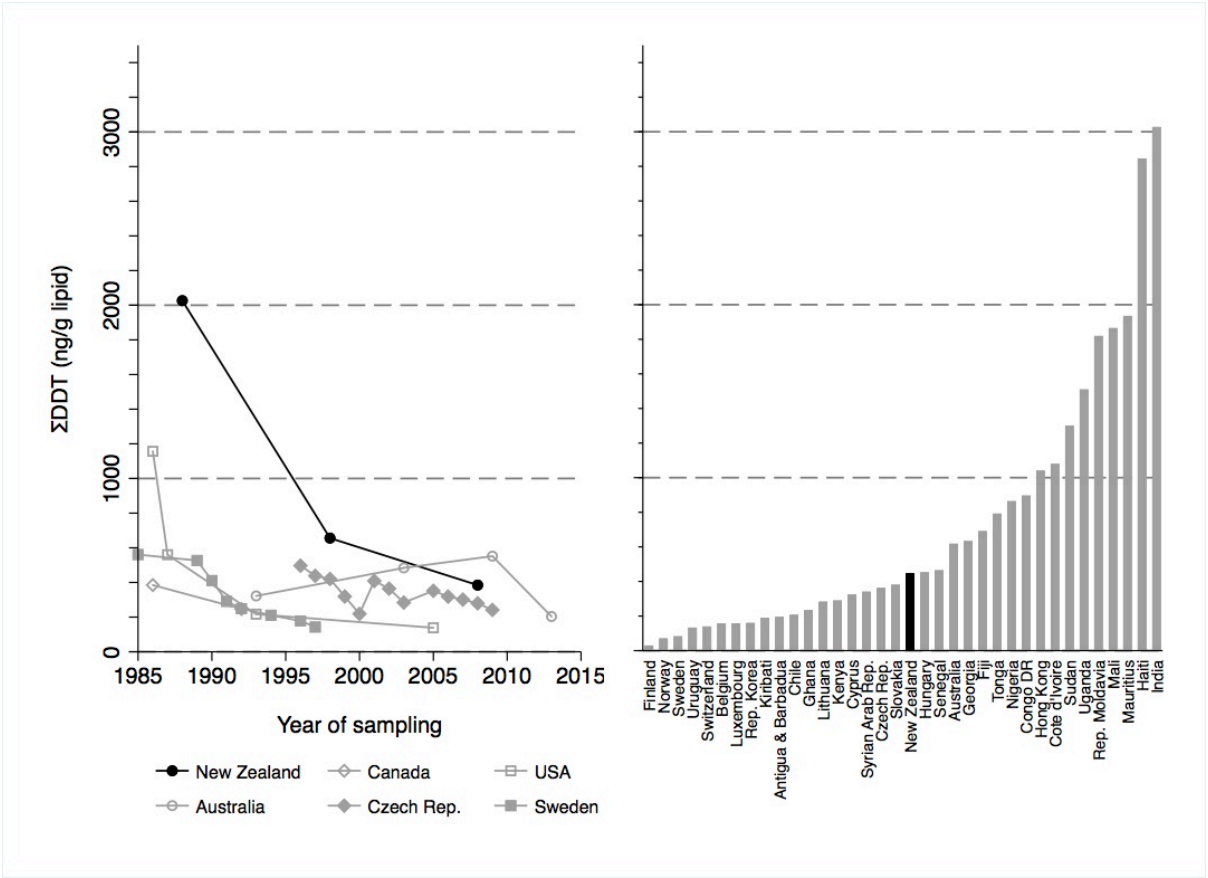

Figure 6. Temporal trend comparison (left side) and most recent country-specific WHO global survey comparison (right side) of the sum of DDT compounds in human milk.

Discussion

The presented data indicate that New Zealand's human milk concentrations of PCDD/PCDF have followed a continuous downward trend since the 1980s, comparable to those reported for other countries. This includes countries of geographic proximity (i.e. Australia) as well as countries of considerable geographic distance (i.e. Sweden), illustrating the effectiveness of international and New Zealand's efforts to control environmental exposure sources of these compounds [2]. The data presented here also show that New Zealand's current PCDD/F concentrations are similar to those observed for other nations of relative geographic proximity, such as Tonga and Fiji. It is noteworthy that a decreasing trend is still evident for the most recent years, even for countries with relatively low PCDD/PCDF concentrations, such as New Zealand. This is encouraging, considering that even for New Zealand, the current estimated intake of dioxin-like compounds through human milk is still above the acceptable daily intake of 1 pg TEQ/kg/day [185]. For most countries time trend data are not available, and there is a clear need for tracking human milk concentrations of PCDD/PCDF for example in countries such as India, for which the current PCDD/PCDF human milk concentrations exceed those observed for New Zealand 30 years ago (Figure 4).

The number of countries that have data on time trends for PCB (TEQ_{05}) human milk concentrations is limited. For New Zealand only two time points are available, as the first human milk study did not determine the levels of all dioxin-like PCBs. Overall, the limited data from New Zealand, Sweden and Canada suggest a decreasing trend for PCBs, similar to that observed for PCDD/F human milk concentrations. Comparing

specific PCB congeners that were determined in all three New Zealand surveys also supports the finding that concentrations of PCBs in New Zealand human milk have decreased between surveys in the period 1988 to 2008 [19]. New Zealand's current PCB concentrations also are similar to those observed for nations of relative geographic proximity, including Australia, Tonga and Fiji. No clear time trend data were observed for Australia, which may be due to the small number of human milk samples (Table 6) or differences in the geographic areas between time points.

Of the six countries with temporal trend data for DDT, New Zealand had the highest historical DDT human milk concentrations, with levels measured in the 1980s (2000 ng/g lipid) comparable to those currently observed in countries where DDT is continued to be used, for example India (Figure 6) which is the largest current global producer and user of DDT for malaria vector control [197]. The phase out and ban of DDT in New Zealand took place during the 1980s – the presented data illustrate a clear decreasing trend in DDT human milk concentrations since that decade, with current levels in New Zealand being in the middle of the range internationally and comparable to concentrations that were measured 30 years ago in countries with relatively low historic DDT use, such as Sweden where DDT was banned in 1975 [196]. Notably, current New Zealand human milk concentrations for DDT equate to an estimated intake of total DDT through human milk of 1600 pg/kg/day, above New Zealand's tolerable daily intake of 500 pg/kg/day [185]. Assuming New Zealand will follow the same time trend as has been observed for Sweden in the past 30 years, it will take at least another 10 years before New Zealand will reach mean human milk

ΣDDT concentrations resulting in an average DDT intake through human milk below the tolerable daily intake.

The relatively high human milk concentrations of DDT compounds in New Zealand, compared to many of the reviewed studies, may be explained by the widespread use of OCPs in New Zealand agriculture until the late 1980s [58, 198]. The New Zealand results for DDT compounds were dominated by the DDE congener, indicating historic exposure to DDT before the 1980s ban was implemented.

The comparisons we have made in this paper need to be considered in light of the significant methodological differences between the selected studies. Not all of the studies were conducted as part of the WHO-UNEP initiative, so not all the participating mothers met the inclusion criteria (i.e. primaparae, healthy, exclusively breast-feeding one child, aged between 20 and 30 years, and resident in the country for at least 5 years). In particular, differences in age of the participants may have affected the results as body burdens of PCDDs, PCDFs, PCBs, and OCPs are higher in older women [30]. The age of the participating mothers was not reported for all studies, limiting our ability to assess this association. For those that did report the mothers' age we found no statistically significant association of TEQ_{05} (PCDD/F), TEQ_{05} (PCB) or sumDDT concentrations and the mothers' mean age, when using multiple regression adjusted for study year. Parity of the mothers will influence POPs concentrations in human milk because POPs are excreted in human milk during previous breast-feeding, prior to the mothers' involvement in the studies. However, information on mother's parity was not provided for all of the studies, so we could not assess this influence. In addition, we are limited in our calculation of TEQ_{05} (PCB)

and the sum of DDT compounds because several of the studies do not report all these congeners. However, all studies report results for the congeners with the highest toxic equivalency factors, and results for the highest DDT congeners, therefore the effect of any missed congeners is unlikely to change the overall findings.

The finding that chlorinated POPs are still found in human milk at detectable levels is cause for concern. In fact, despite the overall substantial decrease in human milk concentrations of chlorinated POPs over time, the estimated daily intakes via human milk remain above the TDI for DDT and dioxin-like compounds for New Zealand [185] and many other countries [187]. PCBs in existing installations (e.g. capacitors and transformers) were phased out of New Zealand in 2016, and there is a commitment from the New Zealand government to manage these hazardous substances appropriately by shipping them to a suitable overseas facility [199]. Other efforts provide some assurance that environmental sources of POPs will continue to decrease, for example air quality standards for dioxin emissions [200] and rules for contaminated sites which define PCDDs, PCDFs, PCBs, and DDT compounds as "priority contaminants" [201]. We consider that New Zealand should continue its effort to identify and manage environmental sources of chlorinated POPs, along with ongoing monitoring of chlorinated POPs in human milk.

Conclusion

The research discussed in this paper confirms the decreasing temporal trend of chlorinated POPs in human milk in New Zealand and internationally. Current concentrations of PCDDs, PCDFs, and PCBs are lower in New Zealand than most

other countries we considered, while concentrations of DDT compounds are in the middle of the international range. These findings, along with related New Zealand research showing exceedance of the TDI for dioxin-like compounds and DDT compounds in nursing infants, show that there remains a potential risk to human health from historic exposure to chlorinated POPs, despite the overall decreasing temporal trend for the past 30 years. Periodic monitoring of POPs in human milk and enforcement of regulations on POPs emissions sources and illegal disposal sites are positive steps to continue to reduce the exposure of infants and their mothers to chlorinated POPs and other toxic chemicals of concern.

Chapter 4. Recruitment methodology of a national survey of adult New Zealanders' serum concentrations of POPs and determinants of response

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Abstract

A national survey was conducted to determine serum concentrations of persistent organic pollutants (POPs) of adult New Zealanders. This paper describes the survey's recruitment methodology and determinants of response in the survey sample and contacted group. Adults aged 19 to 64 years were randomly selected from the 2010 Electoral Roll and stratified according to age group, geographic region, ethnicity (Māori/non-Māori), and sex. Eligible participants were invited to donate a blood sample at a local pathology lab, after which serum was harvested. Serum samples were pooled according to demographic strata prior to analysis of POPs. We evaluated associations between demographic variables and response using multivariate logistic regression. Of the 14,310 invitees, we contacted 2,449 individuals. Of the contacted individuals 2,222 were eligible for the survey. Contact was positively associated with older age, female sex and non-Māori ethnicity, and to a lesser degree with lower deprivation status. Of the eligible, contacted individuals 1,252 refused and 734 participated by providing a serum sample – 236 contacted individuals did not complete the survey. Participation was positively associated with older age, female sex, and non-Māori ethnicity. The overall contact and participant rates were 17% and 5% of the invited sample, respectively. The low contact and participant rates achieved for this survey resulted in an under-representation in the survey sample of adults that are young, male, and of Māori ethnicity. This finding supports the importance of stratifying the survey sample by these demographic characteristics, and using pooled samples, to increase the representativeness of the survey results compared to the source population.

Introduction

Persistent organic pollutants (POPs) are toxic chemicals that are found in humans and the environment around the world. POPs include polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and perfluorinated alkyl substances (PFASs). The measurement of POPs in human biological tissue (e.g. blood serum) is an accepted method to assess human exposure to POPs in the environment [147]. Recruitment of a representative sample of individuals into a population-based biological monitoring survey is a labour intensive process, and there is evidence that response rates for such surveys are in decline [202, 203]. Selection of a survey sample, and the methods used to recruit people from the sample into the survey, are important factors in survey design that influence the interpretation of survey results.

The first national population-based survey of POPs in the serum of New Zealand adults was completed in 2001 [58, 62]. The 2001 survey was carried out in conjunction with the National Nutrition Survey (NNS), which included a blood collection component. Of the 10,600 individuals who were invited to participate in the NNS, 3,376 people provided serum samples of which 1,834 samples were pooled for analysis according to pre-determined demographic groups for age, sex, ethnicity, and geographic region.

The second national survey of POPs in the serum of adult New Zealanders was completed in 2013. The 2013 survey's aims were to provide an evaluation of contemporary POPs serum concentrations in adults and assess the effectiveness of

national POPs reduction measures by comparing the results to the 2001 survey. The 2013 survey used the same strategy for serum sample pooling as the 2001 survey (i.e. according to demographic groups based on age, sex, ethnicity, and geographic region), but used a different sampling frame (i.e. the 2010 Electoral Roll instead of the NNS), and invitation strategy (i.e. mailed invitations to provide a serum sample instead of using samples collected as part of a broader survey). In this paper we describe the recruitment methodology of the 2013 POPs survey, assess response and participation rates, and evaluate how the survey response may influence the representativeness of the survey results. Specifically, this paper investigates how demographic characteristics of the survey sample are associated with (a) the ability to contact individuals, and (b) their willingness to participate once contacted.

Methods

Recruitment:

The 2010 New Zealand Electoral Roll was used as the sampling frame. People in the Electoral Roll were stratified (64 strata) according to the following demographic characteristics (similar to those from the 2001 POPs survey):

- Age: 19−24, 25−34, 35−49, 50−64 years
- Geographic region: Northland/Auckland, Waikato/Bay of Plenty (BOP), Lower North Island, South Island (Figure 7)
- Ethnicity: Māori and non-Māori
- Sex: male and female

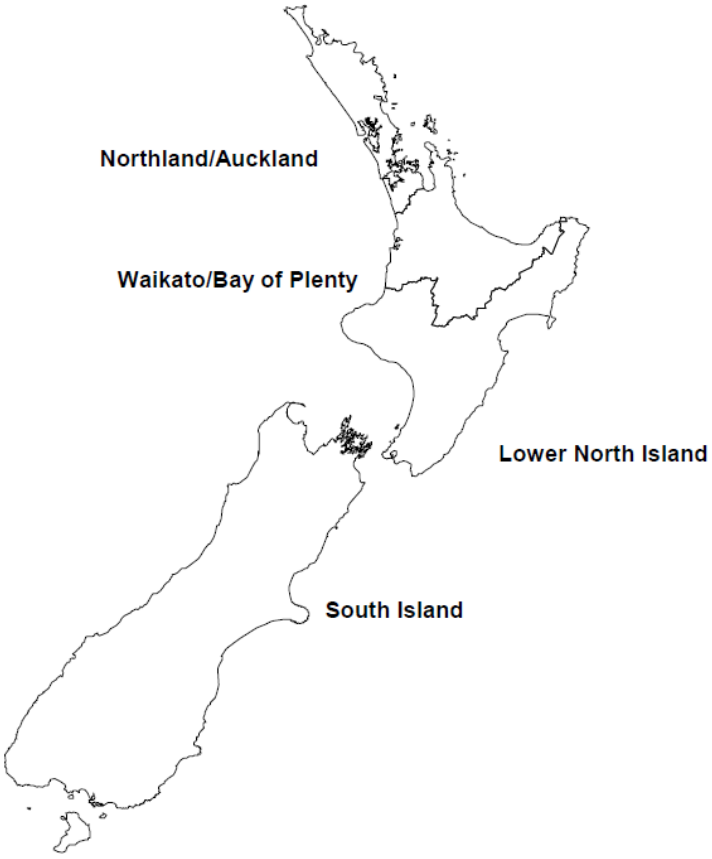

Figure 7. Geographic regions.

Mailed invitation letters, along with an information sheet and reply form, were sent in 6 separate mail-out events between February 2011 and June 2012 to 14,310 people.

If no response to the invitation letter was received, we attempted to contact the non-respondents using telephone numbers from the White Pages and an address-matched list of telephone numbers provided by a professional mailing services provider. We initially attempted to do 3 follow-up telephone calls to non-respondents, however as the survey progressed we focused our follow-up telephone calls on those demographic groups with low response rates (e.g. young males).

Follow-up telephone calls were generally made during days and evenings during the working week.

The survey design sought to obtain equal representation from all demographic groups included in the survey (i.e. equal numbers of participants in each of the 64 strata). During the course of recruitment it became clear that more participants were needed from particular demographic groups because of low contact and response rates. After each mail-out event the number of contacted people in each demographic group was used to determine the number of additional invitations sent out per demographic group in the following mail-out. This approach aimed to weight the subsequent mail-outs towards those demographic groups with relatively low contact rates, in order to increase their recruitment into the survey.

For those people who replied positively to the mailed invitation or follow-up telephone call we conducted a short telephone interview to determine eligibility. The interview collected information on the following reasons for exclusion of a potential survey participant:

1. Current or previous employment in occupations with high exposure to POPs,
2. Medical conditions which would prohibit giving blood, or
3. Non-residency in New Zealand.

If the person was eligible we sent them a package with the necessary paperwork and materials for collection of serum samples at a local pathology laboratory. Participants were offered a $20 MTA voucher to assist with transportation costs.

Serum samples (3 x 10 mL vacutainers per individual taken during a one-off visit) were collected from the participants between May 2011 and April 2013.

Statistical analysis:

The response of each person in the survey sample was classified into one of the following categories:

1. No response (NR) – people who did not reply to mailed invitations and for whom telephone contact could not be established
2. Return-to-sender (RTS) – people who were sent a mailed invitation, but were no longer living at the address we used
3. Contacted, refused (CR) – people who refused our invitation by returning a reply form in the post, or who refused at a later stage of the recruitment process (e.g. during the telephone screening interview or after a blood collection kit had been sent)
4. Contacted, not completed (CNC) – people we contacted by telephone but for whom we lost contact, and eligible people with whom we completed a screening interview, but who did not provide a serum sample within the study timeframe
5. Contacted, participant (CP) – people whose serum samples were analysed for POPs
6. Contacted, not eligible (CNE) – people who had previous occupational exposure to POPs, medical conditions that prevented providing a serum sample, were non-resident in New Zealand, were in prison, were deceased, or did not speak English well enough to complete the study

The Contact rate, Contacted Participant Rate, and Participant Rate were calculated as:

$$\text{Contact rate (CX)} = \frac{CR + CNC + CP}{All - (CNE + RTS)} \times 100\%$$

$$\text{Contacted Participant Rate (CPX)} = \frac{CP}{CP + CR} \times 100\%$$

$$\text{Participant Rate (PX)} = \frac{CP}{All - (CNE + RTS)} \times 100\%$$

Each person in the survey sample was assigned a New Zealand deprivation index score (NZDep) according to address-based meshblock data from the Electoral Roll [204]. The NZDep is a small-area index of relative socio-economic deprivation which was developed based on information gathered in the national census [205]. Deprivation index applies to small geographical areas (meshblocks) of residence. There were 18 individuals whose meshblock information was not associated with a deprivation index, resulting in 14,292 individuals in the survey sample with an NZDep score.

We used multivariate logistic regression to reveal how demographic characteristics are associated with contractibility, and participation of the contacted individuals. All demographic characteristics were included as variables in the regression model, with the dichotimised response indicators as the dependent variable, to determine adjusted response odds ratios.

Results

Summary demographic information for the survey sample, categorised into response categories and response rates, is provided in Table 7. Non-responding individuals (n=11,244) account for 78% of the source sample. We received telephone contact details for 1,288 individuals from responses to our mailed invitations. We conducted a search of the White Pages for 2,472 addresses, which generated an additional 872 telephone numbers (representing 35% of the individuals included in the search). The overall Contact Rate for the survey was 17%. There were large variations in Contact Rate between age groups (9% for the youngest and 31% for the oldest age group), between ethnic groups (13% for Maori and 21% for non-Maori) and deprivation groups (9% for the most deprived and above 20% for the 5 least deprived groups). The overall Participant Rate was 5% (range 2 to 12% for different demographic groups), with female, older, non-Māori, and less deprived groups of individuals having the highest Participant Rates. Of the contacted individuals, 37% participated in the study.

Table 7. Recruitment results.

		NR	RTS	CNE	CNC	CR	CP	Total	CX	CPX	PX
	Total	11,244	723	62	295	1,252	734	14,310	17%	37%	5%
Ethnicity	Māori	6,511	420	29	146	570	293	7,969	13%	34%	4%
	Non-Māori	4,733	303	33	149	682	441	6,341	21%	39%	7%
Sex	Female	5,146	310	25	163	667	457	6,768	20%	41%	7%
	Male	6,098	413	37	132	585	277	7,542	14%	32%	4%
Age group (years)	19-24	3,951	286	17	65	247	97	4,663	9%	28%	2%
	25-34	3,152	245	9	73	269	143	3,891	13%	35%	4%
	35-49	2,526	130	10	77	367	211	3,321	21%	37%	7%
	50-64	1,615	62	26	80	369	283	2,435	31%	43%	12%
Region	Northland/Auckland	2,980	158	14	67	303	168	3,690	15%	36%	5%
	Waikato/BOP	2,937	192	18	73	327	199	3,746	17%	38%	6%
	Lower North Island	2,935	195	25	69	356	190	3,770	17%	35%	5%
	South Island	2,392	178	5	86	266	177	3,104	18%	40%	6%
Deprivation index	Total	11,231	721	62	295	1,250	733	14,292	17%	37%	5%
	1 (least deprived)	805	42	6	22	124	76	1,075	22%	38%	7%
	2	811	55	3	27	133	75	1,104	22%	36%	7%
	3	822	60	8	41	136	85	1,152	24%	38%	8%
	4	872	60	6	24	118	80	1,160	20%	40%	7%
	5	922	89	8	28	131	66	1,244	20%	34%	6%
	6	1,069	73	4	29	120	72	1,367	17%	38%	6%
	7	1,112	81	11	29	125	78	1,436	17%	38%	6%
	8	1,296	91	2	25	118	75	1,607	14%	39%	5%
	9	1,511	80	7	34	126	71	1,829	13%	36%	4%
	10 (most deprived)	2,011	90	7	36	119	55	2,318	9%	32%	2%

NR – No response, RTS – Return to sender, CNE – Contacted not eligible, CNC – Contacted not completed, CR – Contacted refused, CP – Contacted participant CX – Contact rate, CPX – Contact participant rate, PX – Participant rate

Associations between response and demographic variables:

The results of multivariate logistic regression (i.e. adjusted odds ratios) to investigate associations between key response indicators (i.e. ability to contact, participation in contacted individuals, and overall participation in the study sample) and demographic variables are shown in Figure 8, Figure 9 and Figure 10.

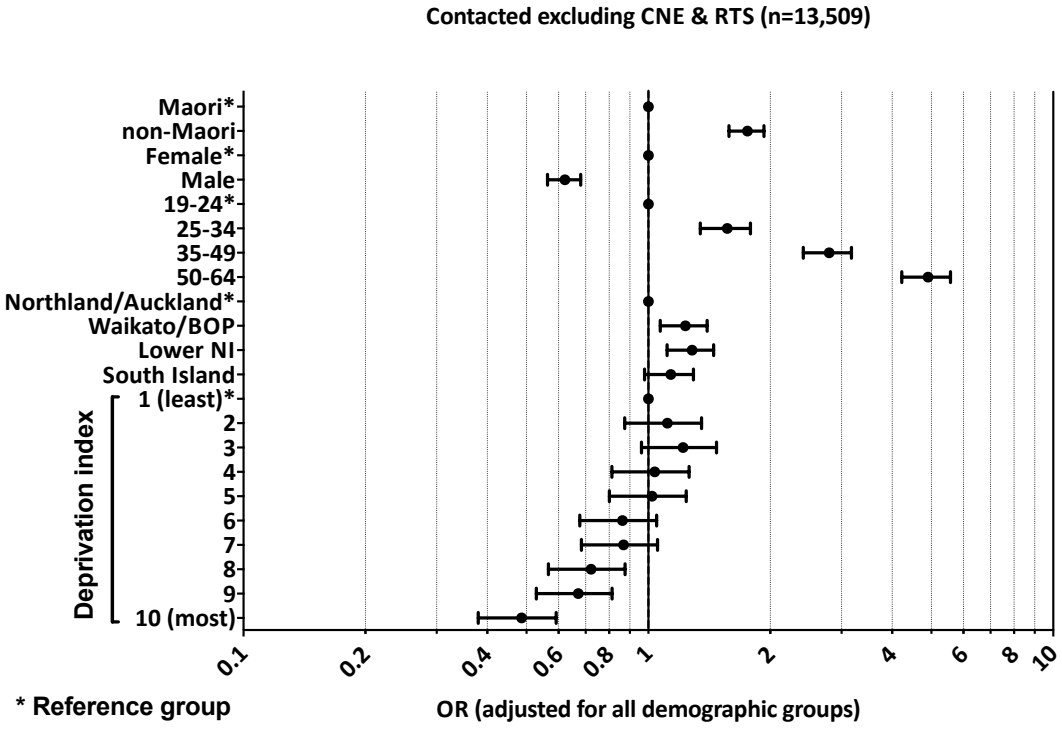

Figure 8. Influence of demographic characteristics on ability to contact individuals.

Overall, non-Māori were 1.8 times more likely to be contacted compared to Māori. Males were 1.6 times less likely to be contacted compared to females. Older individuals (>25 years) were 1.5 to 4.9 times more likely to be contacted compared to the youngest age group. Individuals from the Waikato/BOP and Lower North

Island regions were 1.3 times more likely to be contacted compared to the Auckland/Northland region. Individuals in the three highest deprivation groups were 1.4 to 2.1 times less likely to be contacted compared to individuals from the lowest deprivation group.

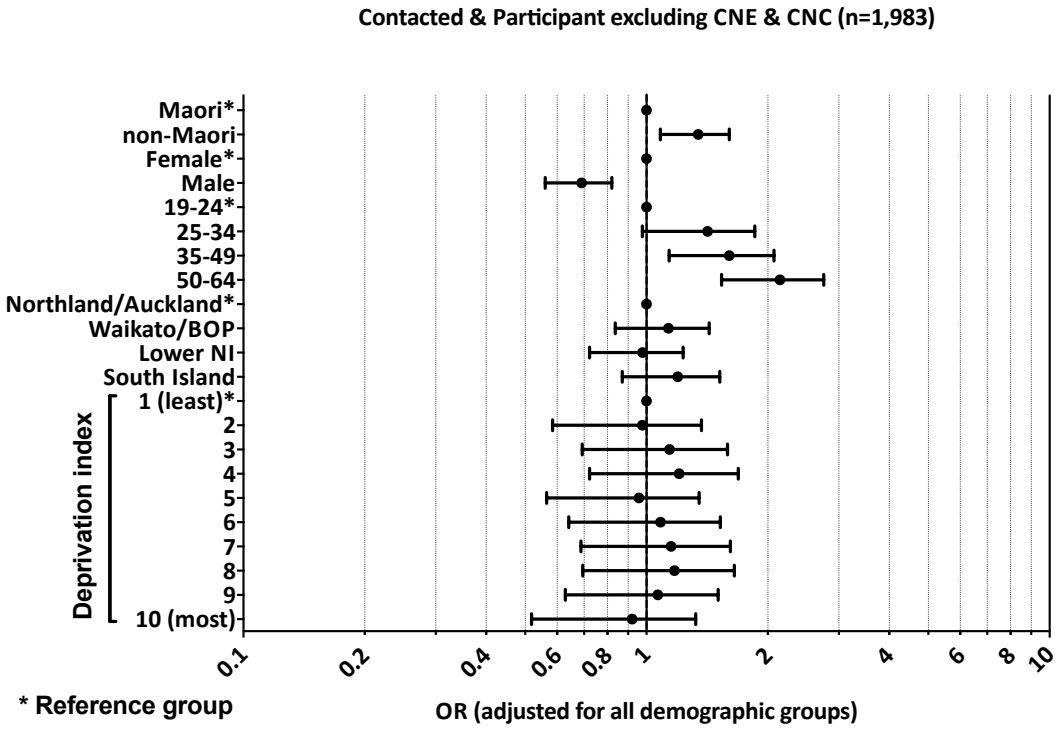

Figure 9. Influence of demographic characteristics on participation in the contacted individuals.

In the contacted group, non-Māori were 1.3 times more likely to participate compared to Māori. Males were 1.5 times less likely to participate compared to females. Older individuals (>25 years) were 1.4 to 2.1 times more likely to participate compared to the youngest age group. There were no apparent

associations between survey region or deprivation and participation in the contacted group.

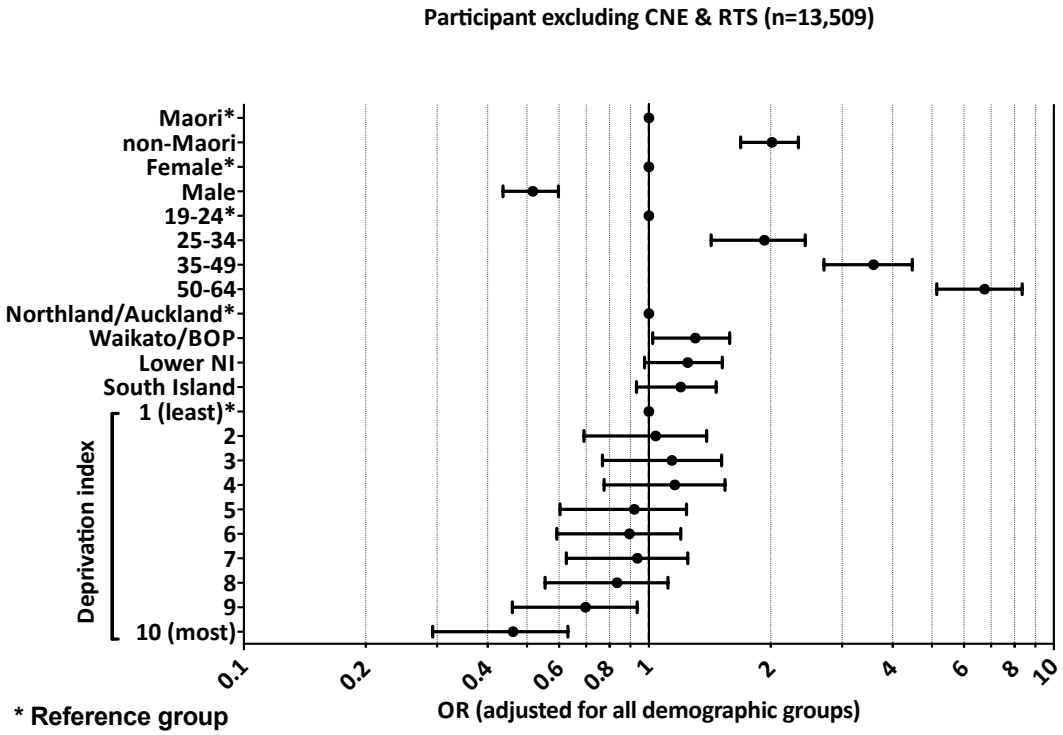

Figure 10. Influence of demographic characteristics on participation in the overall study sample.

Overall, non-Māori were 2.0 times more likely to participate compared to Māori. Males were 1.9 times less likely to participate compared to females. Older individuals (>25 years) were 1.9 to 6.6 times more likely to participate compared to the youngest age group. Individuals from the Waikato/BOP regions were 1.3 times more likely to participate compared to the Auckland/Northland region. Individuals from the two highest deprivation groups were 1.5 to 2.3 times less likely to participate compared to individuals from the lowest deprivation group.

Discussion

The overall contact and participant rates of 17% and 5%, respectively, are relatively low figured compared to similar population-based biological monitoring surveys of POPs. The majority of individuals in the survey sample (adults on the Electoral Roll) did not respond to our mailed invitations and did not have an available telephone number for follow-up contact. We attempted to recruit more people into the survey by targeting groups with relatively low response rates (i.e. young males of Māori ethnicity), however these groups remained difficult to contact and therefore remained under-represented in the survey.

There are several contributing factors to the low contact and participant rates. First, we did not attempt face-to-face contact to recruit individuals (e.g. door-to-door visits). This was a national survey covering a large geographic area and we did not have the resources to attempt face-to-face contact for the non-contacted individuals. Secondly, we did not have access to an established survey for the source sample (e.g. National Nutrition Survey or another current New Zealand population-based survey) with confirmed individual contact details.

The use of the Electoral Roll for selecting the survey sample has limitations. Importantly, telephone numbers are not provided with the Electoral Roll. Access to a more comprehensive source of confirmed telephone contact details (e.g. through a recently completed national population-based health survey) would have resulted in higher contact rates for the survey sample. There is evidence that access to land-line

telephones in New Zealand is decreasing[1] and it is likely that many of the invited people do not own a land-based telephone line and rely on mobile communication, particularly individuals in the younger groups. We did not have access to a searchable database of mobile telephone numbers. In addition, we could not comprehensively assess the accuracy of the address information in the Electoral Roll. Recruitment for the survey was done between February 2011 and June 2012 and the Electoral Roll data was published in August 2010. Some addresses may have been out of date as people moved during the recruitment period, illustrated by 6% of the letters sent to the survey sample were "return to sender".

Non-response bias may exist but the magnitude of this bias cannot be determined. Intensive efforts to contact individuals (e.g. door-to-door visits) may have resulted in further non-response bias because it is likely that individuals in certain demographic groups would be easier to locate. Peytchev [206] showed no relationship between non-response rates and bias in a review of studies, and suggests that efforts to increase response rates can lead to increased bias in survey estimates. Such efforts include (a) more call attempts in telephone surveys, (b) in-person visits, and (c) providing incentives – potentially resulting in recruitment of individuals who will be different on key survey estimates compared to the source population.

Influence of demographic characteristics on contact and participation:

Age is the dominant determinant of ability to contact, and participation in the survey sample. Nearly twice as many invitations were sent to individuals in the youngest

[1] http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/quickstats-about-national-highlights/phones-internet-access.aspx

age group compared to the oldest age group. However, more than 3 times more individuals were contacted from the oldest age group compared to the youngest group. Individuals from the oldest age group were 6.6 times more likely to participate in the survey compared to the youngest age group. Mannetje [207] showed that age influences responses to survey invitations with the youngest age group (19-25 years) 2 times less likely to be contacted, and also 2 times less likely to refuse compared to the oldest group (56-65 years). Alternative recruitment methods for younger people that focus on their lifestyle factors (e.g. use of social media, attendance of events such as university orientation) may result in higher contact and participation rates for this difficult-to-reach group. However, such targeted methods are likely to exclude individuals from certain demographic groups, and the influence of this exclusion would need to be considered in the interpretation of the survey results.

To a lesser extent, Māori ethnicity, male sex, and higher deprivation status were associated with a reduced likelihood of participation in the survey sample. Higher deprivation was inversely associated with our ability to contact individuals in the survey sample, however this association was not present for participants in the contacted group. More people were invited from the higher deprivation categories because of our efforts to recruit younger, male, Māori subjects – this amplified the influence of higher deprivation on survey participation in the survey sample. Since the association of higher deprivation and participation disappeared in the contacted group this is evidence that deprivation status does not influence an individual's decision to participate in the survey once they have been contacted.

The higher likelihood of participation in the older age groups (35-64 years) remained when only the contacted group was considered. However, the magnitude of the age-related association with participation was less in the contacted group compared to the overall survey sample.

Participation in the survey was a relatively time-consuming process for the individuals because they had to visit a local pathology laboratory to provide a blood sample. During the sample collection period we lost contact with younger individuals more than older individuals, which is reflected in the higher proportion of RTS and CNE in younger individuals in the survey sample. Mannetje [207] suggests that a key reason that younger people do not participate as much as older people is increased mobility (i.e. they do not stay contactable at an address as long). Sex and ethnicity are also determinants of participation for the contacted group. However, the magnitude of the association of sex and ethnicity on participation was less in the contacted group compared to the overall survey sample.

An individual's decision to participate in this survey is likely related to the level of commitment required by participants to provide a blood sample, compared to the commitment required for completion of only a mailed questionnaire or telephone interview. The number of health-related studies that ask participants to provide biological specimens is increasing over time [208] and there is evidence that the inconvenience related to collection of biological specimens may result in lower survey participation rates [209].

The detailed reasons for refusal were not collected as part of this survey, but it is reasonable that the reasons for refusal include:

- Reluctance to provide a serum sample, for privacy or health reasons, or a dislike of venipuncture methods for personal or cultural reasons
- Insufficient time or commitment to travel to a local pathology lab
- Lack of interest in the survey objectives or outcomes
- Insufficient incentives (e.g. monetary compensation or payment) to participate

The detailed reasons for participation were not collected as part of the survey, but it is reasonable that the reasons for participation include:

- An interest in the public health outcomes of the survey
- Financial gain through receipt of an incentive (i.e. $20 MTA voucher)

The consistent pattern that Māori were less likely to be contacted and participate is a finding that merits consideration. The need for increased Māori participation in health-related research has been identified [210]. In this survey, Māori were over-sampled in the survey sample by the nature of the recruitment design. In the first mailout for the survey 50% of the invitees were Māori. Over the period of 6 mail-outs we increased the proportion of Māori invitees, so that we could increase the recruitment of this under-represented group (as well as other age, sex, and region-related strata). This was done for practical purposes related to the limitations of laboratory analysis – more young Māori needed to participate so that the collected serum pools were of sufficient volume to enable future laboratory analysis. The ratio of Māori to non-Māori in the survey sample was 7,969/6,341, that is Māori represented 56% of the survey sample. This is in contrast to the ratio of Māori to non-Māori who participated in the survey – 293/441 or 40% of the survey sample.

Specific methods for more effective recruitment of Māori in population-based health research should be sought in future studies.

Survey stratification and sample pooling to increase representativeness:

The low participant rates for this survey were, to a certain degree, accommodated by the survey design. Specifically, the collected serum samples were pooled according to the 64 survey strata defined by age, sex, region, and ethnicity groups. The pooling strategy is outlined in a separate paper [36]. The pooled serum samples are a proxy for estimating central tendency POPs concentrations within each of the survey strata.

Conclusion

Population-based public health surveys are an important tool for assessing associations between health outcomes and demographic determinants such as age, sex, and ethnicity. This survey found that certain demographic groups were more likely to be contacted, and participate, in a population-based survey of persistent organic pollutants in the serum of adult New Zealanders. This finding is supported by New Zealand and international studies. Age is the dominant determinant of participation in this survey, with sex and ethnicity also associated with participation to a lesser degree. Higher deprivation was shown to be associated with ability to contact, but not with survey participation in the contacted group. We made efforts to recruit more individuals from certain demographic groups, however the survey sample is under-represented by young, male, and Māori individuals. The Electoral Roll is a convenient resource for survey recruitment, however it has limitations that should be considered in future population-based biological monitoring studies.

Chapter 5. Chlorinated persistent organic pollutants in serum of New Zealand adults, 2011-2013

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(Published in Science of the Total Environment [36]. See Appendix 6)

Abstract

A national survey was conducted in 2011-2013 to assess serum concentrations of persistent organic pollutants (POPs) in adult New Zealanders. Participants were randomly selected from the 2010 Electoral Roll within 64 demographic strata according to 4 age groups, 4 regions, 2 ethnic groups (Māori/non-Māori) and sex. Eligible subjects (n=734) donated up to 30 mL of blood, after which serum was pooled (n=49) according to demographic strata prior to analysis by GC-HRMS. Associations between demographic variables (age, region, ethnicity, sex) and serum POPs were assessed using linear regression. The weighted geometric mean (GM) of PCDD/Fs was 5.3 pg/g lipid toxic equivalents using the WHO 2005 toxic equivalence factors (TEQ_{05}), which increased by age (3.2, 4.4, 4.8, and 8.1 pg/g lipid for the 19-24, 25-34, 35-49, and 50-64 year age groups, respectively). The weighted GM of dioxin-like PCBs was 1.4 pg TEQ_{05}/g lipid which also increased by age (0.82, 0.86, 1.4, and 2.3 pg/g lipid for the same age groups, respectively). Of the detected OCPs, the highest concentration was observed for *p,p'*-DDE (weighted GM, 220 ng/g lipid) followed by hexachlorobenzene (HCB; 7.3 ng/g lipid), *beta*-HCH (7.0 ng/g lipid), and dieldrin (4.7 ng/g lipid). For most Cl-POPs, concentrations were lowest in the youngest age group, and were similar for men and women and Māori and non-Māori. Serum Cl-POPs were, on average, 50% lower than those measured 15 years earlier in 1997. This survey provides evidence of declining serum concentrations of chlorinated POPs in the New Zealand adult population. Age was the most important determinant of POPs concentrations. Body burdens of PCDD/Fs and PCBs in New Zealand are relatively low by international comparison, while for OCPs they are similar or lower compared to those reported for other developed countries.

Introduction

Chlorinated persistent organic pollutants (POPs) are ubiquitous environmental contaminants which are toxic, resistant to degradation, bio-accumulative, and transported by air, water and migratory species across international boundaries [12, 20, 40, 211]. Humans in non-occupational settings are primarily exposed to POPs through diet, particularly from foods of animal origin (Smith, 2001). Health effects associated with human exposure include cancer, allergies and sensitisation, and disorders of the nervous, reproductive, and immune systems [212]. The most studied POPs are polychlorinated-*p*-dibenzodioxins (PCDDs), polychlorinated-*p*-dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs), and organochlorine pesticides (OCPs) including the historically used dichlorodiphenyltrichloroethane (DDT), and its degradation products dichlorodiphenyldichloroethane (DDD) and dichlorodiphenyldichloroethylene (DDE). Other OCPs historically used in New Zealand (and many other countries) are hexachlorocyclohexane (HCH), dieldrin, pentachlorobenzene (PeCB), and hexachlorobenzene (HCB).

The Stockholm Convention embodies the commitment of member countries to reduce the effects of POPs on human health and the environment, and makes recommendations for member states to monitor POPs in people and the environment [40]. A number of countries have carried out biological monitoring of POPs in the general population in order to establish reference levels and assess temporal trends [30, 39, 155]. New Zealand conducted its first national study of serum Cl-POPs in non-occupationally exposed adults in 1997 [58]. In addition, three surveys of POPs in human milk were carried out in 1988 [63], 1998 [61], and 2008

[19, 186]. These studies showed that intakes of POPs and associated body burdens in human serum and milk in New Zealand are relatively low compared to other developed countries [48, 58, 186]. In addition, they showed that levels of chlorinated POPs in human milk have declined between 1988 and 2008 [19], but there is currently no information on temporal trends of POPs representative for the New Zealand general adult population, including men and older age groups.

The aim of this study was to assess concentrations and demographic determinants of chlorinated POPs in non-occupationally exposed adults in the New Zealand general population. We also assessed temporal trends of chlorinated POPs since the previous New Zealand study conducted in 1997.

Methods

This cross-sectional survey assessed serum concentrations of chlorinated POPs in the adult New Zealand population, using a stratified sampling method. Participants were recruited using the 2010 Electoral Roll from the New Zealand Electoral Commission (www.elections.org.nz). Potential study participants were randomly selected with equal proportions based on age (19−24, 25−34, 35−49, 50−64 years), sex, geographic region (Northland/Auckland, Waikato/Bay of Plenty, Lower North Island, South Island), and ethnicity (Māori, non-Māori). The survey sample was therefore based on 64 strata consistent with the previous New Zealand POPs serum survey conducted in 1997 [213], except for the exclusion of the 15-18 years and 65+ years age groups which were included in the 1997 survey. Ethics approval was obtained from the Upper South A Regional Ethics Committee (reference URA/10/07/054 11 August 2010).

Mailed invitation letters, along with an information sheet and reply form, were sent in 6 separate mail-out events between February 2011 and June 2012 to 14,310 people. For those who replied positively we conducted a short telephone interview to determine eligibility. Exclusion criteria included: current or previous employment in occupations with high exposure to POPs, specifically timber treatment, manufacture and repair of electrical equipment, and application of organochlorine pesticides; medical conditions which would prohibit giving blood (e.g. exposure to certain blood-borne pathogens or other conditions specified by the respondent); or non-residency in New Zealand at the time of the survey.

Eligible participants provided written consent and were asked to visit a local private pathology laboratory to have up to 30 mL of whole blood taken (see Appendix 1). Blood was allowed to clot (30 – 45 minutes) at room temperature, then centrifuged and serum was collected using cleaned glass pipettes. Serum samples and bovine serum quality assurance (QA) samples were stored in amber glass vials at -20^{o}C. Duplicate and replicate samples were included to assess laboratory precision. Duplicate samples from four strata were sent to an accredited overseas laboratory for inter-laboratory comparison.

Sample pooling and laboratory analysis:

A pooling strategy was developed to ensure sufficient serum volume in each pool to achieve suitable laboratory detection limits (i.e. 50 ml) and reduce analytical costs. We did not have sufficient participants in all demographic strata to create pools using equal aliquots, while still achieving a minimum of 50 ml of serum per pool. We estimated the pool-specific 75th percentile volume for the individual samples within each pool and used this figure as the maximum volume that would be aliquoted to the pool from any participant. If a participant's sample serum volume was less than the pool-specific 75th percentile volume, the complete serum sample was aliquoted to the pool. For age strata with very low numbers of participants (i.e., males aged 19-34, Māori females aged 19-24), the samples from the four geographic regions were combined together into one pool.

A 40 mL aliquot of each pooled serum sample was analysed (AsureQuality, Lower Hutt) for PCDDs, PCDFs, and PCBs while a 10 mL aliquot was analysed for OCPs. Lab methods were based on USEPA methods for PCDD/Fs [214], PCBs [215], and OCPs [216]. A matrix spike and reagent blank was included with each batch of samples. Each sample was spiked with ^{13}C labelled internal standards prior to extraction using either C18 SPE (PCDD/Fs, PCBs) or soxhlet extraction (OCPs, after dehydration with sodium sulfate). Clean-up and fractionation was achieved using acid silica, basic alumina, florisil, carbon column chromatography, and gel permeation chromatography. The cleaned extracts were spiked with recovery standards before being reduced to a final volume of 10 µL (PCDD/Fs), 50 µL (PCBs), and 25 µL (OCPs). PCDD/Fs, PCBs, and OCPs were analysed by GC-HRMS using Agilent 6890/7890 GC coupled with Waters Ultima/Premier HRMS. PCDD/Fs were analysed at 10,000 mass resolution. Quantification was performed using Waters QuanLynx software. Internal standards were used for quantification of the target analytes, thus results were recovery corrected. The recovery standard was used for quantification of the internal standards to determine the percent recovery. Testing results from bovine serum QA samples showed no evidence of sample contamination during storage and handling. Mean coefficient of variation (CV) [217] results for duplicate and replicate QA samples were 8% and 22%, respectively, which is acceptable considering that some of the measured POPs were at concentrations near laboratory detection limits. Results from testing of inter-laboratory duplicate samples were also acceptable, with normalised difference (ND) values within 50% for the majority of congeners.

Triglycerides and HDL-cholesterol levels were determined using Roche P800 GPO-PAP and P800 Direct Enzymatic methods, respectively. Serum lipid concentrations were calculated using the formula of Phillips et al. [218]. Results were reported on a lipid adjusted basis as pg/g lipid (for PCDD/F and PCBs) and ng/g lipid (for OCPs). Analyses of OCPs chlordecone, endrin aldehyde, endrin ketone and endosulfan sulphate showed unsatisfactory recoveries and results are therefore not reported for these compounds.

Data analysis:

Toxic equivalents (TEQ_{05}) were calculated for PCDD/F and PCBs using the World Health Organisation 2005 Toxic Equivalence Factors [57]. For analytical results below the laboratory limit of detection (LOD), a value of 0.5 x LOD was assigned. Summary statistics for each analyte (minimum, maximum, weighted geometric mean (GM), weighted geometric standard deviation (GSD)) were calculated using Stata v.11.2 (Statacorp, USA). Weighted summary statistics were obtained by applying weights equal to stratum-specific population counts from the 2010 Electoral Roll. Combined pooled samples weights were based on the sum of individual weights from each of the combined strata.

Analytes were excluded from further consideration if (a) they were at concentrations above the laboratory detection limit in less than 30% of pooled samples (excluded analytes 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9-HpCDF, OCDF, PCB15, PCB19, PCB37, PCB54, PCB77, PCB81, PCB104, PCB155, PCB188, PCB200, *alpha*-HCH, *gamma*-HCH

(lindane), *delta*-HCH, heptachlor, aldrin, heptachlorepoxide, oxychlordane, gamma-chlordane, endosulfan-A, *alpha*-chlordane, *trans*-nonachlor, *o,p'*-DDE, endrin, endosulfan-B, *cis*-nonachlor, *o,p'*-DDD, *p,p'*-DDD, *o,p'*-DDT, and methoxychlor), or (b) the arithmetic mean concentration of the analyte in the serum pools was less than 5 times the arithmetic mean of the analyte in laboratory reagent blanks (excluded analytes 2,3,7,8-TCDF, PCB1, PCB3, PCB4/10, PCB44, PCB49, PCB52, PCB70, PCB101, PCB110, and PeCB).

Multivariate linear regression was used to assess the association between POPs concentrations and demographic characteristics. Demographic characteristics included in the regression model were age group, sex, ethnicity, and study region (as a categorical variable, with Northland/Auckland as the reference region). We also treated age group as a categorical variable to assess age-related associations for each age group with the youngest age group (19-24 years) as the reference. In a separate model we treated age group as a continuous variable to assess the overall trend. Un-weighted natural log-transformed POPs concentrations were used in all regression models.

We compared weighted arithmetic mean (AM) concentrations of chlorinated POPs between the 1997 and 2012 POPs serum surveys to determine percent changes in POPs in the 15-year period between surveys. TEQ_{98} values were used in the comparison because TEQ_{05} values did not exist at the time of the 1997 survey and could not be calculated based on the 1997 published data. The 1997 and 2012 surveys were conducted in different population samples and therefore changes in

serum concentration over time within individuals could not be determined. In order to estimate changes of serum POPs in individuals, we compared the 1997 age-group-specific-concentrations to the 2012 concentrations corresponding to the age group they would have been in 15 years later (e.g., 1997 results in 35-49 year olds were compared to 2012 results in 50-64 year olds).

Results

Survey sample:

Of the 14,310 adults invited, 1,986 were contacted, 62 were ineligible, and 734 participated in the study by providing a serum sample that was used in serum pools (See Appendix 2). Of the contacted eligible individuals the participation rate was 37%. Younger age groups, males and Māori were less likely to participate in the study, but over-sampling of these strata provided sufficient individual samples to contribute to pools. For age strata with very low numbers of participants the four geographic regions were combined together into one pool. As noted in the methods section, for the 19-24 age group the four geographic regions were combined for Māori males, Māori females and non-Māori males. For the 25-34 age group the four geographic regions were combined for Māori males and non-Māori males. The total number of pools was therefore 49.

PCDD/Fs:

Weighted geometric mean concentrations of PCDD/Fs in serum are presented in Table 8. The congener with the highest weighted geometric mean concentration was OCDD at 120 pg/g lipid. The overall weighted geometric mean and weighted arithmetic mean PCDD/F toxic equivalents were 5.2 and 5.7 pg TEQ_{05}/g lipid, respectively. PeCDD was the largest contributor to the weighted arithmetic mean for PCDD/F TEQ_{05}, (42%), followed by 2,3,4,7,8-PeCDF (16%), 2,3,7,8-TCDD (12%), and 1,2,3,6,7,8-HxCDD (11%), with the other congeners each contributing 3% or less.

Table 8. Concentrations of dioxins and furans in 49 pooled serum samples (pg/g lipid).

Congener	% Detected	Min	Max	Weighted geometric mean (wGSD)	Weighted geometric mean (wGSD) for age groups, years				Exponentiated age regression coefficient
					19-24 (n=7 pools)	25-34 (n=10 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	
2,3,7,8-TCDD	37	<LOD	3.2	0.70 (1.9)	0.44 (1.4)	0.47 (1.5)	0.60 (1.7)	1.3 (1.8)	1.5***
1,2,3,7,8-PeCDD	98	<LOD	5.6	2.2 (1.5)	1.4 (1.2)	1.9 (1.2)	2.0 (1.4)	3.2 (1.4)	1.3***
1,2,3,4,7,8-HxCDD	63	<LOD	3.7	0.91 (2.1)	0.48 (1.8)	0.44 (2.3)	0.90 (1.6)	1.8 (1.5)	1.6***
1,2,3,6,7,8-HxCDD	96	<LOD	20	5.3 (1.8)	2.0 (1.3)	3.5 (1.2)	4.9 (1.3)	11 (1.3)	1.8***
1,2,3,7,8,9-HxCDD	86	<LOD	2.9	1.4 (1.6)	1.0 (1.6)	1.1 (1.4)	1.3 (1.5)	2.1 (1.3)	1.3***
1,2,3,4,6,7,8-HpCDD	100	4.3	25	13 (1.4)	7.9 (1.3)	11 (1.3)	13 (1.3)	17 (1.3)	1.3***
OCDD	100	68	260	120 (1.4)	84 (1.1)	96 (1.3)	120 (1.3)	160 (1.3)	1.3***
1,2,3,7,8-PeCDF	61	<LOD	4.1	0.60 (2.1)	0.31 (1.8)	1.0 (1.9)	0.51 (1.7)	0.65 (2.4)	0.98
2,3,4,7,8-PeCDF	100	1.2	5.7	2.8 (1.4)	1.7 (1.3)	2.5 (1.2)	2.7 (1.2)	4.0 (1.2)	1.3***
1,2,3,4,7,8-HxCDF	96	<LOD	3.7	1.5 (1.5)	0.81 (1.5)	1.5 (1.4)	1.5 (1.2)	2.0 (1.5)	1.3***
1,2,3,6,7,8-HxCDF	96	<LOD	3.7	1.6 (1.6)	0.95 (1.5)	1.7 (1.4)	1.5 (1.5)	2.1 (1.4)	1.3***
2,3,4,6,7,8-HxCDF	51	<LOD	1.4	0.51 (1.7)	0.36 (1.8)	0.66 (1.4)	0.45 (1.4)	0.58 (1.9)	0.94
1,2,3,4,6,7,8-HpCDF	98	<LOD	10	3.1 (1.5)	2.8 (1.9)	4.0 (1.4)	2.8 (1.4)	3.3 (1.5)	0.92
TEQ_{05} (PCDD/F)		2.7	13	5.2 (1.5)	3.1 (1.1)	4.3 (1.2)	4.7 (1.3)	8.1 (1.3)	1.4***

1. Only congeners detected in >30% of pooled samples are reported and included in TEQ_{05}. Non-reported congeners are 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9-HpCDF and OCDF. 2,3,7,8-TCDF was detected in serum pools at concentrations less than 5 times the concentrations in laboratory reagent blanks and was excluded. <LOD = below laboratory limit of detection. wGSD = weighted geometric standard deviation.

* p-trend<0.05

** p-trend<0.01

*** p-trend<0.001

PCBs:

Weighted geometric mean concentrations of PCBs in serum are presented in Table 9. The 3 PCB congeners found at the highest concentrations were PCB180, PCB153, and PCB138/163/164 at 11,000, 11,000, and 7,600 pg/g lipid, respectively. The overall weighted geometric mean and arithmetic mean concentration of PCB toxic equivalents was 1.4 and 1.6 pg TEQ_{05}/g lipid, respectively. PCB126 was the largest contributor to the weighted arithmetic mean for PCB TEQ_{05} (67%), followed by PCB169 (26%) while the other PCB congeners each accounted for 4% or less of the PCB TEQ_{05}. PCB congeners combined accounted for 21% of PCDD/F+PCB TEQ_{05}.

Table 9. Concentrations of polychlorinated biphenyls (PCBs) in 49 pooled serum samples (pg/g lipid).

Congener	% Detected	Min	Max	Weighted geometric mean (wGSD)	Weighted geometric mean (wGSD) for age groups, years				Exponentiated age regression coefficient
					19-24 (n=7 pools)	25-34 (n=10 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	
PCB28	100	450	3100	890 (1.5)	750 (1.3)	950 (1.6)	760 (1.3)	1100 (1.5)	1.1
PCB74	100	490	2700	1200 (1.6)	620 (1.2)	940 (1.3)	1100 (1.2)	2000 (1.2)	1.5***
PCB99	100	310	2100	730 (1.6)	370 (1.2)	540 (1.2)	670 (1.2)	1200 (1.2)	1.5***
PCB105	100	140	720	330 (1.5)	170 (1.2)	260 (1.2)	300 (1.2)	530 (1.2)	1.5***
PCB114	98	<LOD	240	100 (1.8)	38 (1.8)	61 (1.3)	99 (1.2)	190 (1.2)	1.8***
PCB118	100	640	3500	1600 (1.6)	820 (1.2)	1200 (1.2)	1500 (1.2)	2700 (1.2)	1.5***
PCB123	73	<LOD	48	19 (1.8)	7.1 (1.5)	13 (1.6)	20 (1.3)	32 (1.4)	1.6***
PCB126	51	<LOD	25	8.7 (1.7)	5.2 (1.3)	4.9 (1.2)	8.6 (1.6)	15 (1.2)	1.6***
PCB138/163/164	100	2800	21000	7600 (1.7)	3500 (1.2)	4500 (1.1)	7500 (1.3)	14000 (1.2)	1.7***
PCB153	100	3500	33000	11000 (1.8)	4400 (1.2)	6000 (1.2)	11000 (1.3)	20000 (1.3)	1.7***
PCB156	100	470	4000	1500 (1.8)	650 (1.2)	820 (1.2)	1500 (1.3)	2800 (1.2)	1.7***
PCB157	100	92	730	280 (1.8)	120 (1.2)	160 (1.1)	280 (1.3)	540 (1.2)	1.6***
PCB167	100	140	980	370 (1.7)	180 (1.3)	210 (1.1)	370 (1.2)	720 (1.2)	1.7***
PCB169	41	<LOD	28	12 (1.5)	7.8 (1.4)	9.3 (1.3)	12 (1.5)	17 (1.4)	1.2**
PCB170	100	1000	11000	3700 (1.9)	1500 (1.3)	1900 (1.2)	3900 (1.4)	7300 (1.2)	1.8***
PCB180	100	2700	33000	11000 (1.9)	4000 (1.2)	5500 (1.2)	12000 (1.4)	22000 (1.2)	1.8***
PCB183	100	240	2600	720 (1.8)	290 (1.2)	410 (1.2)	750 (1.3)	1300 (1.3)	1.8***
PCB187	100	530	6400	2100 (1.9)	750 (1.2)	1100 (1.2)	2200 (1.3)	4100 (1.2)	1.9***
PCB189	100	26	540	190 (2.1)	58 (1.5)	87 (1.3)	220 (1.4)	390 (1.2)	1.9***
PCB194	100	380	7100	1900 (2.2)	500 (1.2)	860 (1.2)	2300 (1.3)	4300 (1.2)	2.1***

Congener	% Detected	Min	Max	Weighted geometric mean (wGSD)	Weighted geometric mean (wGSD) for age groups, years				Exponentiated age regression coefficient
					19-24 (n=7 pools)	25-34 (n=10 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	
PCB196/203	100	240	5000	1400 (2.1)	400 (1.3)	630 (1.2)	1600 (1.3)	2900 (1.2)	2.0***
PCB202	100	41	870	240 (2.1)	77 (1.4)	110 (1.4)	260 (1.4)	490 (1.3)	2.0***
PCB205	78	<LOD	100	37 (2.2)	9.4 (1.2)	18 (1.6)	46 (1.3)	74 (1.3)	2.1***
PCB206	100	61	1200	310 (2.2)	90 (1.4)	130 (1.7)	370 (1.2)	660 (1.3)	2.1***
PCB208	92	<LOD	450	91 (3.3)	20 (2.3)	22 (3.5)	140 (1.5)	230 (1.3)	2.3***
PCB209	100	100	770	280 (1.6)	130 (1.1)	170 (1.1)	320 (1.2)	420 (1.3)	1.5***
TEQ_{05} (PCB)				1.4 (1.6)	0.82 (1.3)	0.86 (1.2)	1.4 (1.4)	2.3 (1.2)	1.4***

1. Only congeners detected in >30% of pooled samples are reported and included in TEQ_{05}. Non-reported congeners are PCB15, 19, 37, 54, 77, 81, 104, 155, 188, and 200. PCB1, 3, 4/10, 44, 49, 52, 70, 101, and 110 were detected in serum pools at concentrations less than 5 times the concentrations in laboratory reagent blanks and were excluded. <LOD = below laboratory limit of detection. wGSD = weighted geometric standard deviation.

* p-trend<0.05

** p-trend<0.01

*** p-trend<0.001

OCPs:

Weighted geometric mean concentrations of OCPs in serum are presented in Table 10. The OCP found at the highest concentration was *p,p'*-DDE at 220 ng/g lipid, which was at least one order of magnitude higher than all other detected OCPs.

Table 10. Concentrations of organochlorine pesticides (OCPs) in 49 pooled serum samples (ng/g lipid).

Congener	% Detected	Min	Max	Weighted geometric mean (wGSD)	Weighted geometric mean (wGSD) for age groups, years				Exponentiated age regression coefficient
					19-24 (n=7 pools)	25-34 (n=10 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	
beta-HCH	100	1.1	65	7.0 (2.8)	2.4 (2.0)	4.5 (1.9)	9.1 (3.1)	9.9 (2.4)	1.4**
HCB	100	4.1	16	7.3 (1.3)	5.9 (1.2)	6.4 (1.3)	6.8 (1.2)	9.4 (1.3)	1.3***
dieldrin	100	1.7	16	4.7 (1.6)	3.9 (1.3)	4.9 (1.4)	4.1 (1.8)	5.7 (1.4)	1.1
p,p'-DDT	100	1.2	6.1	2.5 (1.5)	2.0 (1.2)	2.6 (1.3)	2.0 (1.4)	3.5 (1.3)	1.2***
p,p'-DDE	100	75	680	220 (1.7)	120 (1.3)	160 (1.5)	200 (1.4)	380 (1.3)	1.6***
mirex	94	<LOD	2.8	0.53 (1.9)	0.22 (1.2)	0.39 (1.4)	0.51 (1.8)	0.90 (1.5)	1.5***

1. Only OCPs detected in >30% of pooled samples are reported. Non-reported OCPs are *alpha*-HCH, *gamma*-HCH (lindane), *delta*-HCH, heptachlor, aldrin, heptachlorepoxide, oxychlordane, *gamma*-chlordane, endosulfan-A, alpha-chlordane, trans-nonachlor, *o,p'*-DDE, endrin, endosulfan-B, cis-nonachlor, *o,p'*-DDD, *p,p'*-DDD, *o,p'*-DDT, and methoxychlor. PeCB was detected in serum pools at concentrations less than 5 times the concentrations in laboratory reagent blanks and was excluded. <LOD = below laboratory limit of detection. wGSD = weighted geometric standard deviation.

* p-trend<0.05

** p-trend<0.01

*** p-trend<0.001

Influence of demographic characteristics:

Age was positively associated (p-trend<0.05) with 10 out of 13 PCDD/Fs, 25 out of 26 PCBs, TEQ_{05} (PCDD/F, PCB, and PCDD/F+PCB), *beta*-HCH, HCB, *p,p'*-DDT, *p,p'*-DDE, and mirex. As indicated by the exponentiated age regression coefficients, serum concentrations increased by 40% (regression coefficient 1.4) with each increase in age category for both the PCDD/F TEQ_{05} and the PCB TEQ_{05}. This age gradient was steeper for the dioxins (30-80% higher with each increase in age category) compared to the furans (0-30% higher with each increase in age category). There were large differences in trends with age for individual PCBs with generally no association shown for the lower chlorinated PCBs and a very strong association observed (up to 200% higher with each increase in age category) for the higher chlorinated PCBs.

Associations found for other determinants (sex, ethnicity, and region) were less consistent and did not show clear trends. Male sex was associated (p<0.05) with higher concentrations of 2,3,4,7,8-PeCDF, 14 out of 26 PCBs, dieldrin, and mirex. Female sex was associated (p<0.05) with higher concentrations of OCDD and 2 out of 26 PCBs. Māori ethnicity was associated (p<0.05) with lower concentrations of 2,3,7,8-TCDD, PCB194, PCB196/203, PCB202, PCB206, PCB209, and *beta*-HCH. Māori ethnicity was also associated (p<0.05) with higher concentrations of *p,p'*-DDT, *p,p'*-DDE, and mirex. Residence in the Waikato/BOP region was associated (p<0.05) with higher concentrations of 1,2,3,7,8-PeCDD, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,7,8,9-HxCDD, and TEQ_{05} (PCDD/F and PCDD/F+PCB) compared to residence in the Northland/Auckland region. Residence in the Lower North Island region was

associated ($p<0.05$) with higher concentrations of PCB28, PCB99, *p,p'*-DDT, and *p,p'*-DDE. Residence in the South Island region was associated ($p<0.05$) with higher concentrations of 1,2,3,7,8-PeCDD, 1,2,3,7,8-PeCDF, *beta*-HCH, dieldrin, and *p,p'*-DDE.

Temporal comparison:

Figure 11 shows the overall weighted arithmetic mean of the 2012 concentrations expressed as a percentage of the 1997 concentrations. Concentrations for all POPs determined in both surveys were lower in 2012 by at least 25%. The TEQ_{98} for PCDD/F was 50% lower in the 2012 survey and the largest difference was observed for *p,p'*-DDE (77% lower in the 2012 survey).

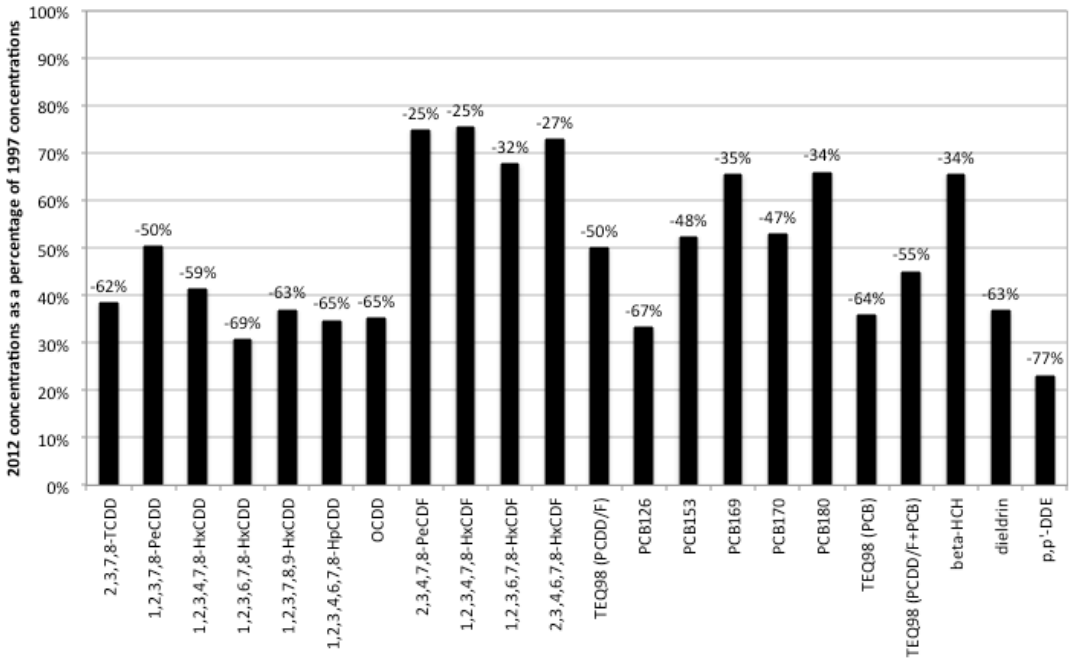

Figure 11. Temporal comparison chlorinated POPs between the 1997 and 2012 surveys.

(2012 concentrations shown as bars representing percentage of 1997 concentrations with percent difference between the 2 surveys shown above bars)

Figure 12 and Figure 13 show the 1997 age-group-specific concentrations (solid black squares) and shifts these to the age groups they would be in 15 years later at the time of the 2012 survey (horizontal arrows). Comparing these concentrations (solid grey squares) to those measured in 2012 (white squares) gives an indication of the reductions in individuals' serum concentrations over the 15 years between the two surveys (as indicated by the vertical arrows). For the majority of POPs, substantial reductions were observed (examples in Figure 12) with some exceptions (Figure 13). Figure 13 indicates that for 2,3,4,7,8-PeCDF, 1,2,3,4,7,8-HxCDF, and PCB180 there was no evidence that serum concentrations in individuals have reduced in the 15 years between the two surveys.

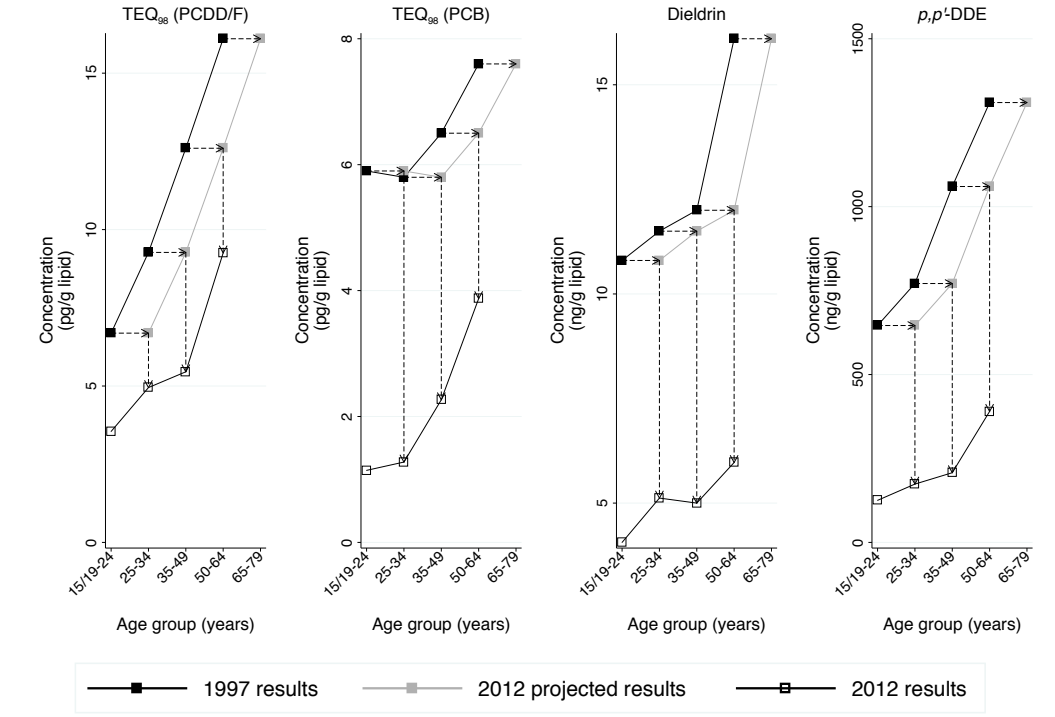

Figure 12. Examples of chlorinated POPs for which serum concentrations have declined in individuals.

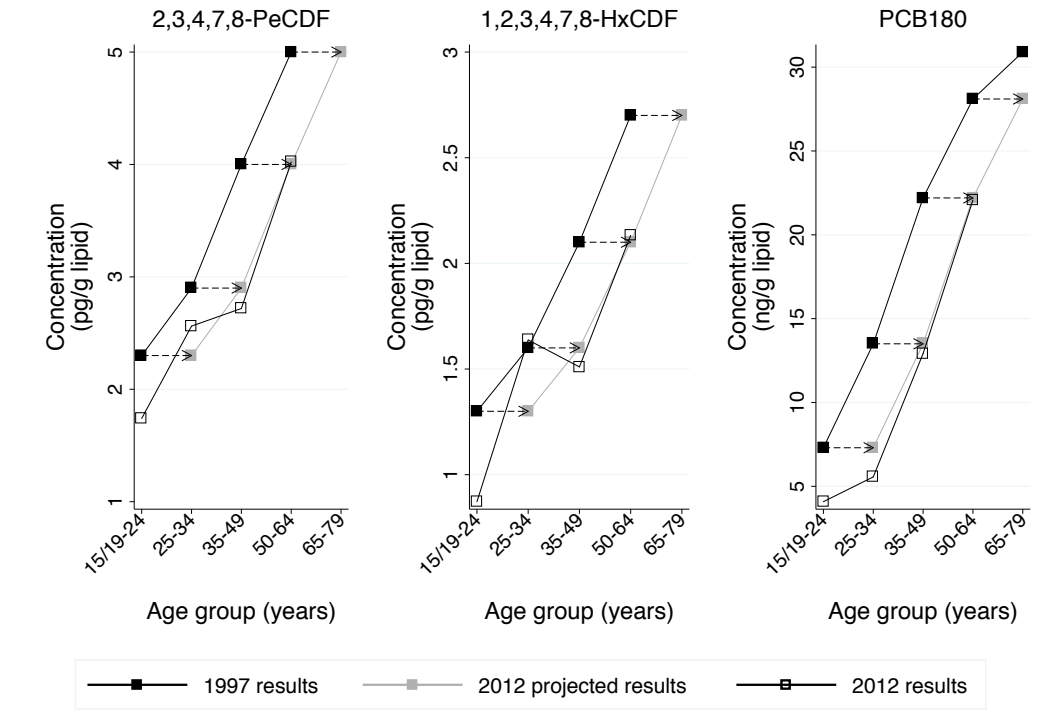

Figure 13. Examples of chlorinated POPs for which serum concentrations have not changed in individuals.

Discussion

This survey provides an estimate of serum concentrations of chlorinated POPs in the general adult population of New Zealand. We observed a clear decrease in overall mean serum concentrations of all POPs for all age groups since the previous survey in 1997, with a 50 to 69% reduction in PCDDs, 25 to 32% reduction in PCDFs, 34 to 67% reduction in PCBs, and 34 to 77% reduction in OCPs.

The observed reduction in serum POPs is consistent with New Zealand human milk surveys which showed PCDD/Fs, PCBs, and OCPs were 40%, 54%, and 34-90% lower, respectively, in samples collected in the period 2007 to 2010 compared to measurements in 1998 [19]. Similar temporal reductions of chlorinated POPs in humans and the environment are shown in international studies carried out between 1989 and 2010 [39], suggesting a global trend of a decreasing background exposure of chlorinated POPs in the general population.

Both the 1997 and 2012 New Zealand surveys showed that within the adult population older people have higher serum concentrations which is highly consistent with other recent international surveys [30, 159, 167, 179]. Our survey also showed that the strength of the association between age and serum concentration is specific for different compounds and congeners. In particular, no association with age was shown for PCB congeners with the lowest chlorination while progressively stronger associations were observed for PCB congeners with increasing chlorination. This pattern may be related to the relatively slow metabolic elimination rate of higher-chlorinated PCBs [219]. The general trend of higher serum concentrations of

persistent organic pollutants in older age groups observed in cross-sectional studies is characteristic of a post-ban situation where emissions and environmental levels of these compounds are past their peak, as illustrated by pharmacokinetic models [28, 180, 220]. For example, individuals in the oldest two age groups in the 2012 New Zealand survey, born between 1948 and 1977, grew up in a period of increasing global POPs emissions [12] and would have accumulated a relatively high body burden of chlorinated POPs. Individuals in the youngest two age groups, born between 1978 and 1993, grew up in a period of decreasing global POPs emissions, and the eventual New Zealand ban of many chlorinated POPs in the late 1980s, and would therefore have had relatively low POPs exposure throughout their life. Therefore, reductions in population levels of POPs over time are at least in part attributable to a cohort effect, with the older more highly exposed cohorts no longer being part of the current population and younger cohorts (born after peak emissions) entering the population. However, in addition to a cohort effect, the two New Zealand surveys also provide indirect evidence that within individuals, serum concentrations have reduced substantially over time (Figure 2). In particular, comparing the results of both surveys suggest that for most of the POPs metabolic elimination is greater than residual intake from food and other sources. For some POPs (i.e. certain PCDFs and PCB180) individual serum concentrations appear to have remained stable between 1997 and 2012, despite an overall decrease in the general adult population (Figure 3). This pattern is also observed in human milk studies which show that concentrations of certain PCDFs are declining at a slower rate than PCDDs after the year 2000 [19, 53, 221], reflecting an equilibrium between current intake and elimination rates for these compounds. For none of the measured

POPs was there evidence that individual serum concentrations had increased over time.

The associations between serum POPs concentrations and other demographic characteristics (sex, ethnicity, study region) were less consistent than the age-related association discussed above. However, the results suggest that male sex is associated with serum concentrations of a number of POPs. Some international studies of POPs similarly find higher concentrations of certain POPs in males [222], while other studies show higher concentrations in females [177, 223], or no sex-related association [164, 179]. The reasons for such sex-related differences are unclear [30], however lifestyle differences (e.g. diet, occupational exposures) and differences in physico-chemical factors (e.g. metabolism and elimination of POPs) may play a role.

Since 2000, comparable surveys of POPs in a representative sample of a national population have been completed in Australia, the USA, and Canada [30] of which Australia is the most comparable to New Zealand in terms of demographic characteristics and scale of industrial and agricultural activity. Comparisons between New Zealand and Australian data (collected in 2003; Harden, Toms, Paepke, Ryan, & Müller, 2007) showed that concentrations of individual PCDD and PCDF congeners were similar. There were some exceptions with 1,2,3,6,7,8-HxCDD 2.0 times higher in Australia, and 2,3,4,7,8-PeCDF 1.7 times higher in New Zealand. Overall, weighted arithmetic mean PCDD/F/PCB TEQ_{05} was lower in New Zealand (7.3 pg TEQ_{05}/g lipid) compared to Australia (11 pg TEQ_{05}/g lipid), although this may be explained by the 10 years between surveys. More recent Australian results from testing of pooled

surplus pathology serum samples collected in 2010/11 and 2012/13 for selected PCBs [165] showed that arithmetic mean concentrations for most PCBs are comparable between Australia and New Zealand, with the exception of PCB206 and PCB209 which were 4 to 10 times higher in Australians during the period contemporary to the 2012 New Zealand survey. The reason for this apparent difference in PCB206 and PCB209 is not entirely clear, but, as noted above, this may be related to the relatively long metabolic elimination rate of higher-chlorinated PCBs [219], or differences in historical exposure conditions between the two countries.

Mean adult PCDD/F TEQ_{05} concentrations in USA adult serum samples collected in 2003/04 were 2 times higher than 2012 New Zealand concentrations. Also, more recent results from the USA [153] show that TEQ_{05} (PCDD/F+PCB) concentrations for the USA adult population in 2005/06 and 2007/08 were 2 times higher than results from the 2012 New Zealand study. Similarly, TEQ_{05} (PCCD/F+PCB) measured in Canadian pooled serum samples collected in 2007/09 [159] was 1.5 times higher than the 2012 New Zealand results. The relatively higher mean concentration of PCDDs, PCDFs, and PCBs in the USA and Canada are likely the result of historical differences in level of industrialisation compared to New Zealand.

OCPs have been measured in pooled Australian human serum samples taken during the period 2002 to 2013, showing an overall decrease of OCP concentrations over this time period [167]. The Australian 2012/13 study-period results were higher than the New Zealand 2012 results for HCB (1.3 times higher) and *p,p'*-DDT (1.7 times higher), similar for *beta*-HCH, and lower for *p,p'*-DDE (a metabolite of DDT; 1.3 times

lower). The differences in OCP concentrations between Australia and New Zealand are not large, reflecting similarities in current and historical agricultural and horticultural activity between the two countries. For further comparison, mean concentrations of *p,p'*-DDE in Canadian (2007/09) and USA (2003/04) adults [224, 225] were higher than the 2012 New Zealand results. USA pooled serum samples collected in 2005/06 and 2007/08 [153] indicated higher concentrations than the New Zealand results for HCB (1.5 times higher), *p,p'*-DDT (3.9 times), *p,p'*-DDE (2.4 times), and mirex (7.2 times), with the exception of *beta*-HCH (1.4 times higher in New Zealand). There were large differences in OCP concentrations between racial groups in the USA, which were not observed consistently in the New Zealand survey.

This survey has strengths and weaknesses. A particular strength of the survey is that results are directly comparable with a previous survey conducted 15 years earlier using essentially the same stratified sample design allowing time trends to be assessed. Similar time trend analyses for POPs in adult serum have only been possible for a few countries such as the USA, Canada, and Australia [159, 165, 226, 227]. While the use of pooled samples does not allow comparisons between individuals in the survey or the evaluation of the impact of outliers, pooled samples do provide a reliable estimate of the general tendency of POPs within demographic groups. The survey had low contact and participation rates, particularly in certain demographic groups (e.g. young males and females, particularly of Māori descent). However, any issues of the sample population not being representative of the source population were mitigated by using serum pools for specified demographic strata,

and survey weights equal to stratum-specific population counts when calculating the population geometric means. We therefore consider that the results are likely to be representative for the New Zealand adult population.

Conclusion

The results of the second national survey of POPs in New Zealand adults show clear decreases of chlorinated POPs in the New Zealand population since the first national serum survey in 1997. As expected, higher levels of chlorinated POPs were found in older age groups. There were no consistent associations of POPs with sex, ethnicity, or geographic region. Concentrations of chlorinated POPs in New Zealand adults are generally lower than in populations of other comparable countries.

Chapter 6. Polybrominated diphenyl ethers and perfluorinated alkyl substances in blood serum of New Zealand adults, 2011-2013

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Abstract

A national survey was conducted in 2011-2013 to assess serum concentrations of brominated flame retardants (BFRs) and perfluorinated alkyl substances (PFASs) in adult New Zealanders. Participants were randomly selected from the 2010 Electoral Roll within 64 demographic strata according to 4 age groups, 4 geographic regions, 2 ethnic groups (Māori/non-Māori) and sex. Eligible participants (n=734; response rate of contacted individuals = 37%) donated up to 30 mL of blood, after which serum was pooled (49 pools for BFRs, 63 pools for PFASs) according to demographic strata. BFRs were analysed by GC-HRMS and PFASs by LC-MS/MS. Associations between serum BFRs and PFASs and demographic variables (age, region, ethnicity, sex) were assessed using regression analysis. The weighted geometric mean (GM) serum concentrations of BDE47, BDE99, BDE100, and BDE153 were 2.0, 0.66, 0.43, and 1.2 ng/g lipid, respectively. The weighted geometric mean (GM) serum concentrations of PFOS, PFOA, PFHxS, and PFNA were 3.4, 2.4, 1.0, and 0.66 ng/mL, respectively. The majority of BFRs showed higher serum concentrations in younger age groups. Conversely, the four PFASs showed higher serum concentrations in older age groups. Concentrations of BFRs and PFASs were generally lower in females compared to males. In New Zealand, both age and sex are important determinants of BFR and PFAS serum concentrations. Serum concentrations of BFRs and PFASs in New Zealand are in the middle of the range of international results.

Introduction

Brominated flame retardants (BFRs) and perfluorinated alkyl substances (PFASs) are synthetic chemicals that can be present in a wide range of products, including consumer goods, electronics, textiles, surface treatments, adhesives and building materials. Due to their wide use and persistence in the environment, exposure to BFRs and PFASs has become universal in humans and wildlife over the past decades. There is evidence that these chemicals adversely affect a range of physiological processes, including disruption of the endocrine system [11, 96, 228, 229]. National surveys that have investigated levels of BFRs and PFASs in humans are scarce [30], but indicate that substantial differences in population levels of these countries may exist between countries and demographic groups based on age, sex, and ethnicity.

The manufacture and use of BFRs has been subject to strict regulatory controls, including outright bans in many countries on common BFR formulations. Tetra- to hepta-brominated BFR formulations are included in the Stockholm Convention on Persistent Organic Pollutants (POPs), and there is a proposal to also include the commonly used deca-brominated formulation (i.e. BDE209) in this international treaty [40]. Internationally, PBDE use has largely been switched to alternative flame retardants such as tetrabromobisphenol A (TBBPA) and hexabromocyclododecane (HBCD), and organophosphate flame retardants (OPFRs) [230]. The import, use and manufacture of BFRs included in the Stockholm Convention are currently not permitted under New Zealand legislation, but estimates suggest annual imports of 15 tonnes prior to this ban mostly for manufacturing of export goods [231]. Human biological monitoring studies of BFRs in New Zealand include a small study of PBDEs

in serum collected in 2001 from 23 adult blood donors in Wellington [99] and a study of PBDEs in human milk [19]. The results of these studies show that BFR concentrations in New Zealand were comparable to Europe, and lower than the USA and Australia. However, given the small size of these previous studies, levels of BFRs in the general New Zealand adult population are unclear.

Less is known in New Zealand about human exposure to PFASs. Similar to BFRs, the import and use of PFOS, its salts, and perfluorooctane sulfonyl fluoride (PFOSF) have been controlled under New Zealand legislation since 2011, but PFOS and PFOA have been previously used in applications such as fire-fighting foams on defence force bases [232]. PFOS and PFOA have been detected in New Zealand wastewater, soil, and sewage sludge [103]. However, there have been no previous New Zealand studies of PFAS levels in humans.

This paper reports the results of the first national survey of BFRs and PFASs in the serum of adult New Zealanders. The results of the survey are compared with human serum concentrations of BFRs and PFASs reported for other countries, and we investigate the significance of demographic determinants of exposure (i.e. age, sex, ethnicity, and geographic region) to BFRs and PFASs.

1

Methods

This cross-sectional survey assessed serum concentrations of BFRs and PFASs, using a stratified sampling method. Participants were recruited using the 2010 Electoral Roll from the New Zealand Electoral Commission (www.elections.org.nz). Potential study participants were randomly selected with equal proportions based on age (19−24, 25−34, 35−49, 50−64 years), sex, geographic region (Northland/Auckland, Waikato/Bay of Plenty, Lower North Island, South Island), and ethnicity (Māori, non-Māori). Ethics approval was obtained from the Upper South A Regional Ethics Committee (reference URA/10/07/054 11 August 2010).

Mailed invitation letters, along with an information sheet and reply form, were sent in 6 separate mail-out events between February 2011 and June 2012 to 14,310 people. For those who replied positively we conducted a short telephone interview to determine eligibility. Chlorinated POPs (i.e. dioxins, furans, PCBs, and organochlorine pesticides) were included in the survey, therefore the exclusion criteria covered current or previous employment in occupations with high exposure to chlorinated POPs, specifically timber treatment, manufacture and repair of electrical equipment, and pesticide application. In addition, participants were not eligible if they had medical conditions that would prohibit giving blood (e.g. exposure to certain blood-borne pathogens or other conditions specified by the respondent), or non-residency in New Zealand at the time of the survey.

Eligible participants provided written consent and were asked to visit a local private pathology laboratory to have up to 30 mL of whole blood taken (see Appendix 1). Blood samples were collected during 2011 and 2012. Blood was allowed to clot (30 –

45 minutes) at room temperature then centrifuged and serum was collected using cleaned glass pipettes. Serum samples and bovine serum quality control (QC) samples were stored in amber glass vials (for BFR analyses) and polypropylene vials (for PFAS analyses) at -20^{o}C. Polypropylene vials were used to avoid potential PFAS contamination from polytetrafluoroethylene (PTFE) lined seals in glass vials, and to avoid adsorption of PFAS to glass vials.

Sample pooling and laboratory analysis:

A pooling strategy was applied to ensure sufficient serum volume in each pool to achieve suitable laboratory detection limits for BFRs to and reduce analytical costs. The pooled serum samples were also tested for chlorinated POPs so the required sample volume was relatively large (50 mL). We did not have sufficient participants in all demographic strata to create pools using equal volume aliquots, while still achieving the required volume of serum per pool. We estimated the pool-specific 75th percentile volume for the individual samples within each pool and used this figure as the maximum volume that would be aliquoted to the pool from any participant. If a participant's sample serum volume was less than the pool-specific 75th percentile volume, the complete serum sample was aliquoted to the pool. For age strata with low numbers of participants (i.e. males aged 19-34, Māori females aged 19-24), the samples from the four geographic regions were combined together into one pool (see Appendix 2). The selected analytical method for PFASs (LC-MS/MS) requires considerably less serum therefore separate pools comprised of equal volumetric aliquots (0.5 to 1.0 mL) were made for this analysis.

The pooled serum samples were analysed (AsureQuality, Lower Hutt) using isotope dilution methods; GC-HRMS for BFRs and LC-MS/MS for PFASs. For BFRs analysis a matrix spike and reagent blank was included with each batch of samples. Each sample was spiked with ^{13}C labelled internal standards prior to extraction using C18 SPE. Clean-up and fractionation was achieved using acid silica, basic alumina, and florisil. The cleaned extracts were spiked with recovery standards before being reduced to a final volume of 50 µL. BFRs were analysed by GC-HRMS (Agilent 6890/7890 GC, Waters Ultima/Premier HRMS at 5,000 mass resolution). Quantification was performed using Waters QuanLynx software. Internal standards were used for quantification of the target analytes, thus results were recovery corrected. The recovery standard was used for quantification of the internal standards to determine the percent recovery. Limit of detection (LOD) for BFRs was calculated based on a signal-to-noise ratio (S/N) of 3.

For PFASs, a 0.5 mL aliquot was spiked with labelled internal standards prior to liquid-liquid extraction. Clean-up was achieved using hexane partitioning. The cleaned extracts were spiked with recovery standards before being reduced to a final volume of 1 mL. PFASs were analysed by LC-MS/MS (Agilent 1200 HPLC, AB Sciex API 5000 triple quadrupole MS). Quantification was performed using AB Sciex MultiQuant software. The internal standards were used for quantification of the target analytes, thus results are recovery corrected. The recovery standard was used for quantification of the internal standards to determine the percent recovery. The results for PFAS are for the linear isomer only, and the results for PFOS include the salts of PFOS and perfluorooctanesulfonyl fluoride (PFOSF). Limit of reporting (LOR)

for PFAS was defined as the concentration of the lowest calibration standard (0.5 ng/mL)

Triglycerides and HDL-cholesterol levels were determined using Roche P800 GPO-PAP and P800 Direct Enzymatic methods, respectively. Serum lipid concentrations were calculated using the formula of Phillips et al. [150] and results for BFRs were reported as pg/g on a lipid adjusted basis. Results for PFASs are reported as ng/mL serum.

Data analysis:

Summary statistics for each analyte (detection frequency, weighted arithmetic mean, weighted geometric mean, weighted geometric standard deviation) were calculated using Stata v.11.2 (Statacorp, USA). For those analytical results below the LOD for BFRs, or the LOR for PFASs, a value of 0.5 x LOD or 0.5 x LOR was assigned. Weighted summary statistics were obtained by applying weights equal to stratum-specific population counts from the 2010 Electoral Roll.

Analytes were excluded from further consideration if their testing results met either of two arbitrary criteria; if (a) they were at concentrations under the laboratory detection limit in more than 50% of pooled samples; or (b) the arithmetic mean concentration of the analyte in the serum pools was less than 4 times the arithmetic mean concentration of the analyte in laboratory reagent blanks. The results of QC testing in this survey were consistent with other surveys of background concentrations of BFRs and PFASs in the general population, with relatively high variability between the limited number of QC and survey samples.

Multivariate linear regression was used to assess associations between demographic characteristics and serum concentrations of BFRs and PFASs. Demographic characteristics included in the regression model were age group, sex, ethnicity, and study region (as a categorical variable with Northland/Auckland as the reference region). We treated age group as a categorical variable to assess age-related associations for each age group with the youngest age group (19-24 years) as the reference. In a separate model we treated age group as a continuous variable to assess the overall trend. Un-weighted natural log-transformed BFR and PFAS concentrations were used in all regression models.

Results

Survey sample:

Of the 14,310 adults invited, 1,986 returned a reply form or were contacted by telephone, and 734 participated in the study (37% participation rate for the contacted individuals). Younger age groups, males and Māori were less likely to participate in the study, but over-sampling of these strata provided sufficient individual samples to contribute to pools. Details of the study sample are reported in a separate paper [36]. The number of pools was 49 for the majority of BFR congeners, except for BDE207, BDE208 and BDE209 where only 42 pools were included due to anomalously high values of BDE209 in one laboratory blank sample.

BFRs:

For 19 out of 40 BFRs, the detection frequency was below 50% (BDE7, 17, 30, 71, 77, 119/120, 126, 138/166, 139, 140, 156/169, 171, 180, 191, 204, 205, PBEB, HBB, and DBDPE). For 16 of the 21 remaining BFRs the blank samples showed detectable levels (BDE15, 28/33, 47, 49, 66, 85, 99, 100, 153, 154, 183/175, 206, 207, 208, 209, and BB153). The arithmetic mean (AM) of BDE49 for the serum pools was less than 4 times the AM in the blanks, so the results for BDE49 are not reported.

Weighted geometric mean concentrations of BFRs in serum are presented in Table 11. The congener with the highest weighted geometric mean concentration was BDE209 at 3.4 ng/g lipid. Weighted geometric mean concentrations for other common PBDE congeners BDE47, BDE99, BDE100, BDE153, and BDE154 were 2.0, 0.66, 0.43, 1.2, and 0.085 ng/g lipid, respectively.

Table 11. Concentrations of brominated flame retardants (BFRs) in pooled serum samples.

Congener	% Detected	Weighted geometric mean (wGSD), pg/g lipid							Exponentiated regression coefficient	
		Age group (years)					Sex			
		19-64 (n=49 pools)	19-24 (n=7 pools)	25-34 (n=10 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	Male (n=20 pools)	Female (n=29 pools)	Age group	Sex[1]
BDE15	100	45 (1.4)	37 (1.4)	41 (1.2)	44 (1.4)	51 (1.5)	43 (1.6)	46 (1.3)	1.1	1.1
BDE28/33	100	120 (1.3)	140 (1.2)	110 (1.2)	120 (1.3)	110 (1.5)	120 (1.3)	110 (1.3)	0.89*	1.3*
BDE47	100	2000 (1.5)	3000 (1.3)	2400 (1.4)	1900 (1.4)	1600 (1.5)	2100 (1.5)	1900 (1.5)	0.78***	1.2
BDE66	86	21 (1.9)	31 (1.9)	30 (1.7)	25 (1.3)	13 (2.2)	21 (1.9)	21 (2.0)	0.67***	1.4
BDE85	94	37 (2.2)	65 (1.7)	29 (4.4)	39 (1.5)	35 (1.8)	34 (2.2)	41 (2.3)	0.72*	1.2
BDE99	100	660 (1.9)	1000 (1.9)	870 (2.9)	550 (1.4)	570 (1.5)	670 (1.7)	640 (2.1)	0.76*	1.1
BDE100	100	430 (1.6)	620 (1.5)	480 (1.9)	420 (1.4)	360 (1.5)	440 (1.5)	420 (1.7)	0.77**	1.3
BDE153	100	1200 (1.4)	1200 (1.2)	1200 (1.4)	1400 (1.5)	1100 (1.5)	1500 (1.4)	1100 (1.4)	0.87*	1.8***
BDE154	98	85 (2.0)	130 (1.6)	89 (2.9)	81 (1.3)	74 (2.4)	88 (1.7)	82 (2.4)	0.73*	1.4
BDE183/175	100	220 (2.1)	150 (1.4)	190 (1.3)	300 (2.8)	180 (1.6)	310 (2.4)	160 (1.4)	0.91	1.8**
BDE184	59	14 (1.9)	17 (1.6)	15 (1.5)	16 (2.2)	10 (1.8)	19 (1.8)	10 (1.8)	0.73***	1.9***
BDE196	80	99 (1.9)	160 (1.3)	100 (1.4)	110 (2.3)	74 (1.7)	140 (1.7)	73 (1.9)	0.65***	2.2***
BDE197	100	720 (1.4)	710 (1.1)	750 (1.1)	760 (1.6)	670 (1.5)	950 (1.3)	560 (1.2)	0.89**	1.7***
BDE201	100	150 (1.4)	190 (1.2)	170 (1.1)	150 (1.5)	130 (1.4)	190 (1.2)	130 (1.4)	0.79***	1.6***
BDE203	84	150 (1.8)	200 (2.0)	140 (1.5)	180 (1.7)	110 (1.9)	200 (1.7)	110 (1.7)	0.67***	2.5***
BDE206[2]	95	300 (1.5)	440 (1.2)	330 (1.4)	330 (1.4)	190 (1.3)	310 (1.4)	280 (1.5)	0.70***	1.4**
BDE207[2]	100	890 (1.3)	1100 (1.2)	950 (1.2)	900 (1.4)	740 (1.2)	1000 (1.3)	810 (1.3)	0.85***	1.3**
BDE208[2]	100	340 (1.5)	510 (1.4)	340 (1.2)	370 (1.7)	260 (1.2)	390 (1.5)	310 (1.5)	0.77***	1.4**
BDE209[2]	100	3400 (1.4)	4000 (1.4)	3400 (1.3)	3700 (1.5)	2600 (1.2)	3700 (1.3)	3000 (1.4)	0.85**	1.3*
BB153	100	420 (1.8)	230 (1.8)	230 (1.4)	510 (1.4)	620 (1.5)	500 (1.6)	360 (1.8)	1.5***	1.4*

Only congeners detected in >50% of pooled samples are reported. Non-reported congeners and their detection frequencies are BDE7 (0%), 17 (18%), 30 (31%), 71 (0%), 77 (2.0%), 119/120 (0%), 126 (2.0%), 138/166 (10%), 139 (45%), 140 (10%), 156/169 (0%), 171 (16%), 180 (14%), 191 (0%), 204 (0%), 205 (0%), PBEB (6%), HBB (41%), and DBDPE (0%). BDE49 was detected in serum pools at concentrations less than 4 times the concentrations in laboratory reagent blanks, and results are not reported. wGSD = weighted geometric standard deviation.

1. Male compared to female
2. N=42 pools. 19-24 years n=7 pools. 25-34 years n=10 pools. 35-49 years n=14 pools. 50-64 n=11 pools. Male n=16 pools. Female n=26 pools.

* p-trend<0.05
** p-trend<0.01
*** p-trend<0.001

PFASs:

For 12 out of 16 PFASs, the detection frequency was below 50% (NEtFOSAA, NMeFOSAA, PFBS, PFDA, PFDoA, PFDS, PFHpA, PFHxA, PFOSA, PFTeDA, PFTrDA, and PFUnA) and results are therefore not reported. None of the PFASs were detected in blank samples.

Weighted geometric mean concentrations of PFASs in serum are presented in Table 12. The weighted geometric mean concentrations for PFOS, PFOA, PFHxS, and PFNA were 3.4, 2.4, 1.0, and 0.66 ng/mL, respectively.

Table 12. Concentrations of perfluorinated alkyl substances (PFASs) in pooled serum samples.

Congener	% Detected	Weighted geometric mean (wGSD), ng/mL							Exponentiated regression coefficient	
		Age group (years)					Sex			
		19-64 (n=63 pools)	19-24 (n=15 pools)	25-34 (n=16 pools)	35-49 (n=16 pools)	50-64 (n=16 pools)	Male (n=31 pools)	Female (n=32 pools)	Age group	Sex[1]
PFOS	100	3.4 (1.4)	2.8 (1.4)	3.0 (1.4)	3.2 (1.4)	4.2 (1.2)	4.1 (1.2)	2.8 (1.4)	1.2***	1.4***
PFOA	100	2.4 (1.3)	2.2 (1.2)	2.2 (1.3)	2.2 (1.4)	2.9 (1.1)	2.9 (1.2)	2.0 (1.3)	1.1***	1.3***
PFHxS	84	1.0 (2.1)	0.75 (2.4)	0.64 (2.4)	1.1 (1.8)	1.3 (1.6)	1.6 (1.6)	0.66 (1.9)	1.3***	1.9***
PFNA	87	0.66 (1.4)	0.54 (1.5)	0.57 (1.6)	0.63 (1.2)	0.82 (1.1)	0.71 (1.3)	0.62 (1.4)	1.2***	1.1

Only congeners detected in >50% of pooled samples are reported. Non-reported congeners and their detection frequencies are PFBS (0%), PFDS (0%), PFHxA (0%), PFHpA (0%), PFDA (1.6%), PFUNA (0%), PFDOA (0%), PFTrDA (0%), PFTeDA (0%), PFOSA (0%), NETFOSAA (0%), and NMEFOSAA (1.6%). wGSD = weighted geometric standard deviation.

1. Male compared to female

*** p-trend<0.001

Influence of demographic characteristics:

Age group and sex were the key demographic characteristics associated with serum BFRs and PFASs (see Table 11 and Table 12). Age was inversely associated (p-trend<0.05) with concentrations for 17 out of 19 PBDE congeners and positively associated for BB153. Age was positively associated (p-trend<0.05) for PFOS, PFOA, PFHxS, and PFNA. Male sex was positively associated (p<0.05) with concentrations of 12 out of 19 PBDE congeners, BB153, PFOS, PFOA, and PFHxS. Associations found for other determinants (ethnicity, study region) were less consistent and did not show clear trends for BFRs. For PFASs we found no associations with ethnicity, however there were inconsistent associations with study region with lower concentrations of PFNA associated with residence in the Lower North Island and South Island (relative to Northland/Auckland).

Figure 14 shows exponentiated age-related coefficients from multivariate regression (with age group treated as a categorical variable, adjusted for sex, ethnicity, and study region), representing the concentrations of BFRs and PFASs relative to the youngest age group (19-24 years). For BFRs the difference between the youngest and the oldest age group (50-64 years) was highest (3.8 times higher in the youngest age group) for BDE196 and lowest (1.3 times higher) for BDE197. Conversely, concentrations of BB153 in the oldest age group were 3.2-times higher than the youngest age group. For PFASs the concentrations of PFOA and PFOS in the oldest age group were 1.4 and 1.5-times higher, respectively, than the youngest age group. For the majority of BFRs concentrations were higher in males compared to females, ranging from 1.3-times (BDE28/33) to 2.5-times (BDE203) higher. For PFASs the

concentrations of PFOS, PFOA, and PFHxS were 1.4, 1.3, and 1.9-times higher, respectively, in males compared to females.

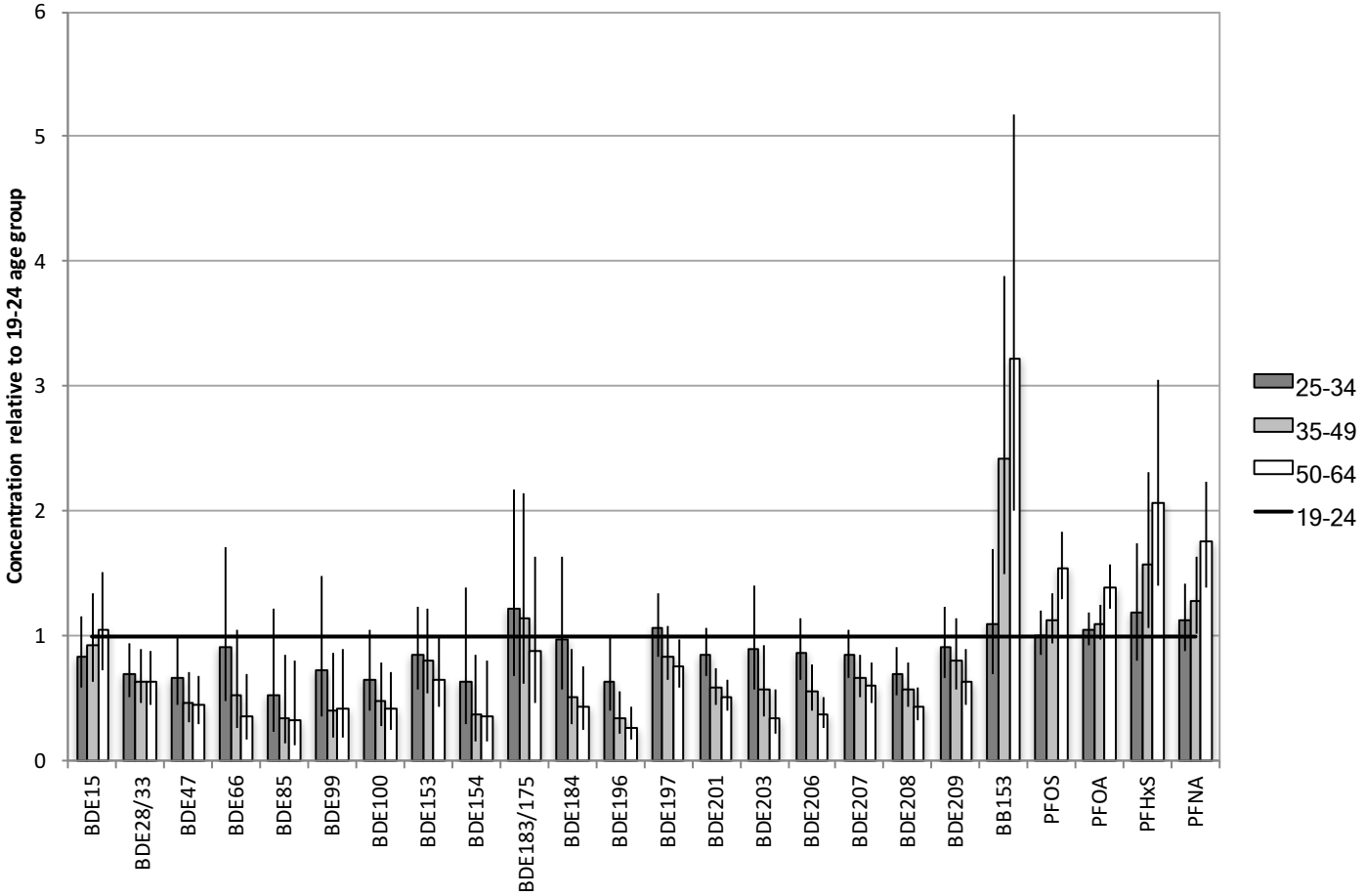

Figure 14. Age-specific concentrations of BFRs and PFASs relative to the youngest age group (19-24 years). Lines represent 95% confidence intervals

Discussion

This survey provides benchmark data for BFRs and PFASs in the general adult population of New Zealand. We observed a consistent pattern of higher concentrations of PBDEs in the younger age groups. Similar age-related associations have been observed in studies of serum BFRs in Australian adults (collected between 2002 and 2009), which showed higher BFR concentrations in younger individuals, decreasing until middle age (i.e. 40+ years) [233]. The 2003/04 NHANES study in the USA showed a linearly decreasing trend of BFR concentrations with age, and the highest BFR concentrations in 12 to 19 year olds [234]. However, the results of later USA NHANES rounds (2005/06 and 2007/08) did not show a difference in PBDE concentrations between age groups [235], attributed by the authors to similar exposure to PBDEs across all age groups, and their relatively short half-lives. A study of BFRs in 42 German adults (serum collected in 2013) also found no association of BFRs with age [179]. The 2001 study of BFRs in New Zealand adults [99] showed no evidence of an age-related association of serum BFRs, however, the study had a relatively small sample size (23 participants). A study of BFRs in New Zealand human milk also showed no association with age, though the sample was limited to mothers 20 to 30 years of age [19]. We found age to be negatively associated with increasing serum concentrations of the higher brominated BDEs, including BDE209. BDE209 has a relatively short human elimination half-life, estimated at 15 days [236], suggesting that the observed age pattern may be explained by ongoing sources of BDE209 in New Zealand, that are particularly relevant for the younger age groups. We have no information on current sources of BDE209 in New Zealand, but previous surveys

confirm BDE209 is the dominant congener in household dust, and is present in human milk [38].

Unlike the PBDEs, BB153 was found at higher concentrations in older participants. BB153 was phased out in the USA in the 1970s and it is likely that the period of peak use in New Zealand occurred around that time. Older participants would have been children during the period of peak exposure to BB153, as contrasted by the PBDEs, which have a period of peak exposure in the 1990s [237]. The human elimination half-life of BB153 is estimated at 12 years [237], so the observed age-related association is consistent with that seen for other POPs with relatively long elimination half-lives (e.g. dioxins, PCBs), in serum samples collected well after the period of peak exposure [28]. A similar age-related association for BB153 has been observed in the USA NHANES 2003/04 round [234].

When PFASs are considered, the results show higher concentrations in the older age groups. A positive association of PFASs with age has been shown in studies from Germany, the USA, and Australia [11, 157, 174]. However, the age-related association is not consistent for all studies, with some studies showing an association for only specific PFAS congeners, and for only one sex. Positive associations with age are generally found in modeled cross-sectional body burden age trends (CBATs) of POPs with long human elimination half-lives (>3 years), but this association emerges for scenarios 20 to 30 years following the period of peak exposure [28, 180]. The human elimination half-lives for PFOS and PFA were estimated in an Australian study to be 4.9 and 2 years for males, with half-lives 12-13% lower in women, and the period of peak human exposure likely occurred between 1984 and 1996 [238]. The

observed positive association with age for PFASs in the current survey suggests that the period of peak exposure for New Zealand adults to PFAS also happened sometime during the 1980s and 1990s, although environmental sampling data of PFAS over time are not available to confirm this assumption.

We observed higher serum concentrations in men for the higher brominated BFRs and 3 out of 4 PFASs. For PFAS, higher levels in males have been reported in the majority of human biological monitoring studies [11]. It is suggested that one reason for lower PFAS concentrations in women is loss in blood during menstruation, cord-blood transfer, and breast-feeding [238, 239]. This is supported by research showing higher concentrations of PFASs in women who have had a hysterectomy and no longer menstruate [240], and lower PFASs in men who regularly give blood or undergo venesection procedures [32, 241].

For BFRs, males had higher concentrations than females in the USA NHANES survey [242] and in a German study [179]. However, in a broader review of human biological monitoring surveys there is not a consistent sex-related association for BFRs [96]. Likewise, the previous study of BFRs in New Zealand 23 adults [99] did not find a sex-related association. The higher serum concentrations in males compared to females observed in this larger New Zealand survey may reflect sex-related differences in intake of and exposure to BFR and PFAS containing materials, though differences in human elimination rates between males and females are likely the primary reason for the observed differences.

This survey showed no consistent associations of serum BFR or PFAS concentrations with ethnicity or study region. Similarly, ethnicity was not associated with serum

BFRs in the USA [235]. In contrast, there was an association of serum PFASs with ethnicity in the USA where Mexican Americans had lower PFAS concentrations than non-Hispanic black and white Americans attributed to lifestyle and diet differences [243]. The lack of an ethnicity-related association in the current survey indicates that sources of BFR and PFAS exposure are similar between Māori and non-Māori, despite consistent evidence of current and historical social and economic disparities between these groups [244]. Serum BFR and PFAS concentrations have been shown to differ by geographic region [11, 96], with local levels of regional urbanisation and industrialisation suggested as the key factors in the distribution of POPs in humans and the environment [245]. The 2008 survey of BFRs in New Zealand human milk [19, 186] showed higher concentrations of the higher-brominated BFR congeners (i.e. BDE184, BDE196, BDE197, BDE201, BDE203 and BDE207) in urban areas, attributed to more sources of BFR exposure in urban environments. The lack of consistent associations with region in the current survey is unsurprising because each of the survey regions included a comparable mix of urban and rural areas.

Some studies suggest that concentrations of certain BFRs in humans and wildlife may be increasing in some areas of the world [85]. As this study represents the first survey to measure BFR concentrations in serum of the New Zealand adult general population, we could not determine a time trend. Comparing this survey to results from a 2001 New Zealand study of BFRs in serum samples taken from 23 adult male and female donors (Harrad & Porter, 2007), suggests higher serum concentrations for BDE47 and BDE100 in 2001, while other congeners (BDE99, BDE153, BDE154, and BDE183) show no apparent differences. However, the differences in methodology

between the two studies mean these findings may not represent actual temporal changes in the general population. The survey results can also be compared to concentrations of BFRs in human milk collected in 2008 from women aged 20 to 30 years [19, 246]. When the 2008 human milk concentrations are converted to serum concentrations using serum:milk partitioning factors based on the published literature [246], the comparison suggests that the majority of BFRs in serum may have increased since 2008. However, the differences in study population and matrix used to determine BFR concentrations preclude firm conclusions.

For PFAS it is not possible to make an assessment of time trends in New Zealand because there have been no previous studies. However, international studies show a clear pattern of decreasing PFASs in adults between 2000 and 2013 [173, 247, 248], and future studies will determine whether this trend is also occurring in New Zealand.

Because the use, fate, and distribution of BFRs and PFASs around the world is rapidly changing over time, we only compare the results to similar population-based biological monitoring surveys conducted within five years of the New Zealand survey, to gain some insight into the relative exposure of adult New Zealanders. A 2008/09 survey of BFRs in the serum of Australians over 16 years of age reports comparable concentrations to New Zealand for the sum of BDE47, BDE99, BDE100, and BDE153 [233]. Concentrations of BDE47, 99, 100, and 153 in New Zealand samples are 4 to 9 times lower than the lowest concentrations in pooled samples from USA adults (>20 years) measured in 2007/08 [153]. This is consistent with other studies showing generally high concentrations of BFRs in the USA [96].

Concentrations of BDE47, 99, 100, and 153 in samples collected in 2009/2010 from the general adult population of Korea (age 20 to 69 years) were comparable to 2012 New Zealand concentrations [249]. Median concentrations of BDE47, 99, 100, 153, and 209 in samples collected in 2010/2011 from the general population of Swedish adults [250] were 2 to 5 times lower than 2012 New Zealand concentrations, with the exception of BDE153 which was the same between both surveys.

Mean concentrations of PFASs in samples taken in 2011 from Australians over 16 years of age [172, 173] were 3.3 and 1.7 times higher, respectively for PFOS and PFOA, than the 2012 New Zealand results. Concentrations of PFHxS, PFOA, and PFNA in the 2012 New Zealand samples were similar to concentrations in USA adults (>20 years) measured in 2011/12, while PFOS levels were 2 times higher in the USA samples [153]. Concentrations of PFASs in the serum of the Korean general population taken in 2008 from residents in a city nearby to Seoul and close to an industrial area, were 2.3 and 1.2 times higher than New Zealand median results for PFOS and PFOA, respectively [251]. Concentrations of PFASs in samples collected in 2011 from adults in Henan, China, a primarily agricultural inland area, were 2 to 16 times lower than 2012 New Zealand concentrations [252].

These comparisons for BFRs and PFASs suggest that current and historic exposure of adult New Zealanders to these environmental chemicals are in the middle of the range of international values. Population density, or proximity to urban areas, has been shown to be associated with higher human serum concentrations of BFRs in a study conducted in the North American Great Lakes [245], and higher serum concentrations of PFASs in a number of studies [11]. The New Zealand survey

included participants from throughout the country's rural and urban areas with a range of population densities. Studies of BFRs in New Zealand household dust, an important exposure source, show that concentrations are similar to the United Kingdom and much lower than North America [38, 97]. There is no information on environmental sources of PFASs in New Zealand. However, it is likely that PFAS exposure sources in New Zealand, primarily through the diet and also through contact with consumer products such as treated textiles, are similar to other countries.

A limitation of this study is that it made use of pooled rather than individual samples. The variability between individuals of the same country may be relatively high for BFRs and PFASs, though there is evidence that the ratio of mean and 95th percentile concentrations remains constant [253]. While some adult New Zealanders may thus have higher body burden of BFRs or PFASs than the mean concentrations of pooled samples reported in this survey, the 95th percentile can be estimated based on published ratios of mean:95th percentile concentrations.

The low contact and participation rates for certain demographic groups (e.g. young males and females, particularly of Māori descent) present another limitation of the study. This was addressed by pooling the collected serum samples by demographic group, and the use of survey weights in the data analysis, in order to achieve results representative for the New Zealand adult population as a whole.

Conclusion

The results of this survey provide the first national estimate of serum BFRs and PFASs in the New Zealand adult population. We observed a trend of higher levels of BFRs in younger age groups, except for BB153, and a trend of higher PFASs in older age groups. In addition, we found evidence that concentrations of BFRs and PFASs are higher in men compared to women of the same age. New Zealand adults' body burdens of BFRs and PFASs are in the middle of the range of international concentrations. Periodic monitoring of BFRs and PFASs in a representative sample of the adult population would allow for determination of temporal trends, providing better information to clarify the age- and sex-related associations observed in this survey.

Chapter 7. Concentrations of polybrominated diphenyl ethers in matched samples of indoor dust and breast milk in New Zealand

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Abstract

Polybrominated diphenyl ethers (PBDEs) are present in many consumer goods. There is evidence that PBDEs are toxic to humans, particular young children. The purpose of this study was to assess indoor dust as an exposure source for PBDEs. Concentrations of 16 PBDEs were determined in dust samples from 33 households in New Zealand, and in breast milk samples from 33 mothers living in these households. Associations between dust and breast milk PBDE concentrations were assessed, and children's PBDE intake from breast milk and dust estimated. Influences of household and demographic factors on PBDE concentrations in dust were investigated. Indoor dust concentrations ranged from 0.1 ng/g for BDE17 to 2,500 ng/g for BDE209. Breast milk concentrations were positively correlated ($p<0.05$) with mattress dust concentrations for BDE47, BDE153, BDE154, and BDE209 and with floor dust for BDE47, BDE183, BDE206, and BDE209. The correlation for BDE209 between dust and breast milk is a novel finding. PBDE concentrations in floor dust were lower from households with new carpets. The estimated children's daily intake of PBDEs from dust and breast milk was below U.S. EPA Reference Dose values. The study shows that dust is an important human exposure source for common PBDE formulations in New Zealand.

Introduction

Brominated flame retardants (BFRs), including polybrominated diphenyl ethers (PBDEs), are a broad class of organic compounds used to reduce fire risk in consumer articles. There has been significant international controversy over the use of PBDEs in domestic articles such as foam-filled furniture [230, 254], resulting in the sole U.S. producer voluntarily ceasing production of two of the most common PBDE formulations in 2004 [255]. In New Zealand, PBDEs have never been manufactured but serum concentrations have been shown to be within ranges reported in Europe, suggesting imported consumer goods are the primary source of human exposure [99]. There is evidence that BFRs are associated with neurodevelopmental effects in children [82, 256] and that humans are exposed to BFRs through air, food, and dust [97, 229, 257-259]. In particular, children have been shown to have high exposures to BFRs through food (including breast milk) and ingestion of indoor dust [168].

A number of studies have investigated BFR concentrations in indoor dust and relationships to BFR body burdens in humans. Some of these found breast milk concentrations of Penta-BDE components to be associated with dust concentrations (Wu et al., 2007; Toms et al., 2009) suggesting that dust is an exposure source for PBDEs. Other studies have looked at the association of PBDEs in human blood and indoor dust, also supporting dust as an exposure pathway for PBDEs in indoor environments [260-264]. Recent reviews have consolidated international information on the exposure of humans to PBDEs through key pathways such as food, including breast milk, and dust with corresponding intake estimates [265, 266].

To date, there has only been one study of PBDE concentrations in New Zealand indoor dust, indicating that PBDE dust concentrations (excluding BDE209 which was not assessed) are similar to those found in the UK and an order of magnitude lower than concentrations in North America [97]. However, associations between dust concentrations and body burdens of PBDEs in New Zealand have not been investigated.

For this study, matched samples of indoor dust and human breast milk from first-time mothers were analysed for PBDEs. The objectives of this study were:

1. To determine the concentrations of PBDEs in samples of living room floor dust and mattress dust collected from New Zealand households (this study is only the second to determine concentrations of PBDEs, and the first to determine concentrations of BDE209, in New Zealand indoor dust).
2. To determine associations between concentrations of PBDEs in matched samples of indoor dust and human breast milk.
3. To study demographic and household characteristics in relation to levels of PBDEs in indoor dust.
4. To estimate the daily intake of PBDEs from indoor dust and breast milk for children.

This study complements a recent study investigating alternative flame retardants (AFRs), including novel brominated flame retardants and organophosphate flame retardants, in the same indoor dust samples [267].

Methods

Households selected for the study were those of 33 mothers who provided breast milk samples for the recent 4th WHO-Coordinated Survey of Human Milk for Persistent Organic Pollutants carried out in New Zealand [186] and for whom at least one living room floor or mattress dust sample was collected. Mothers provided written informed consent to participate in the study and were interviewed by trained staff using a standardised questionnaire to gather information on demographic and household factors.

Dust samples were collected during a single visit to participant houses in two urban (Wellington, Christchurch) and two rural (Wairarapa, North Canterbury) regions. Field staff collected house dust samples with nylon sample socks (25 µm-mesh conical bags, Allied Filter Fabrics Pty Ltd, Australia) mounted on to a furniture attachment on the tube of a common household vacuum cleaner (Nilfisk Sprint Plus 1600W). Samples were taken from the living room floor and the mother's mattress. The living room floor sample was taken in the sitting area of the living room (e.g. in front of the couch). Small pieces of furniture were moved, as required, however larger pieces of furniture (e.g. sofas, book cases) were left in place. Samples were taken by field staff according to the following directions:

- wall-to-wall carpeted floor: 1 m^2 was vacuumed for 2 min;
- completely bare floor: 4 m^2 was vacuumed for 4 min;
- bare floor with rug(s): 4 m^2 of the smooth floor was vacuumed for 4 min, and 1 m^2 of the largest rug was vacuumed for 2 min into the same sample bag.

The whole exposed area of the mother's mattress was vacuumed for a period of 2 minutes. Prior to sampling, duvets, blankets or sheets were removed but under-sheets or mattress covers remained on the bed.

After each sample was taken, the dust sock was carefully removed from the vacuum cleaner, labeled, closed with a zip tie, and stored in a sealed plastic bag. Between samples, the vacuum cleaner fitting was cleaned with tissues and 96% alcohol. The samples were then returned in chilled containers to the Centre for Public Health Research (CPHR), Massey University, together with a field form completed by the field staff while on site. Dust samples were stored at -20^{o}C within 36 h of sample collection until they were sent for laboratory analysis.

Breast milk samples were collected according to the protocol of the 4th WHO-Coordinated Survey of Human Milk for Persistent Organic Pollutants [91] by participating mothers in their second and third month after birth. Full details of breast milk sampling is provided elsewhere [186]. Milk samples were held frozen in mother's home freezers until they were collected by research staff. Milk samples were stored frozen at -20^{o}C until they were sent for laboratory analysis.

Dust samples were analysed at the University of Birmingham (tri- through hexa-BDEs) and Antwerp (hepta- through deca-BDEs) and details of laboratory QA/QC are provided in Appendix 3. Breast milk samples were analysed at AsureQuality, Wellington, according to USEPA Method 1614 Brominated Diphenyl Ethers in Water, Soil, Sediment and Tissue by HRGC/HRMS [268]. Details of the laboratory analysis of breast milk samples, including QA/QC procedures has previously been reported

[186]. Dust and breast milk samples were analysed for BDE17, 28, 47, 49, 66, 85, 99, 100, 153, 154, 183, 196, 197, 203, 206, and 209.

The estimated daily intakes of PBDEs for infants (less than 1 year old) and toddlers (1 to 2 years old) from dust and breast milk were calculated based on the mean measured concentrations of PBDEs in the 33 breast milk and indoor dust samples (non-detects were assigned a value of 0.5 x LOQ). There is no data available on typical concentrations of PBDEs in the air of New Zealand homes, and previous studies have shown relatively low contributions to PBDE exposure from air [257, 269], therefore only floor dust concentrations were used in the exposure calculations. Similarly, we did not have information about contributions of PBDEs from other sources (e.g. foods other than breast milk and sources outside of the home environment) so these are not included in the intake estimate. Mattress dust samples were not available for all participants; therefore only floor dust concentrations were used in the calculation. The majority of New Zealand infants are exclusively breast-fed at 3 months, with partial breast-feeding continuing to 6 months for most infants [270] – concentrations of PBDEs in infant formula or cow's milk were shown to be much less than in breast milk in an Australian study [271] and based on this information we did not consider PBDE intake for infants consuming infant formula. We assumed breast milk intakes of 690 mL/day (<3 months) and 770 mL/day (3 to 6 months) and 0 mL/day (>6 months) [272]. We used an estimated dust intake of 30 mg/day for infants aged 3 to 12 months, 60 mg/day for toddlers aged 1 to 2 years [272], and did not include dust intake for infants less than 3 months. Body

weight was assumed to be 5.9 kg, 7.4 kg, 9.2 kg, and 11.4 kg for children aged less than 3 months, 3 to 6 months, 6 to 12 months, and 1 to 2 years respectively [272].

Conditions for a normal distribution were not met for the majority of the PBDE congeners in breast milk and dust, therefore PBDE concentrations were ln-transformed. Statistical analysis was performed using Stata 11.0 for Windows (StataCorp LP, Texas, USA) and Prism 5 for Windows (GraphPad, La Jolla, USA). To test the hypothesis that concentrations of individual PBDE congeners in breast milk are correlated with those in floor dust and mattress dust, we performed Pearson's correlation for the same congener between matrix pairs (i.e. floor dust and milk, mattress dust and milk, floor dust and mattress dust). Analytical results that were below LOQ were assigned a value of 0.5 x LOQ. For those congener matrix pairs that showed statistically significant ($p<0.05$) correlations, we performed univariate linear regression on ln-transformed data to determine the relationship between dependent and independent variables.

To investigate the household and demographic determinants of PBDE concentrations in dust, we performed univariate linear regression on ln-transformed data to determine the influence of the determinants listed in Table 13. Any analytical results that were below LOQ were assigned a value of 0.5 x LOQ. For PBDE congeners where regression results suggested more than one influential determinant, we performed multivariate linear regression including the associated determinants.

Results

The characteristics of the study participants are summarised in Table 13. The mean age of the 33 participants with matched living room floor dust and breast milk samples was 27 years (range 20 to 31, SD=3.01). The majority of subjects' households had completely (wall to wall) carpeted floors in the living room (91%) and bedroom (88%), with 21% of subjects having purchased new carpets in the past 12 months. Inner spring mattresses were the most common type of mattress used by the subjects (97%) with the average age of mattress 3.5 months (for mattresses <1 year old) and 5.2 years (for mattresses >1 year old). Seventy three percent (73%) of subjects reported owning household furniture that contains plastic foam. Ninety seven percent (97%) of subjects owned a home computer with the average age of the computers of 6.8 years (range 0 – 23 years). There were some differences in these data for those 16 out of 33 subjects with matched living room floor dust, mattress dust, and breast milk samples, but the relative proportions were comparable.

Table 13. Demographic, lifestyle and household characteristics of the study subjects.

	Floor + Milk	**Floor + Mattress + Milk**
N	33	16
Age (y: mean, range)	27, 20 – 31	26, 20 – 31
BMI (kg/m^2: mean, range)	26.1, 20.8 – 31.6	26.1, 20.8 – 31.6
Region		
North Island	22 (67)	8 (50)
Urban	15 (46)	5 (31)
Rural	7 (21)	3 (19)
South Island	11 (33)	8 (50)
Urban	8 (24)	6 (38)
Rural	3 (9)	2 (12)
Ethnicity		
European	31 (94)	14 (88)
New Zealand Māori	1 (3)	1 (6)
Asian	1 (3)	1 (6)
Smoking status		
Never smoked (<100 cigarettes in life)	27 (82)	11 (69)
Ex-smoker	5 (15)	4 (25)
Current smoker	1 (3)	1 (6)
Water supply		
Town supply	25 (76)	13 (81)
Roof collection	6 (18)	3 (19)
Private well or bore	2 (6)	0 (0)
Living room floor covering		
Completely (=wall to wall) carpeted floor	30 (91)	14 (88)
Completely smooth floor with no rugs	1 (3)	0 (0)
Smooth floor with 1 or more small rugs	2 (6)	2 (12)
Bedroom floor covering		
Completely (=wall to wall) carpeted floor	29 (88)	14 (88)
Completely smooth floor with no rugs	2 (6)	0 (0)
Smooth floor with 1 or more small rugs	2 (6)	2 (12)
New carpet purchased in the past 12 months	7 (21)	3 (19)
Type of mattress		
Latex	1 (3)	0 (0)
Inner spring	32 (97)	16 (100)
Age of mattress		
<1 year old (months: mean, range)	3.5, 1 – 6	-
>1 year old (years: mean, range)	5.2, 1.5 – 15	4.9, 2 – 15
Household furniture with plastic foam		
Yes	24 (73)	11 (69)
No	1 (3)	1 (6)
Don't know	1 (3)	0 (0)
No answer	7 (21)	4 (25)
Household computer ownership	32 (97)	16 (100)
Age of home computer (y: mean, range)	6.8, 0 – 23	5.0, 1 - 15

Table notes:
Floor + Milk: Subjects with matched living room floor dust and breast milk samples.
Floor + Mattress + Milk: Subjects with matched living room floor dust, mattress dust, and breast milk samples.
Numbers in parentheses are percentages of N.

The results of breast milk analysis for the 33 subjects are provided in Table 14. The ten most abundant PBDEs in breast milk (median results) were BDE47 (2140 pg/g) > BDE99 (560 pg/g) > BDE153 (517 pg/g) > BDE100 (499 pg/g) > BDE209 (190.5 pg/g) > BDE28 (181 pg/g) > BDE197 (108 pg/g) > BDE85 (45.1 pg/g) > BDE183 (42.3 pg/g) > BDE154 (35.5 pg/g).

Floor dust samples were analysed for PBDEs for 33 subjects and mattress dust samples for 16 of 33 subjects (Table 14). The ten most abundant BFRs in floor dust (median results) were BDE209 (598 ng/g) > BDE99 (31.5 ng/g) > BDE47 (24.2 ng/g) > BDE206 (24 ng/g) > BDE100 (6.4 ng/g) > BDE153 (4.6 ng/g) > BDE154 (3.7 ng/g) > BDE183 (2.7 ng/g) > BDE85 (1.7 ng/g) > BDE49 (1.3 ng/g). The ten most abundant BFRs in mattress dust (median results) were BDE209 (1,018 ng/g) > BDE206 (52.7 ng/g) > BDE47 (46.3 ng/g) > BDE99 (41.8 ng/g) > BDE100 (9.8 ng/g) > BDE153 (6.7 ng/g) > BDE183 (6.3 ng/g) > BDE196 (4.9 ng/g) > BDE197 (3.6 ng/g) > BDE154 (3.1 ng/g).

Table 14. Summary of PBDEs in indoor dust and breast milk.

	Floor dust (ng/g)					Mattress dust (ng/g)					Breast milk (pg/g lipid)				
	N=33					N=16					N=33				
Congener	Mean	Median	Minimum	Maximum	% < LOD	Mean	Median	Minimum	Maximum	% < LOD	Mean	Median	Minimum	Maximum	% < LOD
BDE17	0.1	0.1	0.1	1.0	88	0.3	0.1	0.1	0.9	69	2.4	2.2	0.6	5.6	27
BDE28	0.7	0.6	0.1	1.3	12	1.2	0.8	0.1	7.7	6	217.9	181.0	48.8	751.0	0
BDE47	30.2	24.2	0.3	98.0	3	56.1	46.3	6.5	288.4	0	2673.8	2140.0	317.0	7710.0	0
BDE49	1.6	1.3	0.1	3.6	6	2.1	2.2	0.1	5.0	6	25.6	20.9	6.5	96.4	0
BDE66	1.0	0.8	0.1	3.1	27	1.3	1.1	0.1	7.8	25	31.4	26.2	5.4	103.0	0
BDE85	2.3	1.7	0.1	7.6	21	2.2	1.9	0.1	5.8	25	51.6	45.1	2.2	168.0	6
BDE99	51.8	31.5	3.3	219.1	0	83.9	41.8	8.1	540.3	0	565.9	560.0	66.2	1290.0	0
BDE100	9.7	6.4	0.3	41.1	3	16.1	9.8	0.3	94.1	6	568.7	499.0	70.8	1820.0	0
BDE153	8.8	4.6	0.3	58.9	12	10.6	6.7	0.3	58.2	6	750.4	517.0	142.0	3820.0	0
BDE154	4.7	3.7	0.3	19.8	27	7.1	3.1	0.3	43.1	13	39.0	35.5	6.5	101.0	0
BDE183	12.8	2.7	0.3	238.4	33	7.5	6.3	0.3	21.1	25	66.1	42.3	11.5	512.0	0
BDE196	4.7	0.3	0.3	44.2	55	10.3	4.9	0.3	34.3	25	16.5	12.6	2.5	43.9	6
BDE197	4.7	0.3	0.3	68.0	61	5.6	3.6	0.3	17.5	25	127.9	108.0	50.3	320.0	0
BDE203	2.9	0.3	0.3	25.0	64	8.1	3.0	0.3	30.3	25	18.8	16.5	3.0	45.0	15
BDE206	114.4	24.0	3.2	989.3	0	163.6	52.7	3.5	1253.3	0	30.6	18.0	2.9	195.0	12
BDE209	2505.2	598.0	28.8	27394.3	0	2703.0	1018.0	105.9	21956.2	0	375.6	190.5	65.3	3140.0	3

The estimated mean children's (less than two years old) dust and breast milk PBDE intake values (Table 15) for New Zealand presented in this paper vary with the age of the child and the degree of bromination of the PBDE congener. The estimated intake for infants less than 3 months is dominated by BDE47 (13.1 ng/kg b.w./day), which is consistent with the relatively higher levels of this congener in breast milk than in floor dust found in this study. Estimated intakes for infants aged 3 to 6 months show a higher contribution from BDE209 (11.7 ng/kg b.w./day), with the estimated intake for BDE209 lower for infants 6 to 12 months (8.2 ng/kg b.w./day). Children aged 1 to 2 years had the highest estimated intakes of BDE209 (13.2 ng/kg b.w./day) which reflects the high dust ingestion rate (60 mg/day) used for this group. Estimated intake of tri- to hexa-BDEs is highest in infants less than 3 months (23.5 ng/kg b.w./day), decreases in infants between 3 to 6 months of age (21.4 ng/kg b.w./day), and decreases further for children aged 6 months to 2 years (0.4 and 0.6 ng/kg b.w./day respectively).

Table 15. Exposure factors and estimated intake of selected PBDE congeners (ng/kg/day).

	Age				
	<3 months	3 to 6 months	6 to 12 months	12 to 24 months	RfD[1]
Milk intake (mL/d)[2]	690	770	0	0	-
Dust intake (mg/d)[2]	0	30	30	60	-
Body weight (kg)[2]	5.9	7.4	9.2	11.4	-
BDE47	13.1	11.8	0.1	0.2	100
BDE99	2.8	2.7	0.2	0.3	100
BDE153	3.3	3.0	0.03	0.05	200
Tri- to hexa-BDE[3]	23.5	21.4	0.4	0.6	
BDE209	1.7	11.7	8.2	13.2	7000

Table notes:
[1] RfD = U.S. EPA Reference Dose [273-276]
[2] Values are from U.S. EPA Exposure Factors Handbook [272]
[3] Sum of BDE28, 47, 49, 66, 99, 100, 153, 154

Correlation coefficients for the same PBDE congeners between living room floor dust, mattress dust, and breast milk are provided in Table 16 (full correlation matrices for all congeners in floor/milk and mattress/milk paired samples are provided in Appendix 4 and 5). Associations for the same congener between living room floor dust and breast milk samples were statistically significant ($p<0.05$) for four out of 16 PBDE congeners: BDE47, BDE183, BDE206, and BDE209. We also found positive correlations between BDE209 in floor dust and BDE183, BDE154, BDE100 and BDE47 in breast milk. Similarly, BDE206 in floor dust was positively correlated with BDE209, BDE206, and BDE183 in breast milk. Associations for the same congener between mattress dust and breast milk samples were statistically significant for four out of 16 PBDE congeners: BDE47, BDE153, BDE154 and BDE209. Associations between living room floor dust and mattress dust were statistically significant for three out of 16 congeners: BDE183, BDE206, and BDE209. Scatter

plots of BDE209 concentrations in matched dust and breast milk samples, are shown in Figure 15.

Table 16. Pearson correlation coefficients for PBDE congeners in living room floor dust, mattress dust, and breast milk samples.

	Floor dust/breast milk	Mattress dust/breast milk	Floor dust/mattress dust
	r (N=33)	r (N=16)	r (N=16)
BDE17	NA	NA	NA
BDE28	-0.13	0.21	0.24
BDE47	0.39*	0.52*	0.43
BDE49	0.26	-0.17	-0.08
BDE66	0.34	-0.25	0.05
BDE85	0.18	-0.03	-0.21
BDE99	0.33	0.41	0.35
BDE100	0.17	0.40	0.34
BDE153	0.15	0.74**	0.48
BDE154	0.19	0.58*	0.42
BDE183	0.39*	0.44	0.55*
BDE196	NA	0.49	NA
BDE197	NA	0.19	NA
BDE203	NA	0.17	NA
BDE206	0.36*	0.20	0.52*
BDE209	0.37*	0.50*	0.56*

Table notes:
* $p<0.05$
** $p<0.005$
NA – Not assessed because detection frequency in dust or milk was less than 50%.

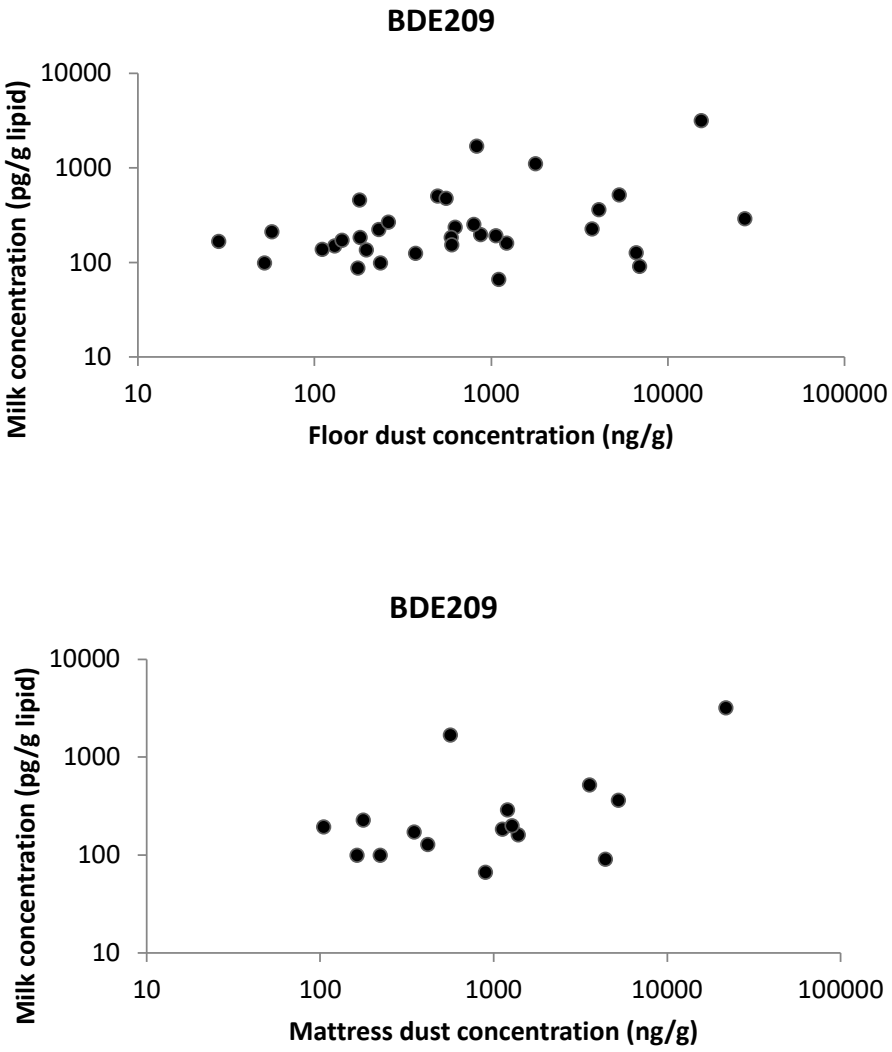


Figure 15. Scatterplots of associations for BDE209 in dust and breast milk.

Regression coefficients from univariate linear regression for the same congener between floor dust and breast milk were 0.25 (R^2=0.15, p=0.03), 0.25 (R^2=0.15, p=0.02), 0.20 (R^2=0.14, p=0.04), and 0.19 (R^2=0.14, p=0.03) for BDE47, BDE183, BDE206 and BDE209, respectively. Regression coefficients for the same congener between mattress dust and breast milk were 0.37 (R^2=0.27, p=0.04), 0.45 (R^2=0.55,

p=0.0009), 0.39 (R^2=0.34, p=0.02), and 0.36 (R^2=0.25, p=0.05) for BDE47, BDE153, BDE154, and BDE209, respectively.

Univariate regression results showed that determinants of PBDEs in dust may be study region (North Island vs. South Island of New Zealand), location (urban vs. rural), and ownership of new carpets (new vs. old carpet). Other demographic and household factors listed in Table 13 were not predictors of PBDEs in dust. The results suggest generally higher floor and mattress dust PBDE concentrations for subjects in the southern region of the study compared to the northern region, though this was only statistically significant for BDE183 (ß=0.97, p=0.04), BDE206 (ß=1.20, p=0.03) and BDE209 (ß=1.50, p=0.01) in floor dust, indicating 2- to 4-fold higher geometric means for dust samples from the south compared to north region. When the regression analyses for PBDEs in dust in relation to study region were adjusted for urban/rural category, there was not an appreciable difference to the regression results. PBDE levels in floor and mattress dust were generally higher in urban than rural samples, but none of the results were statistically significant. PBDEs in floor dust were generally lower in houses with new carpet compared to old carpet although the only statistically significant result was observed for BDE183 (ß=-1.19, p=0.03) in floor dust with the geometric mean of houses with old carpet 3-fold higher.

Discussion

This study is the first study to date in New Zealand investigating PBDEs in matched breast milk and dust samples. Floor dust concentrations of PBDEs in this study are similar to those found in the other New Zealand study [97] that assessed samples taken in Wellington, corresponding to the Northern region of this study, suggesting that these concentrations are representative of PBDE dust concentrations in New Zealand. Living room floor dust concentrations of all PBDEs, excluding BDE209, were similar to concentrations found in the UK and up to 50 times lower than concentrations in dust samples from North America [97]. This study is the first to report concentrations of BDE209 in indoor dust for New Zealand, concentrations of which were 3 to 18 times lower than those reported for UK dust samples [97] and 7 times higher than Australian dust samples [269]. When compared to concentrations of BDE209 in North American dust samples, there is not a clear pattern with some studies reporting 2 to 4 times lower concentrations compared to New Zealand dust samples [97], similar concentrations [260], and 1.8 times higher concentrations in dust samples collected in Boston, USA [277].

This study provides, for the first time, estimated intakes of selected PBDEs from dust and breast milk for New Zealand children less than 2 years of age. Estimated intakes from dust and breast milk were well below available U.S. EPA Reference Dose (RfD) values for BDE47, BDE99, BDE153 and BDE209 [273-276], which is consistent with recent estimates of intake of alternative flame retardants in New Zealand [267]. The relative contribution of PBDE congeners to the estimated daily intake (dust and breast milk only) varied with the degree of bromination, with breast milk exposures

providing a greater proportion of the estimated intake for the lower brominated congeners (BDE17 to BDE203) and floor dust a greater proportion for the higher brominated congeners BDE206 and BDE209. Toms et al. [269] showed a similar result where higher brominated congeners account for a relatively smaller proportion of exposure from breast milk. It has also been observed [246] that breast milk levels of BDE209 are generally 25 times less than levels in serum, while for lower brominated congeners serum/milk ratios are closer to 1, which may partly explain the relatively low contribution of breast milk to infant intake of BDE209 compared to lower brominated congeners.

We showed associations between floor dust and breast milk for BDE47, BDE183, BDE206, and BDE209 suggesting floor dust is an exposure source for components of the Penta-, Octa- and Deca-BDE formulations. Sources of the Penta-, Octa- and Deca-BDE formulations include electrical and electronic appliances, building materials, furniture, and textiles [273-276, 278] which are common items in New Zealand households. In addition, we found associations for BDE209 and BDE206 in floor dust and lower-brominated congeners in breast milk, suggesting a common exposure source for deca- and octa-BDEs within households, or potential debromination of higher brominated congeners BDE209 and BDE206 [279].

Associations between mattress dust and breast milk were assessed for the first time in this study, showing significant correlations for BDE47, BDE153, BDE154 and BDE209. These results indicate that mattress dust is an exposure source for components of the Penta- and Deca-BDE formulation similar to floor dust. In our study, concentrations of PBDEs were marginally higher in mattress dust compared to

living room floor dust, which may indicate that concentrations of PBDEs in mattress dust have not been "diluted" by other components of dust that are more likely to be present in floor dust (e.g. soil, food particles). However, the relative concentrations of PBDE congeners in mattress dust and floor dust were similar suggesting a common PBDE source. Rose et al [280] observed an association between newly-purchased mattresses and higher levels of nona- and deca-BDE in pre-schoolers from California, suggesting mattresses as a source of the commercial Deca-BDE formulation. Similarly, de Wit et al [257] found that household dust concentrations of the penta- and deca-BDE formulations were positively correlated with the number of polyurethane foam (PUF) containing mattresses in the household. This study's finding that mattress dust and breast milk PBDE concentrations are associated for components of the Penta- and Deca-BDE formulations may suggest an important role for exposure by inhalation and possibly dermal contact with PBDE-containing materials during bed rest.

We found a significant correlation between breast milk and indoor dust concentrations for BDE209, a novel finding. The small number of studies that investigated associations between concentrations of PBDEs in dust and breast milk [269, 281] or dust and serum [261-264], generally support dust as an exposure pathway for components of the Penta- and Octa-BDE formulations. In contrast, there is very little evidence to date to support a relationship between BDE209 in dust and breast milk. Toms et al. [269] did not find a significant association for BDE209 between human milk samples and indoor dust. Other studies have either shown a lack of association [262, 281] or had too few study subjects [261] to determine

associations for BDE209 in dust and breast milk. We are aware of only one other study showing significant associations with maternal plasma and dust for BDE209 [263]. If indoor dust is indeed an important exposure pathway for components of the Deca-BDE formulation, this is of particular relevance to human health considering that indoor dust concentrations of BDE209 are generally much higher than those of other PBDE congeners, and the possibility that BDE209 can be debrominated to more toxic compounds [282].

This study showed generally higher floor and mattress dust PBDEs in the southern region of New Zealand, and in homes with older carpets. We came across no information to suggest that the use of PBDE-containing materials differs between the North and South Islands of New Zealand. The concentrations of the majority of PBDE congeners, including components of the Penta-BDE formulation which has historically been identified in carpet underlay before Penta-BDE's withdrawal from the European and North American markets in 2004 [259], were not different between houses with old and new carpet. If there is a trend of higher levels of BFRs in houses with older carpets, this may be explained by increased release of BFRs from older, worn carpet underlay, and higher use of PBDE-containing materials in past carpet underlay manufacture compared to current practice. A New Zealand government report [231] that used portable XRF screening to test for the presence of bromine in consumer articles, did not detect bromine in new carpet and underlay samples, a finding that supports the hypothesis that older carpets and carpet underlays in New Zealand may contain PBDEs and newer ones may not.

Conclusion

This study showed that PBDE concentrations in indoor dust samples were positively associated with concentrations in breast milk for components of the Penta-, Octa-, and Deca-BDE formulations. This suggests that dust is an exposure pathway for New Zealanders to the PBDEs present in consumer articles. The association between dust and breast milk concentrations for BDE209 is a novel finding and warrants further consideration in the light of other international studies. The estimated daily intake of PBDEs from dust and breast milk for New Zealand children less than 2 years old was well below available U.S. EPA Reference Dose values. This study provides an important benchmark for bio-monitoring and exposure assessment of PBDEs in New Zealand and internationally.

Chapter 8. Overall Discussion and Conclusions

Introduction

This thesis reports the results of a national research program to measure the exposure of New Zealanders to toxic POPs chemicals. The research was focused primarily on a survey of POPs in the serum of a representative sample of the New Zealand adult population. The POPs serum survey was the second national survey of chlorinated POPs in adult New Zealanders, and the first time that brominated and fluorinated POPs were measured in the same population. The thesis also provides the results of a related study that investigated, for the first time in New Zealand, the significance of household dust as an exposure pathway for BFRs in human milk. The research is detailed in Chapter 4 to Chapter 7, and each chapter includes a discussion of the results in the context of previous New Zealand research into POPs, and international results.

This chapter provides an over-arching summary of the major findings of the research, and a discussion of the relevance of these findings to our current understanding of the distribution and dynamics of POPs in the New Zealand adult general population. Whilst the research provides answers to several questions about the distribution and dynamics of POPs, there are still a number of areas that warrant further study. For example, temporal trends remain to be established for the brominated and fluorinated POPs. We are now in a position to recommend actions to achieve a better understanding of the public health significance of human exposure to POPs in New Zealand. These recommendations are presented in this chapter along with a discussion of their respective costs and benefits.

The discussion will address whether the following questions have been answered by the research:

- What are the key determinants of POPs in New Zealanders?
- Are concentrations of POPs in New Zealanders changing over time?
- How do human concentrations of POPs in New Zealand compare to the rest of the world?
- What is the importance of dust as an exposure pathway for POPs in infants?
- What are the strengths and limitations of the research, and what can be done to improve future biological monitoring studies in New Zealand?
- How can this research be used by decision-makers to reduce human exposure to toxic POPs?
- What future research and policy measures should decision-makers consider to improve our understanding of the dynamics of POPs in human populations?

The research provides a reference for concentrations of POPs in New Zealand adults. As such, the research is intended to inform future research and decision-making in the field of public and environmental health. While the research did not attempt to find associations between serum POPs concentrations and health outcomes, the findings can be used as a foundation for such research in the future.

Major findings

The following sections provide a detailed discussion of the major findings from the research. In particular, the discussion addresses (a) the importance of demographic factors (e.g. age, sex) as determinants of POPs body burdens, (b) temporal trends of POPs over the past 30 years, and (c) comparisons between the New Zealand research and international data.

Age is an important determinant of POPs concentrations in New Zealand adults

The research showed consistent age-related associations of POPs in the serum of New Zealand adults (Chapters 5 and 6). Serum concentrations of chlorinated POPs (i.e. PCDDs, PCDFs, PCBs, and OCPs) and PFASs were higher for the older age groups, while the concentrations of BFRs were higher for the younger age groups (Figure 16).

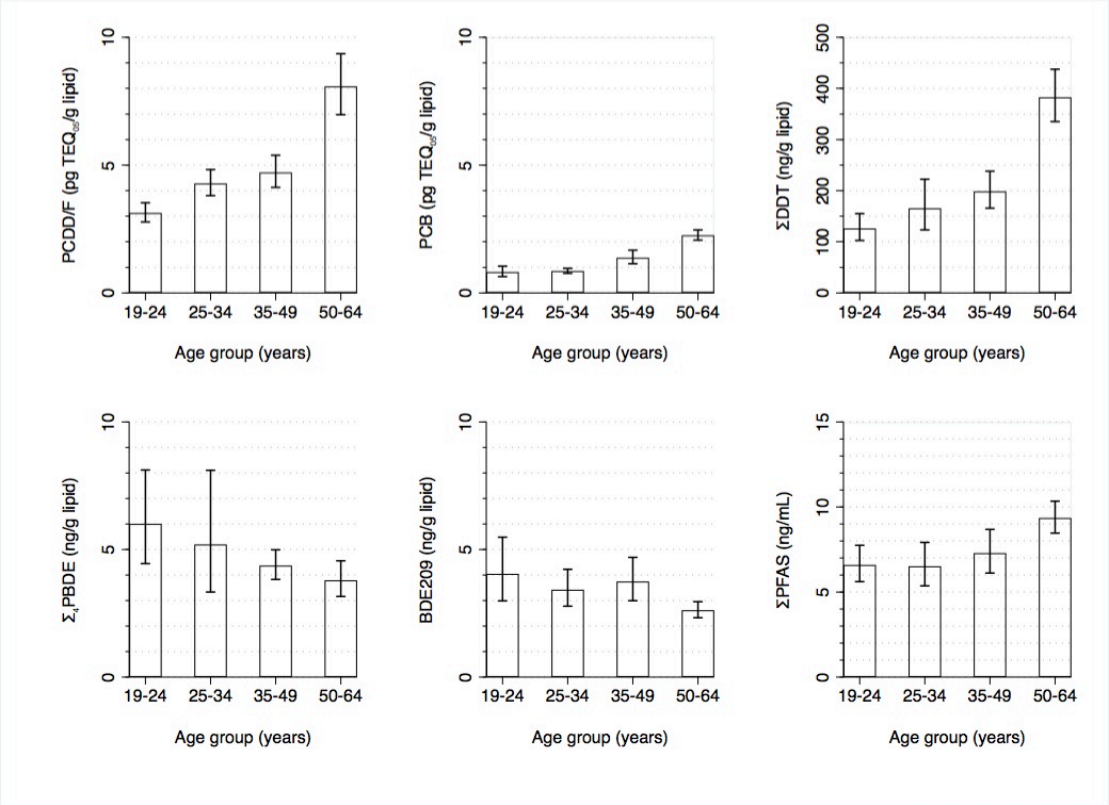


Figure 16. POPs in the serum of adult New Zealanders, by age group.

(ΣDDT=DDT+DDE+DDD, Σ_4PBDE=BDE47+BDE99+BDE100+BDE153, ΣPFAS=PFOS+PFOA+PFHxS+PFNA). (figure is based on Chapters 5 and 6)

A positive association with age for chlorinated POPs is clear from this research, and is consistent with the previous New Zealand serum study [62] and a number of population-based studies around the world [30]. This finding, along with the overall decrease of chlorinated POPs compared to the previous serum study and in the breast milk studies, shows that the body burden of POPs in New Zealand adults is primarily associated with historic exposures (i.e. older individuals had greater exposure during their lifetimes compared to younger individuals). However, the fact that chlorinated POPs are still found at detectable levels in the New Zealand adult

population, regardless of age, is evidence of the long human elimination half-lives of chlorinated POPs, and residual intake from background sources of POPs in the environment and food. Half-lives for PCDDs range from 3.7 years (1,2,3,4,6,7,8-HpCDD) to 10.9 years (1,2,3,4,7,8-HxCDD) in adults, and for PCDFs range from 0.9 years (2,3,7,8-TCDF) to 6 years (1,2,3,6,7,8-HxCDF), with no association of half-life with degree of congener-specific chlorine substitution [283]. Half-lives are associated with age, with longer half-lives in older individuals, and lifestyle factors (e.g. smoking, body fat percentage, and breast-feeding) [283]. In addition, human elimination half-lives are concentration-dependent, with shorter human elimination half-lives associated with higher exposure to POPs in individuals and communities [284-286]. In New Zealand, current exposure to chlorinated POPs is primarily through the diet and this exposure is low by international standards [48]. Therefore, the age-related association confirms that the current exposure of New Zealanders to POPs is different to historic exposure. The importance of diet and other factors to body burdens of chlorinated POPs in New Zealand adults, and the changes in the congener profile of exposure sources, are areas that warrant further research.

The research showed that the strength of the age-related association was similar for all PCDD and PCDF congeners. However, the strength of the age-related association was greater in PCB congeners with high chlorine substitution compared to lower-substituted congeners. A review of published human elimination half-lives of PCBs showed a positive association between the human elimination half-life and the degree of chlorine substitution of the PCB congener [283]. However, this finding is not consistent across all studies. Modelled estimates of human elimination half-lives

for PCBs in Australian and UK adults range from 12 to 30 years, with no apparent difference in half-lives between lower and higher chlorinated PCB congeners [287]. The importance of congener-specific human elimination half-lives to the distribution of POPs in human populations needs further investigation.

The observed age-related association provides insight into the historic exposure of New Zealanders to POPs. The strength of the age-related association reflects the human elimination rate, and the time elapsed since the period of peak exposure [28, 180, 181]. The period of peak exposure to chlorinated POPs in New Zealand has not been established, but it is reasonable to estimate that peak exposure to dioxins, furans, PCBs, and OCPs occurred sometime between the beginning of the 1970s and the end of the 1980s. After this period, international and domestic measures were implemented to control emissions of chlorinated POPs. Therefore, the youngest participants in the serum study (Chapters 5 and 6, 19 to 34 years old) would have experienced lower exposure to chlorinated POPs during their lifetime, compared to the older participants (35 to 64 years old), and would have accumulated a smaller body burden.

The positive association with age for chlorinated POPs shown in the New Zealand research can be expected to remain as long as these chemicals are banned. In addition, the strength of this association (i.e. the relative body burden of chlorinated POPs in older individuals compared to younger individuals) can be expected to increase in the future as each successive generation has lower exposure than previous generations to POPs in breast milk, food, and other environmental sources. Modelled cross-sectional body-burden age trends (CBATs) for PCBs in Swedish

women show that the age-related association for POPs in humans changes from a decreasing to an increasing trend in the decades after PCBs were banned, and the strength of this association increases with time after the period of peak exposure [28].

This research provides the first New Zealand findings on the age-related association for BFRs in adults (Chapter 6). The direction of the age-related association was negative (i.e. decreasing) for BFRs because of their relatively rapid human elimination half-lives, which have been estimated to be less than one year [288]. The period of peak exposure for BFRs was during the 1990s and early 2000s [96] so the age-related association is negative – older survey participants had lower exposure during their lifetimes compared to younger participants. Other studies have shown inconsistent age-related associations for BFRs in adults [96]. A study of Spanish adults [289] found a similar age-related association to the New Zealand research – explained by the relatively recent period of peak human exposure to BFRs, potential differences in the amount of exposure between younger and older individuals, and possibly different human elimination rates between younger and older individuals. It is likely that the observed age association for BFRs was always negative, even during the period of peak exposure, because of the relatively rapid human elimination rates of BFRs in humans [180]. The research supports the theory that, in New Zealand and internationally, younger adults had higher previous and current exposure to BFRs than older adults. Further research into the exposure of younger individuals, including occupational exposure of young adults, would provide information to clarify the observed age-related associations for BFRs.

The observed increasing association of serum PFASs with age in this research (Chapter 6) provides insight into historical PFAS exposure in New Zealand. PFASs have relatively long human elimination half-lives, estimated at 2 to 9 years in Australian adults [238]. The research results suggest that the period of peak exposure to PFASs in New Zealand occurred 20 to 30 years ago (e.g. in the 1980s and 1990s). However, there are no previous data on PFASs in adult New Zealanders so the period of peak exposure can only be estimated.

Data on imports of PFAS-containing materials could be used to estimate the period of peak PFAS use in Zealand. However, such data are not publicly available because these chemicals were only recently the subject to targeted regulation, globally and in New Zealand. Proposed amendments to the Hazardous Substances and New Organisms (HSNO) Act 1996 will allow the New Zealand Environmental Protection Agency (NZEPA) to control the import of PFASs as constituents of manufactured articles [290]. In addition, the amendments enable the NZEPA to issue "non-acceptance notifications" to the Stockholm Convention Secretariat for PFASs that remain in existing New Zealand consumer articles. Prior to this legislation, it is likely that imports of PFAS chemical feedstocks for New Zealand manufacturing occurred to some extent. PFAS imported to New Zealand may have been incorporated into clothing and other textiles, other consumer goods with PFAS-containing surface treatments, and as contaminants in imported food. Food is a key exposure pathway for PFASs, and recent results of testing of Australian foods detected PFOS at levels below the tolerable daily intake and PFOA was not detected [291]. Now that PFOS, PFOA, and their related congeners are included in the Stockholm Convention and

domestic law it is likely that exposure to PFASs in New Zealand will continue to decrease. However, future research will be required in order to confirm this prediction, and to investigate other perfluorinated compounds that are in current use.

The influence of age on human body burdens of POPs is a key factor to consider in public health decision-making related to POPs. There is evidence that New Zealanders continue to be exposed to a wide range of environmental pollutants; for example, elevated levels of PFOS have recently been found in drinking water sources around New Zealand Defence Force bases (www.mpi.govt.nz/food-safety/whats-in-our-food/chemicals-and-food/pfas/). The results of this research can be used as a reference for future assessments of human exposure to environmental sources of POPs, providing reference values for typical adult human body burdens of POPs. In addition, the research highlights the importance of exposure history (i.e. age) in considering assessments of human exposure to POPs in the environment.

Sex is a determinant of concentrations of BFRs and PFASs

The research found no consistent difference in serum concentrations of chlorinated POPs between men and women (Chapter 5). This result is consistent with international results that show few instances of sex-related difference for chlorinated POPs [39, 179]. There may have been a sex-related difference for chlorinated POPs in the past, closer to the period of peak exposure when human body burdens were significantly higher than current levels. Conversely, the research described in Chapter 6 showed a consistent association of sex with current serum

concentrations of most BFRs and all PFASs measured, with males having higher concentrations than females (Figure 17).

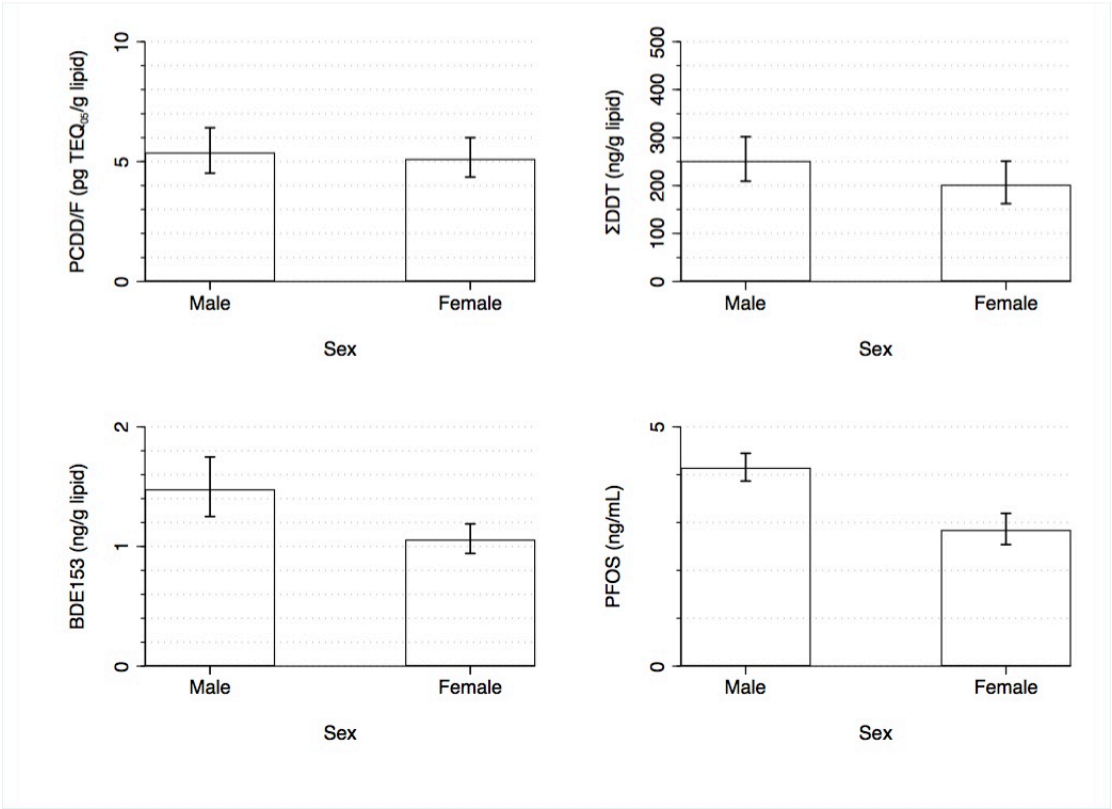


Figure 17. TEQ_{05} (PCDD/F), sum of DDT compounds, BDE153, and PFOS in the serum of adult New Zealanders, by sex. (figure based on Chapter 6)

Other studies do not show consistent associations of BFRs with sex, though there are consistent associations of higher PFASs in males [11, 96]. Important exposure sources of BFRs and PFASs include diet and dust inhalation, and it is unlikely that New Zealand males and females experience these exposure sources differently. Physical and biochemical differences between men and women are likely to play the primary role in these sex-related differences. Females have life stages where

relatively rapid elimination of POPs is likely to occur; namely loss of PFASs bound to blood proteins during menstruation [239], and excretion of BFRs and PFASs in human milk [11, 96]. The role of regular blood loss in elimination of serum POPs has also been shown in males who undergo artificial venesection procedures, such as blood donation and blood extraction as part of the treatment of diseases like hemochromatosis [32, 241]. Such venesection procedures are not experienced by the majority of the adult male population, whereas elimination of POPs in females through menstruation and breast feeding is relatively common.

The findings of different body burdens of BFRs and PFASs in men and women have important implications for public health decisions. Higher body burdens in males may contribute to a greater incidence of adverse health outcomes in this group. For females, loss of BFRs through breast milk may result in a reduced risk for mothers, however there is increased exposure for breast feeding children. Though outside the scope of this research, it is relevant that sex-related differences in serum concentrations of BFRs and PFASs may have developed during childhood and adolescence and persist through to adulthood. Among USA school-age children (7 years old at the time of blood collection), total PBDEs, BDE47, and BDE153 were observed to be higher in males, though only the association of sex and BDE153 was statistically significant [292]. There have been no national studies of BFRs and PFASs in New Zealand youth, so we lack an estimate of the importance of sex-related differences during the most important period of human development.

Dust is a potential exposure source of BFRs to mothers and nursing infants

We found an association between household dust (mattress dust and floor dust) and concentrations of BFRs in human milk. Other studies have found a wide range of POPs, including "novel" BFRs that have been introduced to replace banned and restricted BFRs internationally [87, 97, 98, 230, 293-296] and in New Zealand [267]. The few other studies have investigated BFRs in matched samples of household dust and human milk are consistent with the New Zealand research, showing associations for common BFRs with human milk concentrations [297]. The research showed the estimated intake of BFRs by nursing infants is below reference dose values. However, it is clear that BFRs are one component of a complex, and poorly-understood, chemical mixture of potentially toxic chemicals present in household dust ranging from heavy metals such as lead [298] to a wide range of novel chemicals present in consumer articles.

Māori ethnicity and geographic region are not associated with serum POPs concentrations

The research found no evidence of different human body burdens of POPs between Māori and non-Māori participants. The results suggest that exposure sources of POPs are not affected by socioeconomic factors, as Māori consistently report higher deprivation and mortality rates compared to non-Māori [299, 300]. In addition, there were no consistent differences in body burdens of POPs between geographic regions, with some exceptions for example higher DDE in the South Island (a result

that was also seen in the previous New Zealand serum survey). Regional differences in certain POPs, such as higher DDE in the South Island, may have been present in the past and are related to historic differences in agricultural and industrial activity around New Zealand. It is noteworthy that current serum concentrations of more recent POPs (i.e. BFRs and PFASs) also do not show consistent differences between Māori and non-Māori, or between regions, even though current human exposure is relatively close to the period of peak exposure to these chemicals. However, the use pattern of BFRs and PFASs has been different to historic uses of chlorinated POPs – that is, they are found widely in common consumer goods and are not associated with location-specific agricultural or industrial activity and this may explain the lack of differences we observed based on ethnicity or geographic region.

Concentrations of chlorinated POPs have decreased for all age groups since the previous New Zealand survey

This research provides a second reference point for concentrations of chlorinated POPs in the blood serum of adult New Zealanders (Chapter 5), showing a clear decrease in human body burdens of these compounds (Figure 18).

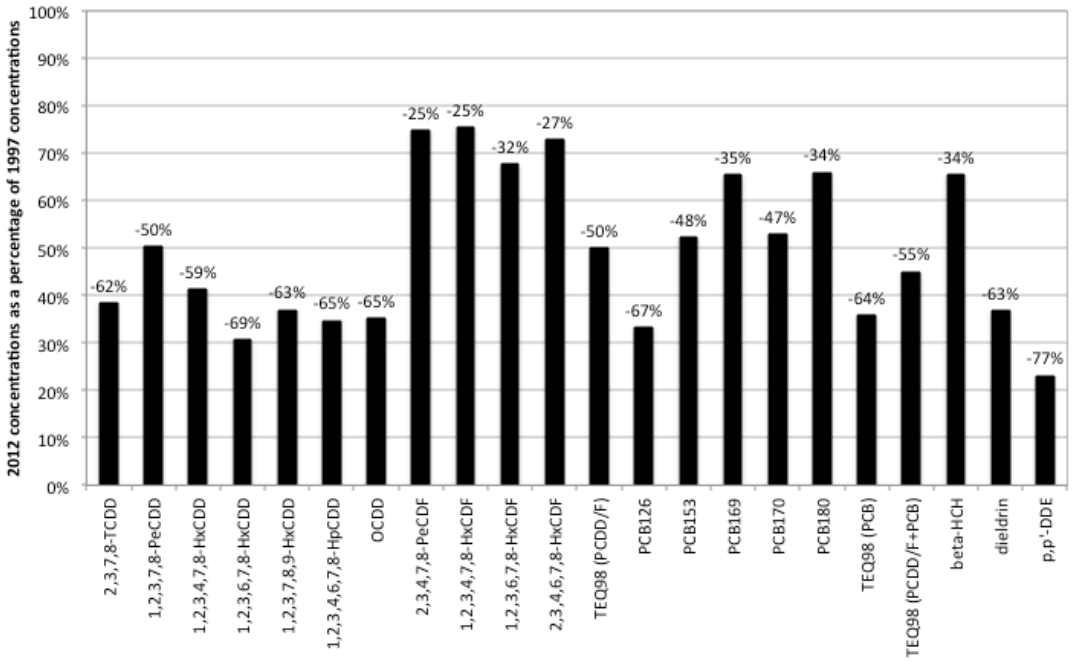


Figure 18. Temporal comparison chlorinated POPs between the 1997 and 2012 surveys. (figure from Chapter 5).

Few countries have completed periodic assessment of POPs in general populations with such a wide age range, so this research is a valuable addition to the international literature. The few repeat surveys of POPs in human serum and milk show that concentrations of POPs are decreasing around the world, attributed to reduced emissions of POPs from industrial and agricultural activities [39, 187]. The implementation of the Stockholm Convention by member countries provides the regulatory framework for action to reduce emissions of POPs to the environment, resulting in reduced human exposure to POPs [40]. New Zealand has committed to a number of measures to implement the Stockholm Convention [2], so the observed reduction of POPs in New Zealand adults reflects lower levels of POPs in the New Zealand environment resulting from these measures.

However, there are still a number of anthropogenic sources of chlorinated POPs in New Zealand and the rest of the world. Sources include ongoing applications of DDT for malaria control in tropical regions, stockpiles of disused agricultural chemicals, contaminated land areas and waterways, consumer products that may be inadvertently contaminated with POPs chemicals, and residues in food [301-303]. The most recent New Zealand Total Diet Survey (NZTDS) [304] showed that DDE was the predominant OCP found in a range of foods, and total DDT compounds decreased during the period 1990 to 2009. Similarly, other OCPs such as dieldrin in food showed a 50-fold decrease during the period 2003 to 2009. The highest concentrations of DDT compounds were found in foods of animal origin (e.g. pork, beef, chicken, and dairy products). The estimated dietary exposure to the OCPs measured in the NZTDS was below Acceptable Daily Intake (ADI) values [305]. The results of this research are in line with the findings of the NZTDS for OCPs, that is New Zealanders have lower exposure to these chemicals than in the past. It is reasonable to assume that dioxins and PCBs are also decreasing in New Zealand food, though more dietary studies would provide useful information to inform estimates of the dynamics of POPs in the general population.

Actions to manage POPs sources result in an overall reduction in the environmental burden of POPs, and this research shows a commensurate reduction in human body burdens. However, if management and remediation actions are not carefully managed they may result in increased exposure of local communities. The remediation of the former Fruitgrower's Chemical Company site at Mapua, New Zealand, one of the largest and most expensive publicly-funded contaminated sites

remediation projects to take place in New Zealand, was completed between 2004 and 2006. It is reported that emissions from the equipment used at Mapua included chlorinated POPs and this may have posed a health risk to local residents [306, 307]. The Priority List for the Contaminated Sites Remediation Fund (http://www.mfe.govt.nz/more/funding/contaminated-sites-remediation-fund/csrf-priority-list) includes a number of existing sites that are contaminated with dioxins and other environmental pollutants. The importance of these and other current environmental POPs sources to public health in New Zealand has not been established.

Higher levels of chlorinated POPs in older individuals is likely a cohort effect

The research showed that, for all the measured chlorinated POPs, mean serum concentrations are decreasing over time in the adult general population (Chapter 5). This decrease may be primarily attributed to a cohort effect – that is, younger individuals with relatively low lifetime exposure to chlorinated POPs enter the adult general population over time, resulting in an overall decrease in the mean adult concentration over time. We did not measure individual serum concentrations of chlorinated POPs in the research or follow individuals over time between the 1997 and 2012 surveys, but we estimated temporal changes at an individual level by investigating temporal changes in mean concentrations within cohorts included in both surveys (i.e. by comparing cohorts 15 years apart).

For each individual within a cohort (e.g. 19 to 24 year-old adults), serum concentrations of chlorinated POPs may be decreasing, increasing, or staying the same depending on an individual's balance of intake (primarily through diet) and elimination (metabolism, weight-gain related dilution, weight-loss related concentration, and excretion). In Chapter 5 we investigated the balance of intake and elimination of chlorinated POPs within cohorts by comparing the serum POPs concentrations measured in 2012 to estimates of 2012 serum POPs concentrations based on a "zero elimination" assumption between the 1997 and 2012 surveys. We presented indirect evidence that, for the majority of the chlorinated POPs congeners, the mean serum concentration in each cohort included in the 1997 and 2012 surveys decreased (i.e. the human elimination rate was greater than the intake rate, see Figure 19 for examples). However, for some PCDF and PCB congeners, the mean serum concentration in each cohort may have reached a steady-state (i.e. the human elimination rate is equal to the intake rate, see Figure 20). We saw no evidence of an increase in mean serum chlorinated POPs concentrations in individuals within a cohort between 1997 and 2012.

This finding supports the theory that the age-related association we observed for all chlorinated POPs (i.e. higher concentrations in older individuals shown in Chapter 5) is the result of a cohort effect. Previous studies have speculated that higher chlorinated POPs in older age groups may result from longer exposure to POPs in the environment and diet, resulting in a higher accumulated body burden in older individuals when measured in cross-sectional surveys [308, 309]. If this theory were true for New Zealand adults, we would expect to see an increase in the mean

concentration of chlorinated POPs for individuals in cohorts in the 1997 and 2012 surveys, which was not shown in this research. However, for certain PCDFs and PCBs elimination is balanced by residual intake, suggesting that human elimination rates are relatively slow for these congeners or there are prevalent environmental sources.

This finding only relates to adults because the balance of intake and elimination of POPs in children and in individuals over 65 years old will be different. Models of human POPs body burdens [28] suggest that the balance of intake and elimination changes markedly during childhood (resulting from relatively high intake from human milk, dust, and other sources) and adolescence (resulting from relatively high growth dilution during puberty). Less is known about the balance of intake and elimination in people over the age of 64, though some research suggests that human elimination rates of chlorinated POPs may increase with age as a result of age-related body fat re-distribution [283]. Further research into current environmental sources (e.g. diet) and the dynamics of human elimination (across a wide age group including children) of chlorinated POPs would provide information to expand on this finding.

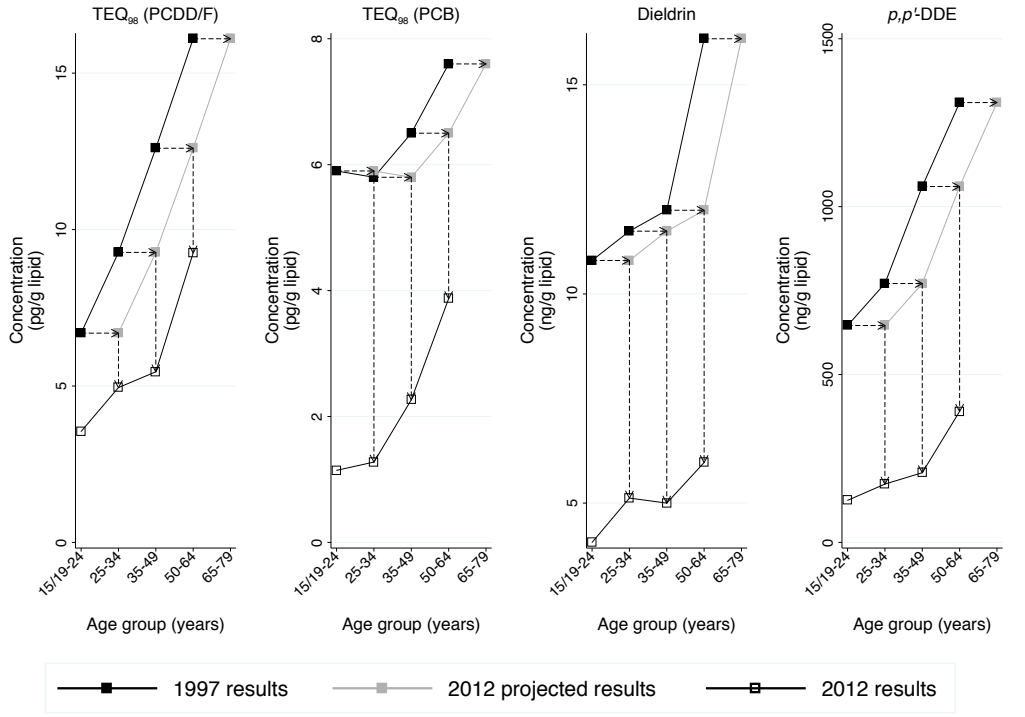


Figure 19. POPs for which mean serum concentrations have decreased for individuals in cohorts. (figure based on Chapter 5)

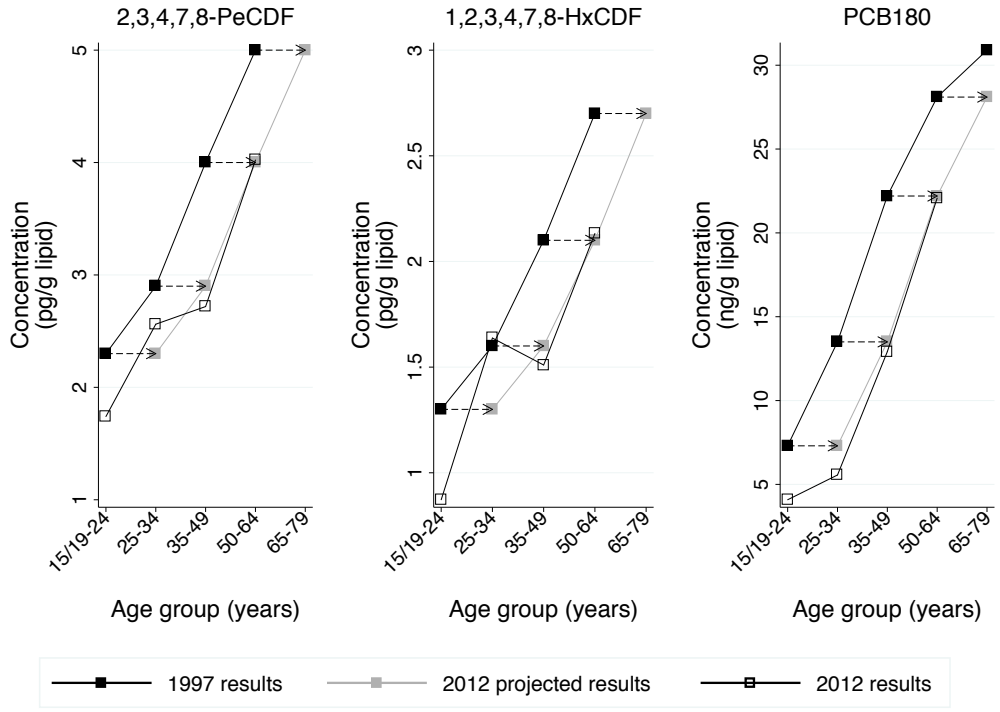


Figure 20. POPs for which mean serum concentrations have reached steady state concentrations for individuals in cohorts. (figure based on Chapter 5).

Concentrations of dioxins and PCBs are generally lower in New Zealand compared to international results

This research confirms previous research showing that concentrations of dioxins and PCBs in New Zealand adult serum are low by international standards (Chapter 5). New Zealand is a relatively non-industrialised nation, with few large manufacturing industries and large-scale thermal combustion processes. Concentrations of dioxins and PCBs are associated with level of industrialisation [155], so it is unsurprising that the concentrations measured in this research are at the low end of the international range.

Diet is the key exposure pathway for chlorinated POPs [310], and studies show that concentrations of dioxins and PCBs in foods of animal origin have been stable since 2000 [311], or are decreasing [312], with concentrations in seafood decreasing [313]. It is likely that levels of dioxins and PCBs in New Zealand food are also following a decreasing trend. The 1998 survey of dioxins and PCBs in New Zealand food [48] stated that "…people in New Zealand are exposed to far lower levels of these contaminants in their food than any other country where a similar survey has been undertaken". We have no information on current concentrations of dioxins and PCBs in New Zealand food, however it is reasonable to assume that New Zealanders' exposure is decreasing in a similar manner to the rest of the world. Future diet studies can be used to confirm this assumption and provide an indication of the current congener profile of chlorinated POPs in New Zealand food.

In Chapter 3 we reviewed international temporal trends of PCDDs, PCDFs, and PCBs in human milk. Similar to the serum research, the human milk results show a decreasing trend of these POPs in New Zealand and internationally over the past 30 years (Figure 21). In addition, the human milk results also show relatively low concentrations of these POPs in New Zealand mothers. With the complete New Zealand phase-out of PCBs in 2016, and a number of regulatory measures in place to control emissions of PCDDs and PCDFs to the environment, it is likely that New Zealand human body burdens of these POPs will continue to decrease.

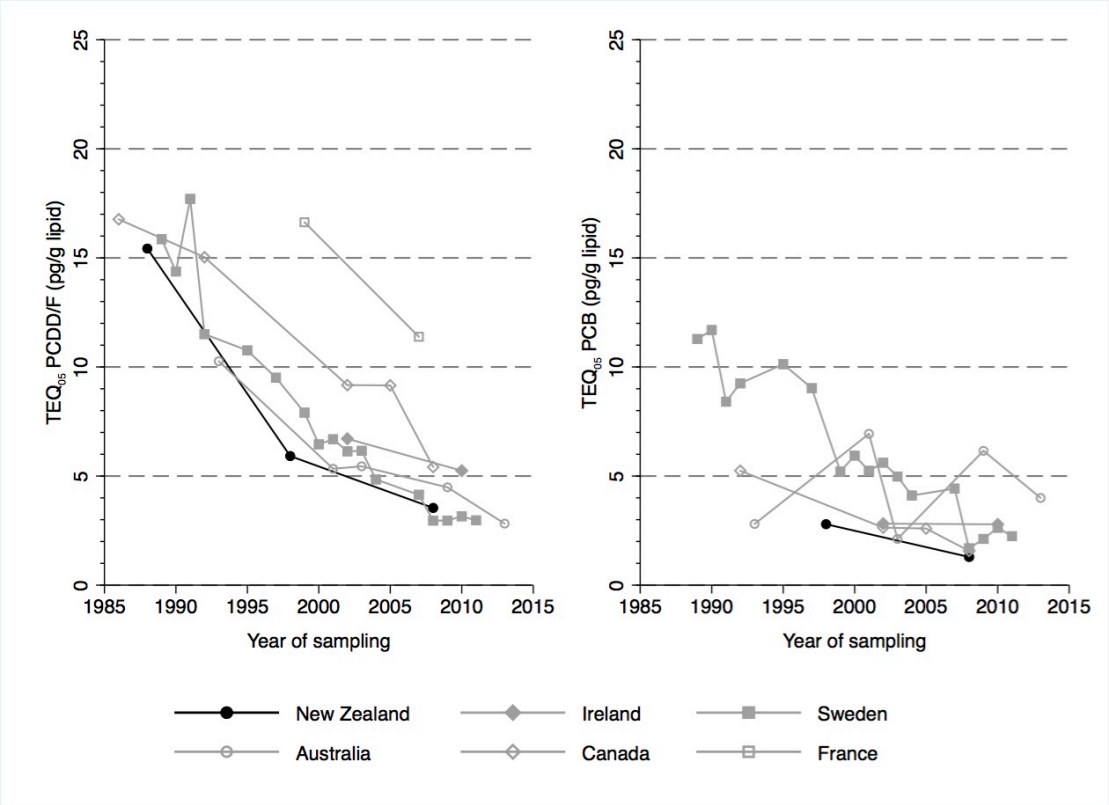


Figure 21. International temporal trend comparison of PCDD/Fs and PCBs. (figure from Chapter 3).

Concentrations of DDT and its breakdown products are relatively high in New Zealand

The research confirms the historic and current exposure of New Zealanders to DDT and its metabolic degradation products DDE and DDD (Chapter 5). Concentrations of OCPs such as DDT are highest in non-industrialised nations [187], resulting from application of agrichemicals and control of other urban and rural pest species. This research showed that concentrations of many OCPs in adult New Zealanders are lower than most comparable countries. However, serum concentrations of DDE (a

product of the metabolism of DDT in humans) in New Zealand adults were higher than a number of countries, most notably Australia.

Relatively high concentrations of DDE in New Zealand adults reflect the widespread historic use of DDT in New Zealand for control of agricultural pests. Previous New Zealand studies of human milk show that the estimated daily intake (EDI) of DDT and DDE was the highest of all POPs measured and was above the tolerable daily intake (TDI) for breast-feeding children [185]. Also, DDE was detected at the highest level of all OCPs measured in a wide range of animal-based food products in the New Zealand Total Diet Study [304].

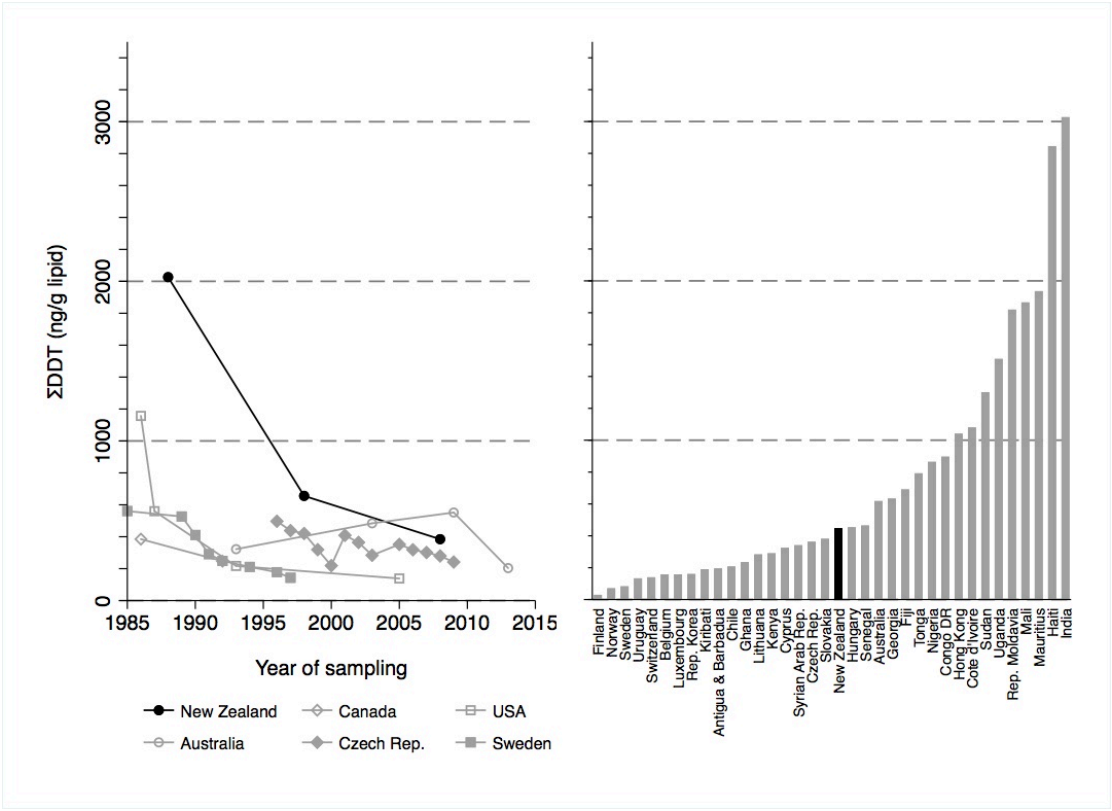


Figure 22. International temporal trend comparison (left side) and country-specific WHO global survey comparison (right side) of the sum of DDT compounds. (figure from Chapter 3).

Similar to the other chlorinated POPs, concentrations of DDT and other OCPs in human milk have decreased over the past 30 years, in New Zealand and internationally (Figure 22, left hand plot). However, the most recent research into DDT compounds in New Zealand human milk [19] shows that concentrations are in the middle of the range of international values (Figure 6, right hand plot), and that breast-feeding children may be exposed to elevated concentrations during a critical period of physical and mental development. Children's exposure to DDT compounds in human milk is an issue that warrants further research in New Zealand.

Concentrations of BFRs and PFASs in New Zealand are comparable to international results

The research provides the first results of BFRs and PFASs in the general population of New Zealand (Chapter 6). Comparison of the research findings with international results shows little difference in the exposure of New Zealanders relative to the rest of the world. Though, such comparisons are limited by differences in study design, study period, study population, and environmental sources of these chemicals between countries. Concentrations of BFRs and PFASs are associated with residency in urban areas [11, 96] and the majority of New Zealanders live in urban areas [314]. Diet is a key exposure route for BFRs and PFASs, though there are few available dietary studies [11]. However, there is evidence that dietary intake of common PFASs, such as PFOS and PFOA, in humans is decreasing since the chemical industry imposed voluntary restrictions on their production in 2002 [157, 243].

There are no PFAS manufacturing facilities in New Zealand, which suggests that New Zealanders may have had lower exposure to these pollutants during the period of peak global use. However, the research shows that New Zealanders' serum concentrations of PFASs are similar to other countries such as Canada, the USA, and Australia. This result is cause for concern because of the persistence of PFASs in humans and the environment, and emerging evidence of health effects in humans, laboratory animals, and wildlife [315-317]. The New Zealand Food Standards Authority (NZFSA) has a program to monitor PFASs in New Zealand food, however at this time there is no published information by NZFSA on this topic. Further research

into PFAS exposure sources in New Zealand, and temporal trends, is recommended to clarify the dynamics of these chemicals in the general population.

Strengths and limitations of the research

A unique aspect of this thesis research is that it includes a large, representative sample of New Zealand adults (Chapters 5 and 6) as well as a small, targeted sample of breast-feeding mothers combined with measurements of BFRs in household dust (Chapter 7). These components of the research provide novel insights into BFR exposure sources. The measurement of BFRs in dust is a useful tool for assessing human exposure to a wide range of flame retardant chemicals [87, 266] and the use of pooled samples in a large, representative sample is an accepted method for estimating central tendency concentrations of POPs [318, 319].

The research showed that analysis of pooled human serum samples is an effective tool for assessing demographic determinants of POPs in humans. While the use of pooled samples provides a good estimate of central tendency concentrations, limitations of this approach include no individual-level data, and no information on current exposure pathways for these pollutants. Due to the high costs per sample for laboratory analysis of POPs it may not be feasible to carry out future large surveys which provide individual results. Future surveys may include a questionnaire on common POPs exposure sources in order to investigate associations with adult body burdens. In addition, field-screening of household items for POPs is a technique that can be employed to better understand exposure pathways for POPs in the environment. Previous research has shown the presence of BFRs in New Zealand household consumer goods [320] and these BFRs accumulate in household dust [38,

267, 321]. Recent research shows that BFRs are also present in kitchen utensils made from recycled plastic [322].

Overall, the research findings provide important information on the current and historic exposure of adult New Zealanders to POPs. The serum samples were collected in 2011 and 2012, and we compared the results to other surveys done within a similar timeframe to the research. We were limited in our ability to directly compare the research to surveys done in the same year and in a directly comparable population, because few other international surveys for such a wide range of POPs were completed at the same time as New Zealand using comparable recruitment methods. Particularly for the BFRs and PFASs, it is important that comparisons between separate surveys are done using contemporaneous samples because of recent changes in the manufacture and use of BFRs and PFASs around the world. However, the comparisons done in this research provide an indication of the relative exposure of New Zealanders and establish a benchmark for future studies.

The POPs survey response rate (Chapter 4) shows that the recruitment methodology used for this research could be improved. A methodology based on random mail-out events to individuals on the Electoral Roll, and follow-up using publicly-available telephone lists was not the most efficient method to recruit a representative same from the general population. In particular, it was difficult to recruit younger individuals, and those of Māori descent. Future surveys should consider alternative strategies to achieve better recruitment efficiency and higher participation rates for those groups with low participation rates.

While the research provides information on the importance of dust as an exposure pathway for BFRs (Chapter 4), we did not investigate other environmental sources of POPs. An understanding of POPs sources including food, air, and water, would provide a more complete picture of POPs in New Zealand. Changes to the global atmosphere, biosphere, hydrosphere, and geosphere resulting from climate change and other environmental pressures will have direct and indirect effects on the fate and distribution of sources of POPs in the environment and people [182, 183]. For example, POPs that were deposited on the polar ice caps and held in place by ice cover may be released to the environment and re-enter the human food chain. In addition, POPs can transform in the environment and wildlife from their original form. For example, soil microbes and fungi can degrade higher-chlorinated dioxins to lower-chlorinated dioxins by the process of reductive dechlorination [323]. The ability of microbiota to degrade POPs in the environment may be affected by a wide range of anthropogenic environmental insults including habitat destruction, destabilisation and erosion of topsoil, and current discharges of pollutants to the environment. While there is little data on the dynamic interactions of POPs chemicals with wider global processes, new policy development should consider the potential for changes to population exposure to POPs from a broad range of environmental factors.

Whilst children were not included in this research, the results of Chapter 7 clearly show that children are exposed to BFRs in their home environments, and during breast-feeding. It is likely that the dynamics of POPs in children's environments are as complex as for adults, however we have no available information on

concentrations of BFRs in New Zealand children. Studies from Australia, Denmark, and the UK show that that children are exposed to high levels of flame retardants in their schools and homes [89, 324, 325]. The toxic effects of BFRs, and other POPs, on the mental and physical development of children is an area of active international investigation [142, 326]. The imperative of protecting the health of children should guide future actions to measure and control these chemicals. In New Zealand, a better understanding of exposure to POPs during childhood should be a priority.

This research provides the first national assessment of BFRs and PFASs in adult New Zealanders. There have been few studies that assess temporal trends of BFRs in human serum [96], so the research provides novel insight into the dynamics of these POPs in adults. However, we are not able to determine temporal trends for BFRs or PFASs at this time, and concentrations of these POPs are rapidly changing in humans around the world in response to regulation and other control measures. BFRs were previously assessed in a convenience sample of residents of New Zealand's Lower North Island [99], but the methodological differences between the previous study and the current POPs survey precludes our ability to assess temporal trends for New Zealand. Internationally, surveys of BFRs in the environment, wildlife, and in humans (including in human milk) show an increasing temporal trend during the 1980s and 1990s and a decreasing temporal trend after 2002 (Law et al., 2014). However, this trend was not consistently shown for the deca-brominated congener BDE209, which increased during periods when lower brominated penta- and octa-brominated PBDEs were decreasing. The ratio of BDE47 (a congener of the penta-brominated PBDEs) to BDE153 (a congener of the octa-brominated PBDEs) decreased, attributed

by the authors to differences in human elimination rates and the chemical industry's attempts to develop and sell substitutes for the penta-brominated PBDEs. BFRs were measured in only the most recent New Zealand study of POPs in human milk, so a temporal trend has not been established for this exposure pathway.

There are a number of analytical challenges related to BDE209 that should be taken into consideration when interpreting the findings of studies of this BFR congener in humans. BDE209 is commonly found in indoor environments [327] and potential contamination, and debromination of BDE209 to lower-brominated congeners during sample preparation, is a current problem with current analytical techniques [328]. The New Zealand research (Chapters 6 and 7) showed that BDE209 was amongst the congeners with the highest concentrations in adult serum, human milk, and dust, raising questions about potential BDE209 contamination of the New Zealand samples. Whilst we cannot exclude the potential for inadvertent contamination during sample handling and laboratory analysis of the New Zealand samples, the observed associations we found (e.g. an association between dust and milk, an association with age in adult serum) suggest that the influence of laboratory contamination is not significant to the overall research findings.

New Zealand adult exposure to BFRs is likely to mirror the exposure of adults in other countries, with some exceptions such as the USA and the UK where regulated use of BFRs was different to New Zealand and certain BFRs are found at relatively high concentrations in humans and household dust [98, 329]. Future biological monitoring surveys and environmental investigations will provide information to clarify temporal changes to New Zealanders' exposure to BFRs. Though the BFRs

measured in this research are ostensibly no longer used in new consumer articles, they have been substituted by other formulations like hexabromocyclododecane (HBCD), and non-brominated flame retardants (NBFRs) such as organophosphate flame retardants [330]. There is no information on current use patterns of HBCD and NBFRs in New Zealand. Unfortunately, efforts to quantify HBCD in the pooled adult serum samples collected in this research were not successful because of insufficient sample volumes to achieve suitable detection limits. Future national surveys should focus on currently-used flame retardants to establish baseline data for New Zealand and allow comparison to international results.

Recommendations

The research presented in this thesis provides answers to a number of questions about the fate and distribution of POPs in the New Zealand adult population. However, there remain a number of key areas where further research and policy development is recommended. The following sections summarise the recommendations that arise from the research and provide a brief discussion of the costs and benefits associated with each recommendation. These recommendations are not comprehensive, as further study into human exposure to POPs will reveal new information and generate new research questions.

1. Researchers may investigate a wider range of methods for obtaining participants and biological samples for studies of POPs and other environmental chemicals in humans. Australian researchers have established agreements with national pathology laboratories for access to surplus pathology samples and this method of sample collection has not been

actively pursued in New Zealand. Another opportunity is for researchers to work closely with government agencies who are conducting health-based surveys. The New Zealand Ministry of Health conducts a number of regular surveys (e.g. the New Zealand Health Survey, the Alcohol and Drug Use Survey, the Nutrition Survey) that could include mechanisms for the collection of samples for assessment of environmental pollutants. The cost of negotiating agreements with pathology laboratories will be time-related costs for researchers to design the study and negotiate agreements with pathology laboratories and government departments, as well as administration costs related to contractual and financial agreements. The study sample from such an approach may not be representative of the general population; though a more representative sample could be identified through a sample selection procedure that is agreed with the pathology lab or government agency. The ethical considerations related to using such samples has not been actively discussed in New Zealand. The benefit is access to potential study participants without expending additional resources on recruitment, as well as access to a greater number of biological specimens (e.g. urine, blood, faeces).

2. Researchers may design study methodologies to assess a wider range of environmental pollutants. The use of more sensitive analytical techniques, such as two-dimensional gas chromatography (GC x GC), provides better quantification of a wide range of POPs with much lower detection limits than are currently available (Mondello, Tranchida, Dugo, & Dugo, 2008). For example, in the current research TCDD was detected in only 37% of serum

samples and the use of more advanced analytical equipment would enable researchers to continue to track the fate and distribution of this highly toxic dioxin congener. In addition, advances in analytical testing methods may result in a much broader range of chemicals that can be quantified in a single sample. Analytical laboratories gather a large amount of data from each sample that could be quantified and considered by researchers. The traditional focus on Stockholm Convention POPs may be limiting our understanding of other current chemicals of concern. Since the work of this thesis was completed, New Zealand researchers have conducted research into concentrations of a wide range of "chemicals of concern" in adults and children. Future national surveys may focus on currently-used POPs to establish baseline data for New Zealand and allow comparison to international results. The cost for revealing additional findings from existing and future analytical surveys will be much less than conducting a new survey. The benefit would be a broader understanding of human exposure to environmental pollutants as well as contributing to emerging research on the human chemome (e.g. metabolomics). Loss of stored biological specimens, for example through accidents and mismanagement of archive facilities, is a risk that may be mitigated by expanding the list of chemicals that are included in future biological monitoring programmes from the outset.

3. Researchers may consider alternative methods to estimate POPs exposure in humans. There are many similarities in the exposure sources and pathways for BFRs and PFASs between New Zealand and other countries, and there is little evidence to suggest that New Zealanders are exposed to these

chemicals differently to the rest of the world. As such, future New Zealand surveys of "traditional" BFRs such as PBDEs may not be warranted. Surveys to develop a New Zealand temporal trend of BFRs in adult serum are expensive, and this cost needs to be weighed against the benefit of temporal trend data. It may be more useful to continue monitoring BFRs in human milk because these studies can be done more efficiently than national studies of POPs in serum and provide information on the exposure of humans during early childhood – a period of critical neurological and physical development. In addition, there is sufficient international data that upper-bound concentrations of BFRs in the general population may be estimated from established ratios between human milk and serum [246] and observations of relationships between central tendency and 95th percentile concentrations [253].

4. Human biological monitoring research should include children wherever possible. It is often challenging to collect invasive biological samples (e.g. blood) from children, however, researchers can work with parents and schools to develop sampling strategies. This sampling may include monitoring of wastewater from schools or child-care facilities, thus providing an opportunity to monitor temporal changes of POPs concentrations over time. A collection of serum samples could be collected in a sub-sample of students, pooled, and tested for a wide range of environmental chemicals along with environmental testing (e.g. analysis of wastewater from schools). Alternatively, researchers can pursue the collection of non-invasive samples such as urine, faeces, fingernails, and hair. BFRs have been measured in

childhood faeces successfully in a group of school-age children in Queensland, Australia [331]. Similar to BFRs, children are exposed to PFASs through diet, including human milk. There is no New Zealand data on levels of PFASs in human milk, though international studies have confirmed this exposure pathway [332]. Future investigations of breast milk to determine early life-stage exposure to POPs is recommended. In particular, New Zealand research should focus on PFAS exposure in children in order to establish reference concentrations and intake estimates for this vulnerable group. As well, researchers should consider investigation strategies that assess the thousands of other PFASs that are still in widespread use and may pose health risks to children [333]. Further research on exposure of children and adolescents to POPs, including BFRs, PFASs, and DDT compounds would provide valuable information on the dynamics and determinants of POPs body burdens through a broader section of the New Zealand population.

5. Targeted biological monitoring programs, such as the investigations into historic exposure of sawmill workers to OCPs [45, 334], may provide complementary information to this research. Future research into POPs in New Zealand may benefit from including targeted investigations on individuals and communities that are likely to have higher exposure to POPs. For example, exposure of workers to BFRs in building materials and electronics, and exposure of fire-fighters to PFAS in fire-fighting foam. Large, population-based surveys of BFRs in blood serum of the general population provide information that can't be gathered from smaller, targeted studies. However, the relatively rapid introduction of new flame retardant chemicals

to the market occurs more frequently than large surveys, which may take several years to complete. The reward for the effort of large HBM surveys is a more complete and representative estimation of current and historical exposure to POPs in the general population; the cost is the significant expense and time that must be dedicated to such surveys. Smaller studies do not provide information to estimate the exposure of the general population, but they can be more targeted and tailored to current chemicals of concern and provide findings in a shorter timeframe. Smaller studies may provide opportunities to more efficiently track chemicals of concern in the general population. Recruitment within a smaller stratum of the general population, or focusing on occupational exposure, will be less resource-intensive, while providing valuable information to assist policy-makers and researchers. The results of this research can be used as a reference for the development and interpretation of future small-scale, targeted studies.

6. Researchers may establish clear protocols for the storage of collected biological specimens. It is important that stored samples are catalogued and any future research involving archived samples is consistent with the ethics approval provided for the original survey. The cost of this recommendation will include the development of secure, temperature-controlled facilities where biological specimens are stored. In addition, there will be ongoing costs for the administration of a database of archived samples. The benefit of this recommendation is that archived samples will be available as a resource for future investigations, within the bounds of the current ethical approvals. The time and expense associated with collection of human biological samples

provides a justification for maintaining high standards in the administration and maintenance of sample storage facilities.

7. Researchers may do more to investigate dietary sources of POPs, for example as part of the New Zealand Total Diet Survey. More information on dietary sources of POPs would provide useful information about this important exposure pathway. There is currently no information on New Zealanders' dietary exposure to BFRs and PFASs; such research is rare internationally and there is an opportunity for New Zealand to lead research in this area.

8. Human biological monitoring can be integrated with field-scale investigation of exposure sources. Field-scale investigation can involve the use of portable screening equipment to identify potential environmental POPs sources, combined with standardised collection of environmental samples for laboratory analysis. Portable X-ray fluorescence has been used in New Zealand and the UK to screen consumer articles for BFRs, and in large-scale contaminated land remediation projects to identify contamination "hot-spots". Regular field-scale monitoring of a selection of consumer goods for POPs would provide valuable information to inform exposure estimates. Biological monitoring data from individuals who use these consumer goods can also be collected, and researchers can investigate associations between exposure sources and body burdens. Such studies will generally be smaller than a national research program, and will likely focus on a particular demographic group, so they can be done in less time with fewer resources.

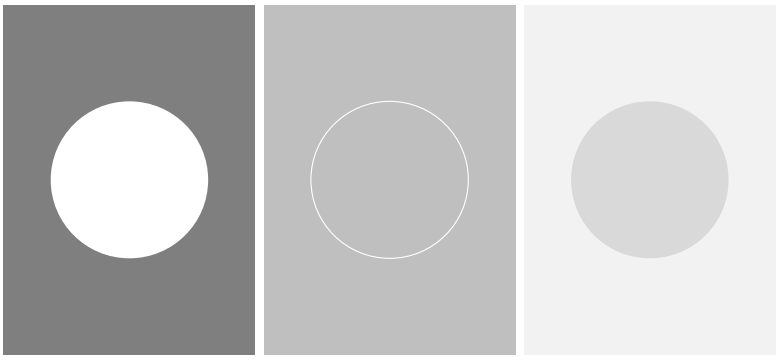
9. Policy agencies should consider the results of the research as a reference for assessing long-term risks associated with hazardous substances.

Organisations such as the NZEPA and New Zealand Food Standard Authority (NZFSA) can incorporate this research as part of their decision-making process for new chemicals, particularly those with slow metabolic elimination rates in humans. The risks and benefits from the use of persistent chemicals should be objectively established by regulatory authorities and be consistent with assessments from independent expert organisations such as the International Agency for Research on Cancer (IARC).

10. Decision-makers on new policy measures to control POPs in humans should consider the potential for changes to population exposure to POPs from a broad range of environmental factors, including climate change. Researchers may consider the influence of these environmental factors when considering temporal trend results for POPs. Policy agencies such as the Ministry for the Environment and the Ministry of Health are in a position to incorporate the research findings into their decision-making process.

Conclusions

The research presented in this thesis provides answers to a number of questions about the body burden of POPs in the New Zealand population. The associations of POPs levels with demographic factors, such as age and sex, provide insight into the distribution of these toxic chemicals. The research provides the first analysis of temporal trends of POPs in the general adult population of New Zealand, providing insights into New Zealanders' historic exposure to toxic POPs chemicals. In addition, the importance of dust as an exposure source for BFRs in human milk has been established for the first time in New Zealand. While the exposure of New Zealanders to the majority of POPs is low by international standards, there are a number of areas where further research is recommended. In particular, the exposure of children to POPs deserves greater focus in research and policy decision-making. The findings provide a key reference for future research into the dynamics of POPs in humans and will hopefully guide public health decision-making related to human exposure to POPs. More generally, the research results enable an assessment of the strengths and weaknesses of the selected methodology for assessing toxic substances in a representative sample of the general population. We recommend that the findings of this research are considered by government agencies to assess the effectiveness of continued domestic and international measures to reduce human exposure to POPs.



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Appendix 1 – Protocol for collection of blood and serum samples

17 February 2011

This protocol has been developed by the Centre for Public Health Research (CPHR) at Massey University to provide guidance to staff at pathology labs who have agreed to assist CPHR with blood and serum collection for the POPs Serum Study.

Blood Collection Instructions:

1. Confirm that the participant has completed the Clinical Form (or equivalent form) and obtain the completed form. If the participant has not completed the form provide time before or after blood collection to complete. The Clinical Form should stay with the study materials at all times during blood and serum collection.

2. The following materials will provided by CPHR for each survey participant:

- 3 x BD Vacutainer® 10 mL red top glass tubes (additive-free).
- 2 x 7.5 mL Qorpak® amber screw thread vials with polypropylene caps.
- 1 x 5 mL Qorpak® Smooth Skirt Polypropylene Cryogenic Vials with screw caps.

Study participants will bring these materials to the pathology lab. Other consumables for blood collection (e.g. tourniquets, gauze, Vacutainer® needles, bandages) are to be provided by the pathology lab or phlebotomist and administered according to standard protocols.

3. Draw blood using the Vacutainer® system into the 3 x 10 mL Vacutainer® red top glass tubes (additive-free). Do not invert or agitate the red top tubes.

4. Allow the blood in the red top tubes to clot for 30 – 45 minutes at room temperature. In some situations it may be necessary for blood samples to remain in the tube for up to 24 hours (maximum) to enable transport to a main blood processing centre. However, the time elapsed between blood collection and further processing should be minimised wherever possible.

5. Complete the "Blood Collection" section of the Clinical Form. If you are sending blood samples to a main processing centre for serum collection ensure that you send the other study materials (vials, Clinical Form) along with the blood tubes.

Serum Collection Instructions:

6. Centrifuge the blood tubes for 15 minutes at 2,900 rpm at a temperature between 17°C and 25°C.

7. Decant as much serum as possible, using glass pipettes (boxes of glass pipettes and rubber bulbs will be provided to you by CPHR for the study), from the centrifuged red top tubes and dispense into the appropriate Qorpak® vial (2 glass vials and 1 polypropylene vial). Each vial should contain the serum from one centrifuged red top tube. Note on the Clinical Form any observations of the collected serum (e.g. hemolyzed, turbid, lipemic, icteric). Fit the cap to the vial and store upright in a freezer at -4°C or less within one hour of spinning.

8. Complete the "Serum Collection" section of the Clinical Form. Fax a copy of the Clinical Form to 04 380 0600 Attention: Jonathan Coakley.

9. We recommend shipping of the serum in the vials to CPHR after a number of samples have been collected; say samples from 20 survey participants (60 separate serum samples in vials) depending on the storage capacity at your pathology lab. We will organise a courier company to pick up the samples from your lab and deliver to CPHR. Please contact Jonathan Coakley on 04 801 5799 ext. 62421 to organise courier pickup.

10. Prior to courier pickup, the samples should be bound together with a rubber band (3 vials from one study participant per rubber band), put in biohazard bags and packed securely in the chilly-bin provided by CPHR. Samples should be packed with ice packs on the bottom and top of the container to keep them cool during transport. Samples are to be shipped to the following address:

POPs Serum Study
Centre for Public Health Research
First Floor, 102 Adelaide Road
Newtown
Wellington 6021
Attention: Jonathan Coakley

Please ensure that the box is clearly labelled "POPs Serum Study", it is well-wrapped, and that all efforts are taken to keep the samples frozen during shipping. We will return the small chilly-bin to you so that you can re-use it to send the next set of samples to CPHR.

For any questions about the study please contact:

Jonathan Coakley
Research Officer
Centre for Public Health Research
Massey University
PO Box 756
04 801 5799 ext 62421
j.d.coakley@massey.ac.nz

Appendix 2 – Number of participants in each region, by age, sex, and ethnicity

Age Group (years)	Sex	Ethnicity	Northland/ Auckland	Waikato/ Bay of Plenty	Lower North Island	South Island	Totals
19-24	Female	Māori	5	5	6	4	20
		Non-Māori	8	15	14	10	47
	Male	Māori	1	2	2	0	5
		Non-Māori	5	7	9	4	25
25-34	Female	Māori	12	11	14	8	45
		Non-Māori	12	14	17	16	59
	Male	Māori	3	6	2	2	13
		Non-Māori	3	11	4	8	26
35-49	Female	Māori	12	12	9	20	53
		Non-Māori	14	22	18	18	72
	Male	Māori	8	8	10	6	32
		Non-Māori	11	18	15	10	54
50-64	Female	Māori	18	14	19	24	75
		Non-Māori	23	23	20	20	86
	Male	Māori	16	12	11	11	50
		Non-Māori	17	19	20	16	72
Totals			168	199	190	177	734

Shaded cells indicate strata that were combined for all regions because of low participant numbers.

Appendix 3 – Laboratory QA/QC information for PBDEs in dust and human milk

The analytical method for PBDEs in indoor dust has been recently validated by Van den Eede et al. (2012) and further described in details by Dodson et al. (2012). Six procedural blanks were analyzed in the same batches as the samples and the results are blank corrected. This implies subtraction of mean blank values (in pg) from the raw PBDE values (in pg) in the samples. Blank values, when detected, were <0.5% of sample values. Compounds consistently detected (found in all blanks) in the procedural blanks were: BDE 47 (20 pg), BDE 85 (15 pg), BDE 154 (40 pg), BDE 196 (10 pg), and BDE 209 (1300 pg). Method limits of detection (LOD) were calculated as three times the standard deviation of blank values and divided by the amount of dust used for analysis (typically 50 mg). For compounds not detected in the blanks, the LOD was calculated based on the signal to noise ratio 3/1, taking into account the chromatogram's characteristics for the respective retention time (co-elution, noisy baseline, etc.). LODs are compound-specific variables and therefore spanned a large range of concentrations. SRM 2585 (Organic Contaminants in House Dust), which has certified values for PBDEs was used to test the accuracy. Concentrations of PBDEs ranged between 0 and 30% relative difference from the certified values (except for BDE196, 197, 203 for which the relative difference ranged between 40 and 50%, see below). Despite a few discrepancies, there does not appear to be a systematic bias to the samples and values were not adjusted. Recoveries of internal standards ranged between 72 and 95 with RSD <12% Apparently, the recoveries of these surrogate standards added to the dust is better than those of the native PBDEs present in SRM 2585 due to a higher accessibility during extraction.

Congener	LOD	Average	SD	Certified	SD	Difference(%)
BDE 28	1	32	1	46.9	4.4	31
BDE 47	2	403	8	498	46	19
BDE 99	2	733	17	892	53	18
BDE 100	2	115	2	145	11	21
BDE 153	2	95	2	119	1	20
BDE 154	2	76	2	83.5	2	8
BDE 183	2	31	5	43	3.5	28
BDE 196	2	23	2	39	4	42
BDE 197	2	17	2	29	3	41
BDE 203	2	18	1	36.7	6.4	52
BDE 206	3	271	14	271	42	0
BDE 209	5	2116	257	2510	190	16

Values are in ng/g unless otherwise specified

The analytical method for PBDEs in human breast milk has previously been described in (Mannetje and others 2010). In general sample data was processed to the Limit of Quantification (LOQ), which is equivalent to a signal to noise ratio of 10:1. In some cases data was processed to the Limit of Detection (LOD), which is equivalent to a signal to noise ratio of 3:1. The LOQ and LOD values were determined by QuanLynx software (Waters Corporation, USA). In all cases an analytical response must have a signal to noise ratio of 3:1 or greater to be considered detected. Prior to extraction each sample was spiked with an internal standard solution containing 13C labelled standards. After extraction and clean up, prior to injection on the GC-HRMS, the samples were spiked with a recovery standard solution. The internal standards were used for quantification of the target analytes; thus sample results are recovery corrected. The recovery standard was used for quantification of the internal standards to determine the percent recovery. The internal standard recoveries were assessed against the limits specified in USEPA Method 1614. Analysis of certified reference materials (CRMs) were not included for breast milk samples. The analysis of a matrix spike was included with each batch of samples. The matrix spike recoveries were assessed against the limits specified in USEPA Method 1614. The analysis of a reagent blank was included with each batch of samples. The results for the blank were reported together with the sample results. No blank correction of the sample data was performed.

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Appendix 4 – Pearson correlation coefficients for living room floor dust in relation to breast milk samples

	Floor dust, r (N=33)															
Milk	BDE17	BDE28	BDE47	BDE49	BDE66	BDE85	BDE99	BDE100	BDE153	BDE154	BDE183	BDE196	BDE197	BDE203	BDE206	BDE209
BDE17	NA	-0.15	0.19	0.001	0.04	0.05	0.17	0.2	0.21	0.2	0.23	NA	NA	NA	0.26	0.2
BDE28	NA	-0.13	0.2	0.13	0.33	0.32	0.16	0.13	0.1	0.06	0.1	NA	NA	NA	0.19	0.21
BDE47	NA	0.006	0.39*	0.39*	0.22	0.22	0.3	0.28	0.21	0.19	0.26	NA	NA	NA	0.34	0.35*
BDE49	NA	0.27	0.43*	0.26	0.34	0.41*	0.41*	0.39*	0.32	0.38*	0.17	NA	NA	NA	0.06	0.08
BDE66	NA	0.1	0.39*	0.3	0.34	0.31	0.34	0.33	0.28	0.27	0.24	NA	NA	NA	0.21	0.24
BDE85	NA	-0.02	0.36*	0.39*	0.14	0.18	0.3	0.26	0.2	0.19	0.21	NA	NA	NA	0.32	0.34
BDE99	NA	-0.01	0.41*	0.35*	0.2	0.17	0.33	0.32	0.21	0.22	0.24	NA	NA	NA	0.32	0.34
BDE100	NA	-0.06	0.26	0.38*	0.21	0.18	0.2	0.17	0.14	0.11	0.21	NA	NA	NA	0.33	0.36*
BDE153	NA	0.11	0.23	0.21	0.3	0.24	0.23	0.21	0.15	0.12	0.12	NA	NA	NA	0.26	0.3
BDE154	NA	-0.11	0.37*	0.36*	0.2	0.22	0.33	0.3	0.23	0.19	0.24	NA	NA	NA	0.33	0.37*
BDE183	NA	-0.19	0.37*	0.32	0.02	0.21	0.31	0.31	0.36*	0.16	0.39*	NA	NA	NA	0.57**	0.62**
BDE196	NA	-0.21	0.2	0.24	-0.2	-0.06	0.19	0.24	0.16	0.16	0.19	NA	NA	NA	0.59**	0.54**
BDE197	NA	-0.2	0.12	0.18	-0.09	-0.12	0.08	0.09	0.05	0.008	0.21	NA	NA	NA	0.55**	0.52**
BDE203	NA	-0.23	0.16	0.03	-0.29	-0.19	0.16	0.21	0.09	0.17	0.22	NA	NA	NA	0.28	0.23
BDE206	NA	-0.16	0.002	-0.05	-0.2	-0.08	-0.002	-0.001	-0.06	-0.01	-0.12	NA	NA	NA	0.36*	0.31
BDE209	NA	-0.05	0.04	0.05	-0.16	0.07	0.03	0.003	-0.04	0.002	-0.08	NA	NA	NA	0.43*	0.37*

Table notes:
* $p < 0.05$
** $p < 0.005$
N – number of matched pairs used in the correlation
NA – Not assessed because detection frequency in dust or milk was less than 50%.

Appendix 5 – Pearson correlation coefficients for mattress dust in relation to breast milk samples

	Mattress dust, r (N=16)															
Milk	BDE17	BDE28	BDE47	BDE49	BDE66	BDE85	BDE99	BDE100	BDE153	BDE154	BDE183	BDE196	BDE197	BDE203	BDE206	BDE209
BDE17	NA	0.24	0.41	0.45	0.44	0.41	0.31	0.42	0.23	0.29	0.08	-0.003	-0.16	-0.12	-0.14	0.08
BDE28	NA	0.21	0.28	0.46	0.34	0.24	0.22	0.26	0.06	0.17	-0.43	-0.56*	-0.47	-0.33	-0.3	-0.21
BDE47	NA	0.32	0.52*	0.56*	0.48	0.46	0.46	0.43	0.62*	0.49	0.05	0.13	0.11	0.26	0.11	0.2
BDE49	NA	-0.02	0.05	-0.17	0.04	0.16	0.13	0.05	0.07	0.23	0.58*	0.28	0.19	0.16	0.22	0.09
BDE66	NA	-0.24	-0.21	-0.08	-0.25	-0.29	-0.3	-0.29	-0.2	-0.33	-0.37	-0.1	-0.02	0.04	-0.18	-0.15
BDE85	NA	-0.19	-0.03	-0.28	-0.09	-0.03	-0.17	0.05	-0.12	-0.05	0.09	0.16	0.08	-0.04	-0.26	-0.27
BDE99	NA	0.3	0.45	0.56*	0.45	0.44	0.41	0.41	0.64*	0.48	-0.04	0.1	0.08	0.27	0.11	0.23
BDE100	NA	0.29	0.45	0.53*	0.43	0.43	0.39	0.4	0.63*	0.48	0.004	0.18	0.13	0.32	0.1	0.21
BDE153	NA	0.38	0.5	0.6*	0.52*	0.52*	0.47	0.49	0.74**	0.58*	0.12	0.28	0.28	0.37	0.18	0.31
BDE154	NA	0.39	0.51*	0.63*	0.53*	0.52*	0.52*	0.47	0.75**	0.58*	0.03	0.14	0.14	0.3	0.21	0.33
BDE183	NA	0.35	0.49	0.4	0.47	0.55*	0.43	0.51*	0.49	0.52*	0.44	0.42	0.46	0.09	-0.06	0.12
BDE196	NA	0.31	0.33	0.07	0.28	0.5*	0.42	0.42	0.53*	0.52*	0.32	0.49	0.29	0.2	0.05	0.14
BDE197	NA	0.49	0.49	0.24	0.46	0.59*	0.55*	0.58*	0.51*	0.6*	0.2	0.32	0.19	0.03	-0.23	-0.1
BDE203	NA	0.3	0.37	0.11	0.32	0.5	0.49	0.43	0.54*	0.54*	0.19	0.37	0.15	0.17	-0.02	0.03
BDE206	NA	0.2	0.31	0.12	0.2	0.44	0.35	0.41	0.52*	0.4	0.16	0.55*	0.34	0.28	0.2	0.37
BDE209	NA	0.09	0.2	0.11	0.11	0.34	0.22	0.32	0.43	0.26	0.11	0.5	0.36	0.23	0.29	0.5*

Table notes:
* $p < 0.05$
** $p < 0.005$
N – number of matched pairs used in the correlation
NA – Not assessed because detection frequency in dust or milk was less than 50%.

Appendix 6 – Statements of contribution to Doctoral thesis containing publications

MASSEY UNIVERSITY
GRADUATE RESEARCH SCHOOL

STATEMENT OF CONTRIBUTION TO DOCTORAL THESIS CONTAINING PUBLICATIONS

(To appear at the end of each thesis chapter/section/appendix submitted as an article/paper or collected as an appendix at the end of the thesis)

We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: Jonathan Coakley

Name/Title of Principal Supervisor: Andrea 't Mannetje

Name of Published Research Output and full reference:

Coakley, J., et al. (2018). "Chlorinated persistent organic pollutants in serum of New Zealand adults, 2011–2013." Science of The Total Environment 615: 624-631.

In which Chapter is the Published Work: 5

Please indicate either:

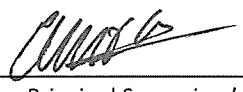
- The percentage of the Published Work that was contributed by the candidate: 90%

  and / or
- Describe the contribution that the candidate has made to the Published Work:

Candidate's Signature

30 October 2018

Date



Principal Supervisor's signature

8/11/2018

Date

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STATEMENT OF CONTRIBUTION TO DOCTORAL THESIS CONTAINING PUBLICATIONS

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We, the candidate and the candidate's Principal Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of Candidate: Jonathan Coakley

Name/Title of Principal Supervisor: Andrea 't Mannetje

Name of Published Research Output and full reference:

Coakley, J., et al. (2018). "Polybrominated diphenyl ethers and perfluorinated alkyl substances in blood serum of New Zealand adults, 2011-2013". Chemosphere 208: 382-389.

In which Chapter is the Published Work: 6

Please indicate either:

- The percentage of the Published Work that was contributed by the candidate: 90%

  and / or
- Describe the contribution that the candidate has made to the Published Work:

Candidate's Signature

30 October 2018

Date

Principal Supervisor's signature

6/11/2018

Date

MASSEY UNIVERSITY
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STATEMENT OF CONTRIBUTION TO DOCTORAL THESIS CONTAINING PUBLICATIONS

(To appear at the end of each thesis chapter/section/appendix submitted as an article/paper or collected as an appendix at the end of the thesis)

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Name of Candidate: Jonathan Coakley

Name/Title of Principal Supervisor: Andrea 't Mannetje

Name of Published Research Output and full reference:

Coakley, J. D., et al. (2013). "Concentrations of polybrominated diphenyl ethers in matched samples of indoor dust and breast milk in New Zealand." Environ Int 59C: 255-261.

In which Chapter is the Published Work: 7

Please indicate either:

- The percentage of the Published Work that was contributed by the candidate: 75%

  and / or
- Describe the contribution that the candidate has made to the Published Work:

Candidate's Signature	30 October 2018 Date
Principal Supervisor's signature	8/11/2018 Date