SOLVENT NEUROTOXICITY IN VEHICLE COLLISION REPAIR WORKERS

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Abstract

Previous studies have shown that vehicle collision repair workers may be at risk of solvent-induced symptoms of neurotoxicity. Changes in industry practices have likely resulted in reduced exposure, but little research has been conducted to assess whether this has reduced the risk of neurotoxicity. This thesis describes a series of studies, which aimed to assess: i) contemporary airborne solvent exposures in collision repair workers; ii) the determinants of airborne solvent exposures; iii) the prevalence of self-reported symptoms of neurotoxicity and objectively measured neuropsychological performance, compared to an unexposed reference group; iv) dose-response associations; and v) the effect of personal protective equipment (PPE) and good workplace hygiene on symptom prevalence.

In total, 370 vehicle collision repair and 211 construction workers (reference group) were recruited. Personal airborne solvent exposure was assessed in 85 collision repair workers, and information on demographics, work practices and symptoms was collected by questionnaire. A sub-group of 47 collision repair and 51 reference workers also completed a battery of neuropsychological tests.

Full-shift, airborne exposures were well below New Zealand and international occupational exposure limits (range, 0.04 – 16.5 ppm). Job title was the strongest predictor of exposure, and non-spraying tasks (e.g. mixing paint and cleaning equipment) were associated with higher exposures than spray painting itself.

Collision repair workers reported significantly more symptoms of neurotoxicity than the reference group, with odds ratios (ORs) of 2.0, 95% CI 1.3-3.3; 2.4, 1.2-4.8; and

6.4, 1.8-23.0, for reporting ≥5, ≥10 and ≥15 symptoms, respectively. They also performed more poorly on neuropsychological tests, particularly those that measure attention/concentration and motor speed/dexterity (e.g. reference vs. collision repair group score on the RBANS total attention scale, -9.5, 95% CI, -15.9, -2.8).

Consistent use of PPE (particularly gloves) and good workplace hygiene practices were strongly protective against symptoms, with reductions in risk of up to 90% for those who most consistently wore PPE.

In conclusion, despite relatively low airborne exposure levels, collision repair workers continue to be at risk of solvent-induced neurotoxicity. These findings provide a strong evidence-base for the development and implementation of intervention programmes to reduce solvent exposures and associated morbidity in this population.

Authors Declaration

This thesis was produced according to Massey University's "thesis-by-paper" requirements i.e. it is based on research that is published. Each individual chapter is set out in the style of the journal in which it has been published. Consequently, some of the chapters are relatively succinct, there is some repetition (particularly in the methods sections) and there are small stylistic differences between chapters.

The published manuscripts include other authors who provided technical expertise and contributed to the writing of the papers, including my PhD supervisors and, in some cases, collaborators in different institutes in New Zealand and the U.K. However, for each chapter, my input was greatest, as reflected by being first author on the paper. I was the lead investigator for the studies described, involved in oversight of study design, recruitment, work co-ordination and data collection, data analysis and preparation of the manuscripts. I was also involved in preparation of the ethics application prior to the conduct of these studies.

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Abbreviations

NIOSH	National Institute of Occupational Safety and Health
CSN	Chronic Solvent-induced Neurotoxicity
CSE	Chronic Solvent-induced Encephalopathy
CTE	Chronic Toxic Encephalopathy
CNS	Central Nervous System
PNS	Peripheral Nervous System
PPE	Personal Protective Equipment
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
IARC	International Agency for Research on Cancer
WHO	World Health Organisation
CAT	Computer Aided Topography
MRI	Magnetic Resonance Imaging
Q16	Neuropsychological Questionnaire 16
PNF	Psychologisch-Neurologischer Fragebogen (Questionnaire)
POMS	Profile of Mood States
NCTB	Neurobehavioral Core Test Battery
NES	Neurobehavioural Evaluation System
BARS	Behavioural Assessment and Research System
CANTAB	Cambridge Neuropsychological Performance Test Automated Battery
BEES	Behavioural Evaluation for Epidemiological Studies
RBANS	Repeatable Battery for the Assessment of Neurobehavioural Status
NART	National Adult Reading Test
JEM	Job-Exposure Matrix
TWA	Time-Weighted Average
TLV	Threshold Limit Values
WES	Workplace Exposure Standards
PEL	Permissible Exposure Limit
OEL	Occupational Exposure Limit
STEL	Short-Term Exposure Limit

ALV	Additive Limit Value
GCMS	Gas Chromatography Mass Spectroscopy
VEM	Video Exposure Monitoring
PIMEX	Picture Mixed Exposure
NSC-60	Neurobehavioural Symptom Checklist
LEV	Local Exhaust Ventilation
OR	Odds Ratio
CI	Confidence Interval
ER	Exposure Ratio
NZ	New Zealand
SIFT-MS	Selected-Ion flow-Tube Mass Spectroscopy
MEK	Methyl Ethyl Ketone
MIK	Methyl Isobutyl Ketone
GM	Geometric Mean
PPM	Parts Per Million
PPB	Parts Per Billion
PPT	Parts Per Trillion
W/W	Weight for Weight (Percentage Mass)
CRA	Collison Repair Association of New Zealand
HRC	Health Research Council of New Zealand
CR	Collision Repair
DASS	Depression, Anxiety and Stress Scale
SME	Small to Medium-sized Enterprise

1 General introduction

Occupational exposure to neurotoxic chemicals is common. In fact, clinical syndromes associated with these exposures comprise one of the ten leading occupational disorders in the United States, and neurotoxic effects are the basis for exposure limit criteria for approximately 40% of the agents considered hazardous by the United States National Institute for Occupational Safety and Health (NIOSH) (1). Of the agents with established neurotoxic effects, solvent mixtures represent the greatest potential hazard, with an estimated 10 million workers regularly exposed in the US alone (1). In New Zealand it has been estimated that 100,000 workers are exposed, which represents a sizeable proportion of the workforce (2).

The intoxicating effects of occupational solvent exposure were recognised as early as the mid-1800s (3), but it was not until the 1960s that an occupational condition referred to as “organic solvent syndrome” or “psycho-organic syndrome” was proposed (4, 5). While a range of acute and reversible health effects (e.g. headaches, nausea) may occur as a result of mixed solvent exposure, long-term, low-level solvent exposures may also result in chronic solvent-induced neurotoxicity (CSN), which may progress to more severe dysfunction (6). When symptoms are chronic and severe, a diagnosis of ‘Chronic Solvent-Induced Encephalopathy’ (CSE) may be made (7). However, despite increased recognition of this condition, data on global incidence and prevalence of clinical and subclinical CSN, particularly outside of Europe, are limited. This is in part due to a lack of routine screening among at-risk populations and the lack of universally accepted diagnostic criteria (8). The available data on solvent-induced adverse health effects also generally relate mostly to clinically diagnosed cases, so

there is limited data on sub-clinical neurobehavioural effects which, although less severe, may nonetheless significantly affect quality of life (9).

Industrial and vehicle collision repair spray painters (who are regularly exposed to mixed solvents) have been consistently over-represented among cases of CSE both globally (10, 11) and in New Zealand (12). With an estimated 700 to 1000 collision repair workshops in New Zealand (employing 2-15 workers each), there is potentially a large population of workers at risk.

Although there is some evidence that airborne solvent levels in the collision repair and other industries may have declined over the past 20 years internationally (13), a lack of research in the past decade means it is unclear what impact this may have had on the risk of solvent-induced neurotoxicity in this workforce. This is particularly true in New Zealand, where very little research on solvent exposures and related health effects has been conducted (12).

A detailed understanding of the determinants of exposure is important for development of effective interventions. In the collision repair industry, the use of administrative and engineering controls, workplace conditions and economic factors (e.g. workplace practices, behaviours and processes, workload, turnover, etc.) have been shown to affect exposure to isocyanates (14) (a chemical agent used in the majority of modern spray paint formulations, and a known cause of occupational asthma in sensitised workers (15)), but few studies have included an assessment of the determinants of solvent exposure, or included a quantitative assessment of solvent exposure levels.

A number of studies on symptoms of neurotoxicity have been conducted in the collision and repair industry over the past 50 years internationally, including those involving subjective assessments of neurobehavioural symptoms and/or objective clinical tests to assess neuropsychological (cognitive) performance (16-19). While an increased risk of neurotoxicity has been observed, findings have often been inconsistent, particularly regarding the results of objective neurobehavioural testing (20, 21). This has led to suggestions that collision repair and other workers with long-term, low-level solvent exposures may be at risk of only 'mild' and reversible symptoms (20). Also, many studies have not found clear dose-response relationships with airborne solvent exposures (16, 22, 23), which may be due to 'healthy worker survivor' bias (where a proportion of workers develop effects and leave the industry, and those remaining are less affected by solvents) (16). Alternatively, dermal exposures, which are often not measured, may play an important role, potentially obscuring a clear dose-response association with airborne solvent exposure (24-26). Finally, most research does not take into account intense peaks in airborne exposures, which may act as a 'tipping point' in the development of symptoms (27, 28).

A small number of studies in spray painters (29, 30) and other solvent-exposed workers (31-34) have shown that the use of personal protective equipment (PPE) is associated with reduced exposure, but few studies have directly assessed the impact of PPE use on the prevalence of neurobehavioural symptoms (30, 31, 34-36). In addition, very few recent studies have reported quantitative data on the type, quality and maintenance level of PPE, or the consistency of its use in the collision repair industry (29). Also, despite the importance of preventing or limiting the exposure of

workers to solvents already being recognised in the mid 1800's (37), very few intervention studies have been conducted in this industry, and those which have, did not assess the effects of the intervention on either exposure levels or health effects (38).

Thus, despite decades of research, many questions in this area remain unanswered. The aims of this thesis are therefore to assess:

- Contemporary airborne mixed solvent exposure in vehicle collision repair workers in New Zealand;
- The determinants of airborne solvent exposures in collision repair workplaces;
- The prevalence and nature of self-reported symptoms of neurotoxicity in New Zealand collision repair workers and compare this to an unexposed comparison group;
- The prevalence and nature of objectively measured neuropsychological performance in New Zealand collision repair workers and compare this to an unexposed comparison group;
- Dose-response associations between duration of employment in the industry and symptoms of neurotoxicity;
- Whether the use of personal protective equipment and good workplace hygiene affects the risk of symptoms of neurotoxicity.

1.1 Outline of the thesis

Chapter 1 – General introduction

This chapter provides a brief introduction to the thesis, including what is currently known about occupational solvent exposures and associated health effects, with a focus on the vehicle collision repair industry. The aims of the thesis are then presented, followed by an outline of the chapters.

Chapter 2 – Literature review

This chapter comprises a review of the literature on occupational solvent exposures and associated health effects, with a specific focus on collision repair workers. It also provides further background information relevant to the topics addressed in the remaining chapters of this thesis, including: the uses and properties of solvents; methodologies for assessing occupational solvent exposures; solvent exposures and their determinants in the collision repair industry; mechanisms of solvent toxicity; the epidemiology of solvent-induced neurotoxicity; and exposure controls to reduce morbidity in the collision repair industry (and potentially other industries that use solvents).

Chapter 3 - Determinants of airborne solvent exposure in the collision repair industry (Keer et al., Ann Work Expo Health, 2018, 62(7) 871-883),

This chapter describes the results of an investigation of the determinants of personal airborne solvent exposures in 18 collision repair workshops. The results of 97 personal

airborne exposure measurements in 85 workers are summarised, and data on potential determinants (environmental conditions, workplace practices, engineering controls and work tasks) collected as part of the questionnaire study (chapter 4, see appendix 1 for a copy of the questionnaire) and on-site workplace hygiene surveys are presented.

Chapter 4 - Solvent neurotoxicity in vehicle collision repair workers in New Zealand (Keer et al, Neurotoxicology, 2016, 57, 223-229).

This chapter presents the results of a questionnaire-based study, which assessed the prevalence of symptoms of neurotoxicity in 370 solvent-exposed collision repair workers compared to an unexposed reference group of 211 construction workers. In addition, the associations between duration of employment in the industry (as a proxy for cumulative exposure) and symptom prevalence are reported.

Chapter 5 - Neuropsychological performance in solvent-exposed vehicle collision repair workers in New Zealand (Keer et al, PLoS ONE, 2017, 12(12): e0189108)

This chapter presents the results of objective neuropsychological testing in a subgroup of collision repair (n=47) and comparison workers (n=51) who took part in the larger questionnaire survey (chapter 4). Test scores in relation to duration of employment are reported, along with the results of analyses assessing the potential severity of cognitive effects.

Chapter 6 - Effects of personal protective equipment use and good workplace hygiene on symptoms of neurotoxicity in solvent-exposed vehicle spray painters (Keer et al, Ann Work Expo Health, 2018, 62(3), 307-320)

This chapter presents data on the use of personal protective equipment (PPE, including respirators, gloves and protective clothing) and the presence of workplace hygiene practices. It also reports associations and dose-response trends between PPE use and good workplace hygiene practices and symptoms of neurotoxicity amongst vehicle repair spray painters (n=267).

Chapter 7 - General discussion

This chapter summarises the main findings and conclusions of the studies described in this thesis, and discusses their relative strengths and limitations. It provides recommendations for future research, including the development of intervention programmes to reduce occupational solvent exposures and associated morbidity.

Appendices

Appendix 1: Occupational exposures and health status Questionnaire

Appendix 2: Flow diagram of study participants included in the results chapters of this thesis (3, 4, 5 and 6).

Appendix 3: Statements of contributions to Doctoral thesis containing publications

Appendix 4: Letter confirming ethics approval from Multi-regional Ethics Committee

2 Literature review

Given the volume and scope of literature on occupational solvent exposures and solvent-induced health effects, it is not practicable to give a comprehensive overview of all aspects of the literature. The following review will therefore focus on issues most relevant to the upcoming chapters of this thesis, specifically:

1. The uses of solvents in industry, including how they are classified, their general properties, and the industrial processes for which they are used.

2. Methodologies for assessing solvent exposures in occupational settings. Solvent exposures in the collision repair industry (and others where relevant) and their determinants are also reviewed, including the impact of engineering controls, administrative controls and other workplace factors on solvent levels.

3. Health effects associated with occupational solvent exposures, including historical perspectives on their toxicity, the pathways and processes by which they enter the body, the pharmacokinetics, and the mechanisms of solvent toxicity (with a focus on neurotoxicity). The neurochemical, neuropsychological and neurobehavioural effects of solvents, and other systemic effects (e.g. carcinogenicity) are also described.

4. The epidemiology of chronic solvent-induced neurotoxicity (CSN), including the methods and tools used to assess it, in particular the subjective and objective assessment of neurobehavioural/neuropsychological function. Data on the global

incidence and prevalence of CSN and CSE (including the occupational groups known to be at risk) are also reviewed.

5. The results of studies in vehicle collision repair and industrial spray painters which assessed potential solvent-related neurobehavioural and neuropsychological (cognitive) effects. Where relevant, studies in other solvent-exposed workers are also reviewed.

6. The effectiveness of personal protective equipment (PPE) at controlling solvent exposures and reducing solvent body burden in exposed workers, and the factors which influence its effectiveness.

2.1 Solvents – Uses, properties and classes

2.1.1 Properties and classes

Organic solvents have a broad range of chemical structures and physical properties, but share the common ability to dissolve or extract substances not usually soluble in water, such as fats, oils and resins (39). They may be grouped into general classes (table 2.1), although a number of chemicals usually described as solvents fall outside these definitions, for example carbon disulphide (10, 40). They are generally volatile at room temperature, of low molecular weight and many are soluble in water (in addition to fats, oils and resins). Despite their disparate chemical and physical properties, they are all lipophilic, and therefore have a propensity to affect the fat-rich tissues of the nervous system (39). Their effects on neurobehavioural and other bodily functions in exposed workers have been observed and studied for over a century; a brief history of this research is provided in section 2.3.

Table 2.1. Organic solvent classes and example compounds – industrial applications*

Group	Example compound	Occupational environments/industries	Primary industrial uses (occupational)
Hydrocarbons			
Aromatic	Toluene	Industrial and vehicle spray painting, rotogravure printing, leather tanning and production, production of pharmaceuticals	Degreasing and cleaning products, lacquers, paints, adhesives, paint thinners
	Styrene	Reinforced plastic, polymer and fiberglass manufacturing, boat building	resins, fillers, aviation fuel
	xylene	rubber and textile manufacturing, industrial and vehicle spray painting and printing industries, production of polyester	adhesives, inks , paints, lacquers, dyes, cements
Aliphatic	n-hexane	shoe making, rubber industry, Industrial and vehicle spray painting	paints, lacquers, adhesives, inks
Chlorinated	Trihloroethylene/ Perchloroethylene	automotive and engineering industries (degreasing), leather and textile industries	paint strippers, adhesives, metal/parts degreasers
	Methylene Chloride	paint and coating removal, automotive and engineering industries (degreasing)	paint strippers, heavy-duty degreasers, refrigerants, propellants
	Trichloroethane	paint and surface coating removal (dip tanks),leather and textile manufacturing, printing, electronics and fumigation industries	inks, paints, adhesives, cutting fluids, degreasers, insecticide
	Carbon tetrachloride	laboratory work, dry cleaning industry, production of refrigerants, fire fighting	refrigerants, degreasers, cleaners, fire suppressant
Esters	Ethyl acetate	electronics and beauty industries, painting	circuit board cleaners, nail varnish remover, paints, degreasers
Ketones	Methyl ethyl ketone/ Methyl Isobutyl ketone	surface coating, paint and coating removal, textile manufacturing	paints, dyes, cleaners, adhesives
Alcohols	propanol, butanol, ethanol, methanol	multiple	Degreasers, cleaners, general purpose solvents

*(Compiled from Wypych (41))

2.1.2 Industrial uses

Hundreds of millions of tons of organic solvents are produced each year globally and used extensively in a wide variety of domestic and industrial applications (table 2.1) (1, 13, 42). They are used in large quantities in the chemical, paint, plastic and rubber production and processing industries, and in a wide variety of industries that utilise the resultant chemicals and products. Specific industrial processes may require the use of a single solvent (43, 44), but for reasons of increased efficacy and wider-reaching application, they are predominantly used in mixtures (39). A range of occupational groups are at risk of exposure to solvents, including textile dyeing and processing workers, dry cleaners, printers, metal fitters and turners, floor layers and plumbers, and they are used in particularly large quantities as carriers for surface coatings in industrial, metal, construction and vehicle spray painting (table 2.1). Collision repair workers, which include vehicle spray painters and bodywork repair technicians, or 'panel beaters', are particularly at risk of elevated and sustained solvent exposures, both via inhalation and dermal absorption [39], as the vehicle refinishing process requires the use of large quantities of solvent mixes for preparation work and subsequent spraying of solvent-based paints.

2.2 Occupational solvent exposures

2.2.1 Exposure assessment methodologies

Exposure assessment

Assessment of solvent exposures in occupational settings is rarely a straightforward process, making it difficult to determine whether exposure is, or has been, 'sufficient' to cause symptoms of neurotoxicity (10). An assessment of historical and current solvent exposures can be made by questionnaire (administered to workers and employers), but retrospective assessment by recall of a person's lifetime exposure is prone to inaccuracies and errors in exposure estimation potentially resulting in bias (7). A retrospective assessment of employer records, job histories, trends in operating procedures and workplace hygiene records may be undertaken, provided these resources are available and are sufficiently detailed (40). However, this is rarely the case, particularly for small-to-medium sized enterprises with a lack of dedicated health and safety staff or resources (45, 46), and exposure monitoring is often not done.

Crude measures of lifetime exposure based on duration of employment (e.g. years of employment in an industry or job) may also result in misclassification, as a result of changes in exposure levels over time due to changes in the solvent-content of products, improved workplace practices and behaviours, and the improved effectiveness of engineering and administrative controls (47). Repeat on-site exposure monitoring, hygiene assessments and/or direct measurement of solvent body burden in workers (through serum, urine or other biological sampling) provides the most accurate indication of contemporary exposures, if the sampling methods and

protocols used are sufficiently sensitive and representative (48-50). However, for the reasons noted above, they are often unsuitable for the assessment of historical/cumulative exposures and, in the case of biological markers of exposure, are generally only able to assess exposure to individual solvents (40, 50-52).

On the basis of current (and historical where available) exposure monitoring data and retrospective exposure estimates, a cumulative exposure index can be developed and used to classify workers according to their exposure history. This may take the form of a job exposure matrix (JEM), where job or even task-specific exposures can be estimated and, using a workers detailed occupational history, provide an estimate of working life cumulative exposure (53-55). However, the validity of such measures/tools is highly dependent upon the quality of the data that has been used to develop them (56). As a result, a combination of methods is often employed, including evaluation by an exposure assessment expert/occupational hygienist, which is generally agreed to be the most accurate means of defining the cumulative exposure status of workers (55, 57). Expert assessment involves identifying the hazardous agent, and establishing the level of confidence that exposure will occur and the likely intensity of it (e.g. low, medium, highly-exposed). This is based on job title and work tasks performed, workers self-reported exposure, technical and scientific literature and historic hygiene assessment records related to the specific industry, discussions with industry representatives and specialists, and the expert's own expertise and perception (58). However, this approach is currently not feasible in New Zealand, due to the lack of prior studies and routine monitoring of occupational solvent exposures.

Airborne exposure sampling

Solvent levels in the work environment can be measured with ambient, static sampling or personal dosimetry, or a combination of these methods (described further below) (50). Samples may be collected over short periods to assess exposure levels during a specific task, or monitoring may be conducted over a full work-shift (50), allowing for comparison with the relevant regulatory exposure standards (discussed below).

A range of 'passive' and 'active' methods are available for sampling of airborne volatile compounds in the workplace (50). Passive dosimeters (a small capsule filled with activated carbon or other sorbent material) are worn by the worker, usually clipped to the upper chest, and the target compound is absorbed and concentrated on the sorbent medium by passive diffusion (50). The sample is then extracted by chemical or thermal desorption (see below) (59). From this, an 8 hour-TWA can be calculated (assuming measurements were collected during a full or close to a full work-shift), and corrected for sampling duration and sample recovery efficiency (50). Sorbent may also be packed into glass or stainless steel sampling tubes for active sampling, where air is drawn through the tube at a constant rate using a portable air pump. This method has the benefit of more accurately representing exposure by inhalation, as the volume of air sampled by a pump can be determined (from flow rate and sampling time), allowing for concentrations to be calculated for a given volume of sampled air (e.g. ppm, mg/m^3) (60).

A disadvantage of both passive and active sampling using a sorbent medium is that subsequent desorption of the sample and laboratory analyses is often time consuming

and expensive (61). The absorption and desorption properties of activated charcoal and other sorbent mediums (e.g. porous polymers) also vary by target compound, and some sorbents and associated desorption methods are unsuitable for certain solvents, particularly less stable ones (e.g. thermal desorption and cyclohexanone (62)) (63). 'Whole-air' sampling involving active sampling of air into an impermeable/semi-impermeable sampling bag or canister (usually stainless steel) largely avoids this issue (60, 61, 64). This method has a significant advantage of being able to collect, store and analyse samples without altering the concentration of the target compound, and is therefore not subject to the same issues regarding absorption speed and desorption efficiency associated with sorbent mediums (50, 61, 63). Whole air sampling systems are however bulkier, more complex and, particularly in the case of sampling bags, can suffer from problems with sample stability/longevity (63-65). Whole-air sampling is also a relatively new method, particularly to the field of occupational hygiene (64), with passive or active sorbent sampling being the primary method used to monitor occupational solvent exposures, including in the collision repair industry (17, 45, 66-69).

In addition to using different sampling devices, a variety of sampling strategies have been used in studies of solvent-exposed workers, making it difficult to compare airborne exposure levels between studies (70). For example, static monitoring of work stations has been used in some studies to quantify worker exposures, which may be less representative of actual exposure levels than personal dosimetry (where the sampler is worn by the worker) (71). Other studies have also monitored exposures during specific tasks (e.g. spray painting in/around the spray booth (72)) or for parts of

a work-shift, making it difficult to compare their findings with studies which have assessed full-shift exposures. Differences in the presentation of exposure monitoring data also make it difficult to compare results. For example, exposure data may be presented as arithmetic or geometric means with geometric means inherently representing a lower, more conservative estimate than arithmetic means (73).

Dermal exposure sampling methods

Due to the many potential pitfalls and impracticalities of dermal sampling, relatively few epidemiological studies of solvent exposed workers have included a direct assessment of dermal solvent exposures. A combination of airborne and biological exposure monitoring has more often been used instead, and dermal contributions estimated from these data (26, 74). A number of complex models have been developed for indirect estimation of dermal exposures, which allow for both current and historical dermal exposures to be estimated on the basis of airborne and biological monitoring data from multiple experimental, quasi-experimental and observational studies (25, 26).

A number of methods are available for the direct assessment of dermal exposures, including full body suits, sorbent (e.g. activated carbon) dermal patches (placed at specific locations around the body), removal or washing techniques (e.g. wiping of the skin after a worker has performed a task, washing of the hands in a liquid collection medium (e.g. methanol) and visualisation of exposure by fluorescent labelling of the product being sprayed/applied (75). To determine the quantity of an agent likely to be absorbed by the skin, a number of environmental and person-specific parameters

must be assessed, including exposure intensity and frequency, the surface area of skin exposed, and skin contact duration (24). One of the biggest issues with these methods is they have a tendency to overestimate exposure, as they measure the total mass of chemical deposited on the skin rather than the amount actually absorbed (25, 75). This is particularly relevant for solvents and spray painters, as a great deal of the volume deposited on the skin will evaporate before being absorbed (26). Also, as discussed in more detail in section 2.3.2, airborne solvent vapour is also absorbed dermally, and may contribute considerably to overall exposure (74), whereas few of the methods described above would be capable of sampling airborne vapours (e.g. removal/washing and visualisation techniques) (75).

Each dermal sampling method has advantages and disadvantages. For example, samples taken using sorbent patches can be used to proportionally estimate dermal exposure across the whole body; however, the lack of defined procedures for selecting sorbent materials, patch sizes or patch locations has led to considerable variability in the sampling strategies used between studies, limiting their comparability (25).

Biological monitoring

The relative contribution of both airborne and dermal exposures to overall exposure can be assessed though biological monitoring, which provides the most accurate direct indication of 'absorbed' solvent (76), i.e. the body burden of solvents (25, 26, 48, 77). The amount of 'unchanged' (not metabolised or otherwise biologically transformed)

solvent in serum and urine may be quantified, but more commonly the relative metabolite of the specific solvent is quantified, particularly in urine (48, 50). These metabolites are specific to their parent compound (e.g. hippuric acid, the urinary metabolite of toluene), which has implications for the monitoring of exposure to solvent mixtures. In particular, in this scenario, one component of the solvent mixture can be used as a marker of total solvent exposure, but only if the relative composition of the mixture being used by the worker is known (48).

Peak exposure sampling methods

Traditional sampling techniques such as sorbent dosimeters, charcoal tubes or whole-air samplers can be used to measure average exposures during specific job tasks, and then levels can be compared between tasks and, for example, to average levels measured over the whole work shift (28). This can give an indication of which tasks may be associated with the highest exposures, and those which contribute most to average exposure. However, they do not provide information about peak exposures, which may play a role in solvent-induced health effects (see chapter 3). To overcome this limitation, 'direct reading' instruments to monitor exposure in real or near real-time may be used, providing a more detailed indication of the frequency, intensity and duration of exposure peaks (78, 79). The instrument either logs data internally for extraction and analysis at a later stage, or exports it to an external device (e.g. a laptop computer) where the operator can both log the data and review it in real-time. In the case of solvents, a photo-ionisation detector, or PID is used (discussed in more detail in chapter 3). Video cameras can also be used to record the task being

performed, and the movements and behaviour of the worker. This allows for assessment of the characteristics of peak exposures, and identification of the tasks and processes they are associated with. This can, in turn, be used to target intervention strategies to reduce exposures (78). This technique is known as 'Video exposure monitoring' (VEM) (78), and was developed in Sweden in the 1980s under the name 'Picture Mixed Exposure' (PIMEX) (80) and in the US (VEM systems™) (81), and has since been further developed and used in research elsewhere (82-84). VEM has been used to assess peak exposures to solvents during spray painting of furniture (mixed solvents) (85), construction painting (mixed solvents) (86), surface coating of woodwork (mixed solvents and formaldehyde) (87), hospital and pharmaceutical laboratory work (toluene, ethyl ether, dichloromethane, chloroform, and benzene) (88, 89), fiberglass boat building (styrene) (90), vehicle refuelling (solvent mixtures) (91) and dry cleaning operations (trichloroethylene) (92). It has also been used to assess peak exposures to other hazardous agents, including wood dust (93), ultrafine particulates (94), noise (95) and ultraviolet radiation (96), amongst others (78). However, to the author's knowledge, it has not been used to assess peak solvent exposures in the vehicle collision repair industry.

Sample analysis

Gas chromatography mass spectroscopy (GC/MS) methods have traditionally been used to identify and quantify solvents in samples collected for occupational exposure monitoring (50, 52, 97-101), but liquid chromatography mass spectroscopy (LC-MS) may also be used (50). The process by which GC and LC/MS identify and quantify

different compounds in a sample have been described in detail elsewhere (102), and are outside the scope of this review. The particular procedure used depends upon the sampling method, and the resultant form of the analyte (substance to be analysed). Whole air samples can generally be introduced into a GC/MS instrument directly, but where solvents have been concentrated on a sorbent medium, (including passive badges and active tubes used for airborne sampling, and dermal patches, see above) the analyte needs to be extracted from the medium first (50, 60, 61). This is achieved either by thermal desorption, which produces a vapour phase analyte that can be analysed with GC/MS, or chemical extraction, often by desorption with carbon disulphide (63). Desorption with carbon disulphide produces a liquid analyte, which can (with some preparation) be introduced directly into an LC-MS instrument, or the vapour phase of the liquid analyte can be analysed using 'head-space' GC/MS (the liquid analyte is placed in a specialised head-space vial and a sample is drawn from the void above the surface of liquid) (103). Thermal desorption of solvents has proven superior in terms of recovery efficiency (see above) compared to extraction with carbon disulphide, but it is not suitable for use with all sorbent materials (e.g. some types of active carbon) (63).

The issue with traditional chromatography/MS analysis is that it is usually time consuming and expensive to conduct. This is at least in part due to the need for the instrument to be calibrated using high purity standards for each of the target compounds of interest (i.e. what is expected to be in the sample), and prior to each round of sample analysis (102). An alternative method, which is faster and cheaper, is selected ion-flow tube MS, or SIFT-MS (59, 104, 105). A SIFT-MS instrument does not

require calibration prior to each round of analysis; instead, data on reaction rate coefficients and ratios of products for the target compounds is held in a library on board the SYFT-MS instrument, (collated from the results of compound-specific validation studies (106-108)). Before sample analysis, a certified gas standard is used to confirm that the instrument-based parameters are standardised, and that the instrument is measuring the compounds in the certified standard correctly (59, 104). The compound-specific data library is then used to detect and quantify the target compounds in the sample. Although the limit of detection (LoD, the lowest concentration at which a substance can be distinguished from the absence of that substance (109)) using SIFT-MS may be higher than traditional GC or LC/MS methods, this can still be in the parts per trillion (ppt) range (104), which is likely to be adequate for risk assessment purposes in occupational settings (where exposure limits (see below) are generally in the tens of parts per million (ppm) range(110).

Biological samples (urine, blood/serum) can be analysed for either the metabolites of target compounds (e.g. hippuric acid, the primary urinary metabolite of toluene, can be quantified using simple visual absorption spectrophotometry (111)), or unchanged solvents using headspace GC/MS. Headspace GC/MS has been used successfully to identify and quantify levels of unchanged solvent in the urine of workers exposed to benzene, toluene, xylene and styrene, and has the added advantage of being able to identify and quantify levels of multiple solvents in a single sample (rather than with analysis of metabolites, which are specific to their parent compound, see section 2.3.2) (77, 111, 112). Analysis of unchanged solvents have also been shown to provide

a more accurate estimate body burden of solvents than urinalysis of metabolites (51, 77).

Workplace Exposure Standards

'Safe' exposure levels for the majority of hazardous agents encountered in the workplace have been set by various regulatory authorities and scientific advisory groups worldwide, and are referred to as workplace exposure standards (WES) (113), Threshold Limit Values (TLV) (110), Permissible Exposure Limits (PEL), or Occupational Exposure Limits (OEL) (114). These limits, which vary by country and regulatory/advisory group, are based on evidence from epidemiological, clinical and animal studies as to the level at which harm may occur; for example, an 8 hour TWA WES is defined as the level at which *nearly all workers* could be exposed (for 8-hours a day and 40 hours a week over an average working lifetime) without experiencing *significant* adverse health effects (110). Other important exposure limits include: 'ceiling' levels, - a maximum concentration that should not be exceeded, not even briefly; a short term exposure limit (STEL) – the maximum permissible exposure over a 15 minute period; and 'excursion' limits – these apply where no STEL is available for the specific agent, and are defined as an exposure of three-times the 8-hour TWA standard for 15 minutes (110, 114). In addition, the 'Additive Limit Value' (ALV) can be calculated for exposures involving multiple compounds. To calculate an ALV, a weight is assigned to each individual compound detected in the sample, based upon its relative workplace exposure standard (e.g. the American Conference of Industrial and Governmental Hygienists, Threshold Limit Values (ACGIH TLVs) (110)), and these

values are summed together, with an ALV >1 indicating that the exposure standard for that combination of compounds has been exceeded (110). Eight-hour TWAs and ALVs are most commonly reported In epidemiological studies of workers with low-level, long-term exposure to solvents, as 8-hour (i.e. a full work shift) thresholds are designed to protect the vast majority of workers from long-term health effects (110).

As discussed in detail later in this review, dermal exposures may contribute considerably to a workers body burden of solvents (and risk of symptoms) (25, 26). For that reason, the ACGIH add skin 'notations' for specific chemicals to their standards, including for solvents, which apply where exposure by the dermal route has the potential to contribute significantly to an individual's overall exposure (110). However, unlike airborne exposures, there are currently no workplace exposure standards for dermal exposure, due to difficulties with quantification of dermal uptake, a lack of standardised exposure assessment methods, and limited data regarding the health risks posed from dermal exposures (25, 115).

As discussed in chapter 4, short-term, high intensity peaks in solvent exposure may be important triggers in the development of neurobehavioural effects (27, 28, 116). Peak exposures may either contribute relatively little to full-shift average exposure, as has been observed with some solvents (117), or they may account for the majority of a workers daily exposure, as has been shown for other types of exposures in other industries (118). STELs and ceiling limits are most relevant to the control of peak exposures (50, 110), but peak exposure data are rarely collected routinely, or as part of epidemiological studies (27, 28, 116).

2.2.2 Solvent exposures in the vehicle collision repair industry

Assessments of global trends of occupational solvent exposures indicate a steady decline in levels across a range of industries over the past 40 years, most likely as a result of changes in product formulations, workplace conditions, worker behaviours and health and safety practices (13, 42, 119, 120). However, relatively few studies have assessed exposure levels in the collision repair industry, particularly in the past decade. As it is beyond the scope of this thesis to review the results of exposure monitoring conducted in all solvent-exposed workers, only results of personal airborne exposure monitoring from studies in the collision repair industry are shown in table 2.2.

Table 2.2. Results of solvent exposure monitoring in the vehicle collision repair industry

Study (date)	Number of samples	Sampling method/device (sorbent medium)	Average sample duration	Number of solvents measured	Mean (mixed) solvent level (ppm)	Percentage of relevant exposure standard (at the time of the study) - Additive limit value (ALV) ɣ
Hänninen, Eskelinen (72) (1976)	54	-	1 hour (task-based)	9	61.3	31.8
Elofsson, Gamberale (19) (1980)	106	-	not specified	12	62.3	30.0
De Medinilla and Espigares (121) (1988)	11	Active - tubes (activated carbon)	30 minutes (task-based)	18	117.0	160.0
Daniell, Stebbins (66) (1992)	137	Passive - dosimeters (activated carbon)	full-shift	2	16.4	8.4
Daniell, Stebbins (45) (1993)	67	Passive - dosimeters (activated carbon)	full-shift	6 (most prevalent)	33.2*	19.3*
Winder and Turner (122) (1992)	70	Active - tubes (activated carbon)	4-7 hours (full shift)	15	52.3	19.0
Moen and Hollund (21) (2000)	30	Active - tubes (activated carbon)	15 min - 5 hours (combination of task-based/full shift)	12	13.7	-
Böckelmann, Darius (17) (2002)	-	Passive - dosimeters (activated carbon)	3-5 hours (full-shift)	6	4.6	-
Bråtveit, Hollund (100) (2004) (solvent-based workshops/ water-based workshops)	51/28	Active - tubes (activated carbon)	6-8 hours (full-shift)	10	2.3/0.84	19.0/7.0
Vitali, Ensabella (68) (2006)	8	Passive - dosimeters (activated carbon)	4-5.5 hours (full-shift)	5	22.5	<100
Caro and Gallego (48) (2009)	6	Active - tubes ('Tentax TA' polymer resin)	3 hours (full-shift)	18	20.2	-

* Includes exposed combination workers (workers who performed mostly panel beating, but also some spray painting, 'low exposure') painters assistants ('medium') and spray painters ('high')

ɣ Exposure indices for total summed solvent levels. These were calculated by dividing the concentration of each compound detected in the sample by its relevant exposure standard, and summing the resultant values together (values taken from the manuscripts for each study, therefore the method used to calculate the ALV varies between studies, e.g. due to changes in exposure standards over time). If this number exceeds 1, it is deemed that the exposure standard has been exceeded for the mixture.

As shown in table 2.2 average mixed solvent exposure levels in earlier studies were generally higher than in later studies, which is consistent with suggestions that occupational solvent exposures may have declined globally (13, 42, 119). However, due to a lack of studies particularly in the past decade, a decline in exposures has not been confirmed. Also, suggestions of a decline in occupational exposures are based primarily on European data, and may therefore not be applicable to the industry in New Zealand, and other countries where workplace conditions differ (13).

2.2.3 Determinants of exposure in the collision repair industry

Although generic determinants of airborne exposures such as job tasks, environmental conditions, workplace practices and equipment characteristics have been reported for some exposures (123), most are unique to specific industries and sometimes individual workplaces (124-131). In the collision repair industry no studies have focused on the determinants of solvent exposures, and only a small number of contemporary studies have included any assessment of solvent exposures (144). In contrast, the determinants of exposure to isocyanates (used in most modern paint formulations (132, 133)) have more frequently been studied, as have determinants of other health hazards (e.g. grinding dust, noise) (14, 15, 100, 122, 134-143). Because of some similarities with isocyanate exposure in this industry, findings of studies on the determinants of isocyanate may shed some light on exposure determinants of solvents. Studies in the US collision repair industry (14, 136) identified process, personnel, business and emission control factors as significant determinants of

isocyanate exposures, with spray painting, particularly of clear and sealant coats, showing higher isocyanate exposures (136) than mixing paint, sanding vehicle bodywork, or other non-spraying work conducted in the vicinity of spray operations (14). The quantity of paint sprayed was also a significant exposure determinant as were personnel and economic factors such as the number of painters at work, the shop size, the number of cars painted per month, and the shops annual income. Engineering controls and workplace behaviours such as use of a spray booth, the type of spray booth used and the proximity of non-spraying work from spray painting were also associated with isocyanate exposure. Although, as noted above, the determinants of isocyanate exposures are likely to be similar to those of solvents (as they are both used in spray paint formulations), differences in the use of the two in collision repair work (e.g. solvent-based cleaning and degreasing products used for preparing vehicle bodywork do not contain isocyanates), and their disparate chemical properties (particularly volatility (133)) means this may not always be the case. Also, as a result of changes that are likely to have occurred in this industry since these studies were conducted (described below), exposure determinants may have changed, both for isocyanates and solvents, and results from previous studies may no longer be relevant to contemporary collision repair workshops.

Although not confirmed (see above), solvent exposures in this industry may have declined over the past 10 years (13). If true, technological advances in the products, equipment and exposure control measures used may be partially responsible. These include advances in paint technology, allowing for the development of lower-solvent content paint formulations and waterborne paints (144), both of which have been

associated with significantly lower airborne solvent exposures (100). The first waterborne colour paints for automotive use were introduced in the 1980s, basecoats in the 1990s, and in more recent years clear-coat (final, clear sealing coat applied after colour paint) formulations have been developed. Apart from reducing solvent exposure, they have a number of practical advantages over solvent-based formulations, including their ability to be thinned for application with water, and the ease with which spraying equipment can be cleaned (144).

Engineering control technologies have also improved, and their use has become more consistent over the past decade, not only because of increased pressure on the control of workplace exposures and regulation of environmental emissions (25, 144), but also, specifically for the vehicle repair industry, the higher standard and consistency of paint finish they provide (139, 145). Evidence also suggests they are effective in reducing worker exposures (13, 119, 146). Local exhaust ventilation (where point extraction is positioned in close proximity to the emission source), has been shown to be effective in the reduction of both local and general exposure levels of various airborne contaminants, including solvents (125, 147-149). In the collision repair industry, ventilation is typically in the form of spray booths, which have been shown to be highly effective at controlling exposures (particularly 'Down-draft' style booths, discussed in detail in chapter 3)(139) (14, 140), mechanical ventilation/extraction of specific work areas (e.g. the paint storage and mixing room) and the main workspace, with passive ventilation in the form of open roller doors and windows (14). Local exhaust ventilation is generally in the form of 'on tool' extraction, with extraction ducted directly into equipment cleaning machines (140, 142).

2.3 Health effects associated with occupational solvent exposures

2.3.1 A historical perspective

The earliest reports of the risks posed by occupational exposure to solvents were made by a French physician Auguste Delpech who published two papers in 1856 (3) and 1863 (150) describing his observations of the health of workers extensively exposed to carbon disulphide in the rubber processing and manufacturing industry (37). He noted that carbon disulphide exposure could lead to effects on every bodily system, but psychological symptoms were amongst those most commonly reported:

"Troubles intellectuels- Affaiblissement de la memoire; vague et confusion dan les idees. Access alternatifs de gaiete folle et d'emportement maniaque. Insomnie; agitation plus ou moins vives; reives penibles; reveils en sursant la nuit. Lejour, somnolence, abattement, etat de torpeur et d'inertie."

("Intellectual disorders- Impairment of memory; vagueness and confusion of ideas. Alternation between crazy happiness and maniacal outbursts. Insomnia; variable state of agitation; distressing dreams; waking up at night. During the daytime; drowsiness, despondency, state of torpor and inertia").

Delpech described a profile of both acute and chronic symptoms among exposed workers, including persistent headaches, dizziness, itching, fatigue, insomnia and in some cases the development of analgesia, loss of sensation in the extremities, and essential tremor and muscular atrophy (37). He also noted that the urine and breath

of workers smelt strongly of carbon disulphide, and unless removed from exposure individuals were shown to become increasingly anaemic and frail. As a cure he advocated removal of workers from exposure and a life of “sobriety”. He noted the commonality of these symptoms with those of exposure to other agents such as alcohol and lead (150), but argued that many were unique to carbon disulphide poisoning and went on to define a syndrome labelled “carbon disulphide neurosis” (37). Delpech also discussed the importance of duration of exposure and age in the development of symptoms, and observed that once removed from exposure, workers usually recovered fully from acute symptoms, but that continued exposure could lead to permanent impairments (3). From this, he theorised that there were two stages of carbon disulphide neurotoxicity, which would now be describe as ‘acute’ and ‘chronic’. He also made recommendations for the prevention of carbon disulphide poisoning, including improvement of ventilation in factories and separation of the various production processes (to reduce clustering of emission sources).

In the 1880s both Charcot (151) and Marie (152) built on the work of Delpech, further describing the effects of carbon disulphide exposure and theorising as to the neurobehavioural and neurological domains affected, and mechanisms involved. They argued that the “neuroses” (at the time meaning any symptom or disorder of the nervous system that could not be explained physiologically) observed in exposed workers were not unique to carbon disulphide exposure (as argued by Delpech), but were simply “vulgar neuroses” common to any “hysteria” caused by intoxication or trauma (37).

In the early 1900's Jump and Cruice (153) suggested that not all the effects of carbon disulphide poisoning were the result of "hysteria" (i.e. psychological disturbance), as suggested by Delpech and Charcot, rather some were evidence of peripheral neuropathy (37).

In the 1930s German physician Karl Bonhoeffer described neurobehavioural symptoms in several cases of carbon disulphide poisoning (reviewed in (37)), detailing a syndrome of sensory deficits indicative of peripheral neuropathy and a "toxic psychosis", including memory impairment, mood lability and episodes of reduced consciousness, which occurred after repeated exposures. He noted that in workers with a hereditary predisposition, exposure could hasten the onset of a mental disorder (e.g. schizophrenia) (37).

These early studies identified many issues which could be seen as integral to contemporary research of occupational solvent exposures, including: the importance of differentiating between acute and chronic effects and the functional domains affected, the impact of cumulative exposure and exposure intensity on disease severity and long-term prognosis, the need to remove affected workers from exposure as soon as possible, and the importance of controlling exposures in the workplace through identification of exposure determinants.

By the 1940s and 50s advances in occupational medicine, epidemiology, psychology and toxicology had allowed for greater characterisation of the neurotoxic effects of a wider range of industrial solvents. For example, Forssman (154) and Grandjean (155) showed that workers exposed to trichloroethylene had an increased risk of symptoms of psychiatric disturbance, and amongst some workers a diagnosis of "psycho-organic

syndrome" was made (155). However, it was not until the mid-1960s and the work of the Finnish psychologist Helena Hänninen that the potential for solvent-related effects to become chronic and irreversible began to be more fully understood. Also, there was an increased understanding that workers from a variety of industries exposed to a wide range of solvents may be at risk of solvent-induced neurotoxicity. Hänninen suggested there was an association between sustained exposure at levels lower than those observed in earlier studies (3, 150, 152, 153) and the development of chronic, irreversible central nervous system (CNS) effects (5). Further studies in the mid-1970s by Hänninen and others (72, 156) showed exposure to mixtures of organic solvents (the form in which solvents are most commonly used by workers in industrial settings (39)) could result in similar effects. On the basis of these studies a new occupational syndrome, "painters' syndrome" or "organic solvent syndrome" was proposed (10). Improved clinical and experimental data on the mechanisms by which solvents act on the brain and nervous system added further credibility to the existence of such a syndrome (40); these mechanisms, along with how solvents enter and are processed in the body are briefly described in the following sections.

2.3.2 Mechanisms of solvent absorption and neurotoxicity

The potential toxicity of solvents depends on many factors, including how they are taken up by the body and transported to target organs, how they are bio-transformed and the relative toxicity of their metabolites, the mechanism by which they cause damage or affect function in target tissues, and the speed and efficiency with which they are able to be excreted by the body (49, 157-159).

As compounds with small molecular structures which are soluble in water and/or lipids, solvents are soluble in both blood and the soft tissues of the body (49). They are also usually able to readily migrate across biological membranes, and can thus be absorbed through the mucosal membranes (nasal passages and lungs), pass through the skin, and be absorbed via the digestive system when ingested (66). The same property allows them, once in the body, to migrate across the blood-brain barrier (a membrane which separates circulating blood from extracellular cerebrospinal fluid (160)) and be readily taken up by the lipid-rich tissues of the brain and nervous systems (49).

Pharmacokinetics

Lung Uptake

As the majority of solvents are volatile it is generally agreed that absorption of solvent vapour through the lungs by inhalation is the main pathway of exposure (66). Factors that affect the extent of uptake through inhalation are the concentration of solvent in the air inspired, the rate of alveolar ventilation, the blood/alveolar air solvent

gradient, the rate of blood perfusion through the lungs (i.e. cardiac output) and the duration of exposure (161).

Skin uptake

Absorption of solvents through the skin is a more complex process, with more modifying factors (26, 74), although it represents a significant potential route of exposure (25, 75). Solvents are absorbed primarily though passive diffusion, the rate of which is dependent upon the location and surface area of the exposed site, and factors specific to that site, such as thickness of the skin and skin condition (i.e. skin barrier function), blood perfusion and temperature (161). Penetration of the skin is also related to the physical properties of the solvent itself. Those that have been shown to pass through the skin readily include toluene, methyl ethyl ketone, and butanol (25). The rate of skin absorption of one solvent may also be affected by the presence of another, which is highly relevant where solvents are primarily used in mixtures, which as mentioned previously is common to many industrial processes, including the collision repair industry (16, 24, 39, 67, 69, 162).

Although dermal absorption may contribute less to total body burden of solvent compared to uptake from inhalation, where controls targeted at airborne exposures are in place, it has been estimated that it may contribute up to 50% of the body burden (25, 30, 74). This contribution may be vastly increased where large quantities of liquid solvent are deposited on the skin, through either spillage or from direct cleaning of soiled body parts (particularly the hands), by immersion, or by direct

application (26). In contrast, where liquid solvent exposure control measures are effective, workers are likely to be exposed to higher volumes of airborne vapour than liquid solvent, especially where the solvents being used are (as is usually the case) highly volatile and the industrial process requires aerosolisation of solvents (e.g. spray painting) (74). Dermal uptake of solvent vapour, although a slower process than dermal deposition of liquid, may therefore comprise the majority of a workers dermal exposure (74). The same environmental factors that affect the dermal uptake of liquid solvent affect vapour absorption (74, 163).

Factors affecting uptake rate

Physical work load is associated with increased uptake of solvents through higher ventilation rate and cardiac output, and the associated increase in volume of inhaled solvent vapour and higher pulmonary and bronchial blood flow leads to a greater perfusion of solvent throughout the tissues of the body (161). Certain work tasks that require strenuous physical activity may result in solvent uptake up to 5 times higher than when at rest, and these tasks may also be those that are associated with release of solvents, increasing solvent uptake further (161, 164). Factors such as clearance rate from the lungs, blood solubility of the solvent and the rate at which the solvent is metabolised interact in a complex way with uptake rate. For example, uptake of highly soluble and quickly metabolised solvents such as xylene and styrene may be limited almost entirely by ventilation rate of the lungs, whereas the uptake of less soluble solvents (e.g. methylene chloride) may be limited by removal of solvent from the lungs, or transformation and subsequent excretion (161).

Metabolism

The metabolism of solvents, primarily in the liver, is a complex process involving a number of intermediate metabolites (157). Different solvents follow different metabolic pathways, resulting in the formation of a range of potentially cyto- and neurotoxic intermediates, which may play a major role in the toxicity of solvents (39). For example, toluene is first metabolised by the liver into benzyl alcohol, which in turn is oxidised further to benzoic acid, which, through conjugation with glycol, is converted to hippuric acid and then excreted in urine (165). A small proportion of toluene is also converted directly to o- and p-cresol, much of which is excreted unchanged in urine, but also in glucuronide or sulphate-conjugated form. Along with unchanged toluene, these metabolites may also be cytotoxic and/or neurotoxic (161).

In addition, these metabolic pathways may be influenced by the presence of other compounds, including other solvents though concurrent exposure (e.g. *o, m,* or *p* – xylene), and prescribed or recreational drugs (158). These interactions are complex, making assessment of pharmacokinetics in the occupational setting difficult. For example, individual solvents in a mixture may simply be additive, or augment or facilitate the toxicity of one another through synergistic or potentiating mechanisms, and may inhibit or proliferate the formation of respective metabolites (16, 166, 167). An important example is concurrent exposure to ethanol and toluene, which increases systemic toluene concentrations and suppresses the conversion of toluene to hippuric acid (161, 168, 169). Another example is concurrent exposure of methylene chloride and aromatic hydrocarbons (e.g. benzene, toluene, xylene), which can inhibit the metabolism of methylene chloride (170), or if exposure to aromatic hydrocarbons

occur 20-48 hours prior to methylene chloride exposure, potentiate its metabolism, leading to elevated carboxyhaemoglobin levels, and potentially acute hypoxia (171).

Effects on the central nervous system

The mechanisms by which solvents interact with the structure and function of nerve tissue at the macro and micro level are still not fully understood (161). However, animal models (168, 172) and some studies in humans (particularly involving persons who intentionally inhaled solvents for recreational purposes (173, 174) and individuals diagnosed with CSE (7, 175-177)) have provided insight into the neurochemical, neurophysiological, and cognitive effects of solvents. These are discussed briefly below.

Neurochemical changes

Solvents have been shown to: interfere with the chemical structure of cellular membranes and the mechanisms by which molecules are transported across them; cause cellular component damage (i.e. destruction of DNA, RNA and mitochondria) through encouragement of the production of reactive oxygen species (49), leading to nerve cell death through oxidative stress (157); and interact with ion channel systems and neurotransmitters (178). In addition, exposure to methanol, toluene or solvent mixtures has been associated with Parkinsonian symptoms in cases of CSE (e.g. resting tremor, reflex impairments), which implies interference with functioning of the

dopamine system (179). This interference is also implicated in relation to reduction in olfactory function, along with direct effects on neuroepithelial tissues (179-181).

Neurophysiological findings

Long-term exposure to solvents may also result in neuroanatomical damage to the brain through destruction of white matter, followed by atrophy in the cerebrum and cerebellum, all of which have been noted in cases of CSE (182). At the cellular level, demyelination is usually seen, along with other evidence of abnormal cell function. More widespread changes such as white matter lesions in the thalamus and basal ganglia can occur, along with abnormal nerve signalling in the brainstem suggestive of diffuse cranial nerve demyelination (182). However, findings of electroencephalographic assessments of sensory function using evoked potentials (i.e. measurement of electrical activity in the brain and nervous system by stimulation) have generally been inconclusive in studies of suspected or confirmed cases of CSE (6-8) and solvent-exposed workers (19, 156, 183, 184), with results showing normal, increased and decreased evoked response magnitudes (10, 184).

2.3.3 Neurotoxicity and other health effects of solvents

Solvent exposure may result in a range of systemic effects, including organ damage and carcinogenesis. As the focus of this thesis is on the neurotoxicity of occupational solvent exposures, the following section of this review will focus on these effects, but will also include a brief description of effects in other target organs and systems.

Acute solvent-induced neurotoxicity

Symptoms associated with acute exposure to solvents are well documented (185-187) and include irritation of the mucosal membranes (rhinitis, sore/itchy eyes, etc.) (99, 188), nausea, dizziness, feelings of intoxication and headache (21, 39). The transient effects of solvents on brain chemistry are largely responsible for these acute symptoms, and are unlikely to reflect actual neurotoxic damage. On the other hand, damage to the CNS and peripheral nervous system (PNS) and an increased risk of permanent and evident neurological damage has been associated with one-off incidents of extremely high exposure, as well as low-level exposures over a period of years to decades (10). These chronic effects are the focus of this thesis, and are described below.

Chronic solvent-induced neurotoxicity

In 1985, two working groups, one from the World Health Organization (WHO) (189) and one convened in Raleigh, North Carolina, USA ("Workshop on neurobehavioral

effects of solvents", (190)) developed clinical diagnostic and disease stage criteria for CSN. Both WHO (189) and the Raleigh group (190) defined three clear stages of disease progression (table 2.3), but differed on some criteria (16, 189-191). The first type (Type I or 1) includes subjective symptoms indicating effects on mood, behavioural control, energy and memory and concentration, but no evidence of objectively measured neuropsychological dysfunction; these will resolve upon cessation of exposure. The second (Type II or 2A and 2B) expands to include sustained changes in mood, memory, learning capacity, energy, attention and psychomotor performance (Type II and 2A) and may include impairments of intellectual capacity (Type 2b); effects may be reversible with sufficient recovery time (type II and 2a) or only partially reversible (type 2b). The third (type 'III' or '3') includes the same impairments as the second stage but more pronounced, in addition to diffuse impairments in memory and intellectual capacity indicating clear, clinically significant encephalopathy; effects are usually irreversible but remain stable with cessation of exposure, and may result in a diagnosis of CSE (8).

Despite the WHO and Raleigh criteria having been available for many years, and the large evidence-base relating to the development of chronic neurotoxic effects with occupational exposure to solvents, there is still no universally accepted or applied criteria for the clinical assessment of CSN, or diagnosis of CSE (2, 10, 191).

Cognitive effects

The neurocognitive functions most often affected in cases of CSE and workers occupationally exposed to solvents are associated with memory, especially working memory, processing speed, motor function and aspects of attention (16). Activation of areas of the pre-frontal cortex not typically used when performing working memory tasks have been observed in workers exposed to solvents, which indicates compensation for neural damage (184). Further effects on neurone function and subsequent reductions in dopamine production have been shown to effect the normal transmission of information through relevant brain circuitry, and in turn affect psychomotor speed and other associated functions. Reduced dopamine receptor functioning may also lead to problems with attention and cognitive flexibility (10, 179, 182). These outcomes in combination have led to suggestions that solvents may accelerate the rate of cognitive decline that results from normal ageing (192, 193).

Table 2.3. WHO and Raleigh Criteria for classification of solvent-induced effects on the central and peripheral nervous systems (adapted from van der Hoek, Verberk (191))

WHO Criteria				Raleigh Criteria	
Pathophysiology	Course	Manifestations	CNS function deficits	Category	Effects
Unclear	Days to weeks, no long-term effects	Mood disturbances, behavioural control, lack of energy and memory and concentration problems	None	Type 1: symptoms only Symptoms Course Cognitive deficits	 non-specific symptoms; fatigue, memory impairment, difficulty in concentration, lack of initiative Reversible if exposure discontinued No objective evidence of neuropsychiatric dysfunction
Unclear	gradual onset over weeks to months, reversibility questionable	Sustained changes: fatigue, mood disturbances, memory complaints, attention/concentration difficulties	psychomotor performance (speed, attention, dexterity), short-term memory	Type 2a: Sustained personality and mood change Symptoms	 marked and sustained change in personality, fatigue, mood lability, impulse control, lack of drive/motivation
Unclear: often associated with CNS damage	gradual onset (indefinite), usually irreversible but stable with cessation of exposure	Loss of intellectual capacity, memory impairment, impaired social and occupational functionality, issues with judgment and abstract thinking, personality change, other disturbances suggestive of cortical dysfunction.	Diffuse cognitive impairments similar to type II but more pronounced, some neurological deficits, abnormal nerve conduction, electromyographical and/or neuroradiological findings.	Type 2a: Impairment of intellectual function Symptoms Cognitive deficits Neurological findings Reversibility Type 3: Dementia Symptoms Neurological deficits Reversibility	 difficulty in concentration (attention), impaired memory, decreased learning capacity Symptoms are accompanied by objective evidence of dysfunction Potentially minor neurological signs Effects may be only partially reversible Marked global deterioration in intellect and memory Often accompanied by neurological signs and neuroradiological abnormalities Poor reversibility at best, but no further progression upon cessation of exposure.

Other health effects

Hepatotoxicity

The liver is the primary organ involved in metabolising potential toxins and is therefore a target organ for many solvents (194). The main agents responsible for liver damage are the toxic metabolites produced during the metabolism of potentially hepatotoxic solvents (e.g. trichloroethylene, xylene and toluene) (157, 195-198). The mechanisms involved include alterations in liver cell function, cell death, interruption of bile flow and damage to the bile duct by excreted toxic metabolites (157, 194, 199, 200). Oxidative stress is also implicated in the development of recurrent fatty liver disease (194, 200). Effects on liver function have been reported in workers occupationally exposed to solvent mixtures (101, 158, 195, 201), but in general very little is known about the incidence or prevalence of occupational solvent-induced hepatotoxicity (194).

Carcinogenicity

According to the classifications of the International Agency for Research on Cancer (IARC), a number of solvents are carcinogenic (Group 1 carcinogens), probably carcinogenic (group 2a) and possibly carcinogenic to humans (group 2b). Details of their carcinogenic classification and that of other relevant solvents are shown in table 2.5. Solvent carcinogenicity is mediated primarily through oxidative stress and resultant cytotoxicity in target organs including the liver, kidneys and lungs (202). An

increased risk of various lymphohematopoietic cancers has also been observed, including various lymphoma subtypes (202-204).

Table 2.4. IARC carcinogenicity classification of various industrial solvents (adapted from Lynge, Anttila (202))

	Animal carcinogenicity		Human Carcinogenicity			
Solvent	**Target organs**	**IARC evaluation[1]**	**Target organs**	**IARC evaluation[1]**	**IARC Group[2]**	**Year of evaluation**
Benzene	liver, kidney, bone marrow	S	Leukaemia	S	1	In preparation
Trichloroethylene	liver, kidney, lung	S	liver, biliary tract, non-Hodgkin's lymphoma	L	1	2014
1, 1, 1 - Trichloroethane		I		I	3	1999
tetrachloroethylene	liver, bone marrow	S	Oesophagus, cervix, non-Hodgkin's lymphoma, bladder	L	2A	2014
methylene chloride	liver, lung	S	biliary tract, non-Hodgkin's lymphoma	L	2A	2017
carbon tetrachloride	liver	S	non-Hodgkin's lymphoma	I	2B	
chloroform	liver, kidney	S		I	2B	1999
toluene		L		I	3	1999
xylene		I		I	3	1999
styrene	Lung	L		L	2B	2002

[1] Evaluation by the International Agency for Research on Cancer – S = Sufficient, L = Limited and I = Inadequate evidence

[2] 1= carcinogenic to humans, 2A = probably carcinogenic to humans, 2B = possibly carcinogenic to humans, and 3 = not classifiable as carcinogenic to humans

Other target organs and tissues

Increased risks of reproductive effects have been observed in solvent-exposed workers and their offspring (205), including spontaneous abortion (206, 207), congenital malformations (208), and preeclampsia (209) with maternal exposures, and low birth weight (210) and anencephaly (211) with paternal exposures. An increased risk of renal diseases such as glomerulonephritis have also been reported (212, 213), along with cardiopulmonary effects, including exacerbation and development of reactive airway disorders, coronary artery disease and cardiac arrhythmia (214-216).

The association between occupational solvent exposure and skin diseases (e.g. dermatitis) is also well recognised (217, 218).

Solvents have also been shown to affect central auditory function, largely through damage to the outer hair cells of the cochlear (219). Studies have shown a higher prevalence of hearing loss amongst solvent-exposed workers (compared to unexposed workers), including those exposed to carbon disulphide (220), styrene (221), toluene (222) and ethyl benzene (223). Also, solvents have been shown to potentiate the ototoxicity of noise in both humans and animals in a synergistic manner, and at sound pressures not normally associated with noise-induced hearing loss (220, 221).

2.3.4 Epidemiology of chronic solvent-induced neurotoxicity

The following section includes a description of the methods used to assess CSN in occupational epidemiological studies, a brief review of data on global incidence and prevalence of CSN/CSE, and a review of population-based studies which focused on vehicle collision repair workers and industrial spray painters.

Methods for assessing solvent-induced neurotoxicity in epidemiological studies

A small number of epidemiological studies have included assessments of various neurological and neurophysiological outcomes, including nerve conduction velocity tests, computer-aided brain tomography (CAT) scans and neuroradiological and magnetic resonance imaging (MRI) investigations (19, 156, 183, 184). However, as discussed above (section 2.3.3), findings from these assessments have been somewhat inconclusive, or have correlated poorly with symptomatology (10, 183, 184). These tests are also complex and time consuming to conduct (184), and therefore generally impractical for use in epidemiological studies involving larger samples of workers (10). Instead, self-reported symptom questionnaires and tests of cognitive performance have generally formed the basis of assessments applied as part of epidemiological studies in solvent-exposed workers (16, 70). A number of subjective and objective testing platforms and individual tests have been developed or adapted from existing tests to assess the spectrum of psychiatric, cognitive and psychomotor functions that may be affected by neurotoxins (8, 16, 49, 191). These are reviewed briefly below.

Assessment of Subjective symptoms

Earlier studies in workers exposed to solvents often assessed self-reported symptoms using a variable combination of questions covering neurobehavioural functions shown or believed to be affected by solvents (4, 72, 155). As understanding of 'typical' symptom profiles improved, these question batteries were refined, improving their validity and applicability across different occupational groups (224). A number of questionnaires have been developed since these earlier studies in response to the need for a defined set of validated questions that can be applied in a variety of settings, facilitating comparisons between studies (224). One of the earlier questionnaires was the Swedish Questionnaire 16 (Q16), which was originally developed in the 1980s for monitoring early neurobehavioural effects in workers occupationally exposed to solvents (225), but has also been used to assess the effects of other neurotoxic agents (226, 227). The questionnaire consists of a set of 16 items which require simple yes/no answers and is easily administered and understood. The ease of question interpretation and the reliability and validity of the questionnaire has been assessed in depth (228, 229). It has proven somewhat useful in assessing the extent of symptoms of neurotoxicity, including progression over time/with increasing cumulative exposure, but is generally agreed to have limited sensitivity and specificity (228-230). Q16 was used extensively up until the early 1990's, but has been largely replaced by the EUROQUEST questionnaire (231, 232).

The EUROQUEST, developed by the EURONEST collaborative network in the early 1990's is a more extensive questionnaire consisting of 59 core items covering a range of neurobehavioural domains (231, 233). These include: neurological disturbances

(e.g. numbness and tingling in the extremities, loss of sensation, dropping things unintentionally, etc.), mood lability (irritability, shortness of temper, mood swings, lack of drive or enthusiasm) , psychosomatic disturbances (nausea, dizziness, stomach cramps, and other non-specific symptoms), immediate and long-term memory problems (having to write notes to remember things, difficulty with remembering names and dates, forgetting what you were about to say or do, having to go back to check things, etc.), concentration difficulties (feelings of confusion when concentrating, daydreaming, etc.), fatigue (falling asleep when not in bed, lack of energy, etc.) and sleep disturbance (trouble falling asleep, waking up too early, etc.), as well as a brief section covering acute and irritant symptoms (5 items). Additional questions on anxiety (6 items) and self-reported general health and wellbeing (4 items) are also included to assess personality traits, which may lead workers to over or under-report symptoms (234). Experimentally it has proven sensitive and specific in the differentiation between cases and non-cases of CSE (175) when validated against clinical criteria. It is also effective in the detection of early symptoms of neurotoxicity in solvent-exposed workers (175, 231-233).

A number of other general questionnaires have been developed, including the German Psychologisch-Neurologischer Fragebogen (Psychological-Neurological Questionnaire, PNF)(235) the Profile of Mood States (POMS) and the Dutch Neurotoxic Symptom Checklist-60 (NSC-60) (236), all of which have been used in epidemiological studies of solvent-exposed workers (43, 237-239). The PNF includes questions covering similar functional domains to the EUROQUEST, but is targeted at German-speaking populations. The NSC-60 also covers similar domains, but is less

comprehensive than the EUROQUEST (224). The POMS also covers some of the same domains as the EUROQUEST, but is primarily focused on assessing mood states (e.g. tension and anxiety, anger and hostility, etc. (237)).

Assessment of neuropsychological function

In addition to subjective symptom questionnaires, objective measures of neuropsychological/cognitive performance have been used to assess solvent-related effects since the 1970's (16). Clinicians and researchers have access to a large repertoire of tests developed over the last century covering a wide variety of nervous-system functions. A 1990 review by Anger (240) of 185 occupational epidemiological studies identified over 250 separate tests which had been administered individually or as part of a test battery. A more recent meta-analysis by Meyer-Baron, Blaszkewicz (16), which focused on studies of neurobehavioural performance in solvent exposed workers was able to analyse forty-eight separate test variables across the 46 studies included. Due to the complicated nature of the nervous system and the variety of functions it is responsible for, a set, or battery, of neuropsychological tests is most commonly applied, in order to gauge potential effects across multiple functional domains (241).

Test batteries developed since the 1970's are generally applicable to the investigation of neurotoxicity associated with multiple neurotoxic agents, although they are often adapted by including or excluding specific tests. Test selection is based on a review of the toxicological and epidemiological literature relative to the agent. A description of

the individual tests most widely used for the assessment of possible solvent-induced effects, and the functional areas they assess, are shown in table 2.4. Broadly speaking, these tests cover the domains of attention (concentration), construction, concept formation, reasoning, memory and motor performance (motor speed and dexterity) (16), with some tests being sensitive to changes in more than one domain (e.g. Trails A and B assess aspects of both visual attention and reaction time (242)).

Table 2.5. Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Attention			
	Simple reaction time	Measures simple reaction time, general alertness and motor speed through revealing a known stimulus at a known position to produce a known response, but at an unknown time.	Blackburn and Benton (243)
	Digit span (forward and backward, sum or difference between forwards/backwards)	Measures attention and immediate memory through delivery of a random sequence of numbers which must then be recalled accurately, both in the order delivered (forward) and in reverse (backwards).	Wechsler (244), Wechsler (245)
	Digit symbol	Measures attention and processing speed. Test consists of number/symbol pairs, followed by a list of symbols. The participant must write down the corresponding digit underneath each symbol in the list as quickly as possible. The number of correct digits in a defined time (e.g. in 90 sec.) is measured.	Smith (246)
	D2 Test	Measures selective and sustained attention. The participant is given a stimulus sheet with the letter "d" placed randomly amongst other false targets (the letter "p") in a line. They must cross out all the letter d's on the line with two marks of any kind as quickly as possible. After a maximum of 20 seconds they are prompted to move to another line and repeat the task.	Brickenkamp (247)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Attention			
	Trail making A and B	Measures visual attention/task switching. The test consists of two parts, for the first part (part A) the participant must connect a series of numbered dots (1-25) as quickly and accurately as possible. The second part (part B) includes a set of both numbered dots (1-13) and dots with letters of the alphabet (A-L) which the participant must connect, in order, alternating between the two sets (1-A-2-B-3-C etc.).	Reitan and Wolfson (242)
	STROOP Colour word (word score, colour score, colour/word score, interference, errors)	Measures attention with interference and reaction time. Subjects are required to read aloud three different lists as quickly as possible. The first is a list of colour-words (e.g. red, blue, green) printed in black ink, the second is a series of different colour patches (red blue or green ink), and the third is colour-words printed in an inconsistent colour ink (e.g. the word "red" is printed in green ink). For the third task participants must name the colour of the ink instead of reading the word. Scoring is based in the number of correct responses uttered in a set time (e.g. 45 seconds).	Golden (248), Scarpina and Tagini (249), Stroop (250)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Attention			
	Switching attention (side, direct and time)	Measures 'executive' function. Participants are required to switch between performing multiple different individual tasks. Participants must switch attention between the direction or location of an arrow on a computer screen, selecting left or right based on queues given.	Laabs and Stager (251)
	Cancellation (speed and errors)	Measures visuospatial function and attention. Participants are given one or more digits to cross out from a list of numbers. The resulting score is calculated by misusing the incorrectly crossed out numbers from correctly crossed out numbers.	Saykin, Gur (252)
	Choice Reaction time	**Measures** attention/alertness and motor speed. This test is similar to the simple reaction time test, but participants are required to choose between two possible stimuli and two possible responses, introducing uncertainty regarding both the stimulus and response.	Stone (253)
	Continuous performance	Measures sustained and selected attention. Participants are required to maintain focus over a period of time whilst performing a repetitive and banal task involving a response to targets or avoiding a response to false targets. Tests may use numbers, symbols, or sounds.	Rosvold, Mirsky (254), Greenberg, Kindschi (255)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Memory			
	Associate learning	Measures immediate (short term) memory. Participants are delivered paired stimuli and responses, usually words, and must recall the response when given the stimulus word.	Cohen (256)
	Benton visual retention (errors and # items recalled)	Measures visual perception and memory. The participant is shown 10 designs one at a time and required to reproduce (draw) each from memory on paper.	Benton (257)
	Benton visual reproduction	Measures visual memory. The participant must draw between one and three basic figures (10 subtests in total) after having reviewed them for 10 seconds. The number of correctly drawn figures is used to score the test.	Benton (257)
	Immediate memory	Measures immediate (short-term) memory. Participants are given lists of simple words and must recall them.	Wechsler (258), Saffran and Marin (259)
	Delayed memory	Measures delayed memory. The participant is required to recall a list of words (often the list of words administered for the immediate memory test) after a set period of time involving other, unrelated tasks, which can be adjusted to increase task complexity.	Wechsler (258), Randolph, Tierney (260)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Memory			
	NES Pattern Comparison (score and time)	Measures immediate memory and processing speed. Participants are required to decide whether two stimuli presented to them side by side on a screen are identical or not. They are given 90 seconds to respond to as many as possible.	Baker (261)
	Visual reproduction	Measures visuospatial function and immediate or delayed memory. Participants are asked to draw a simple stimulus picture as accurately and completely as possible. Then after a delay involving other, unrelated tasks, re-draw the picture.	Wechsler (258)
Motor performance			
	Simple reaction time (right and left)	As above	Blackburn and Benton (243)
	Finger tapping (dominant and non-dominant hand)	Measures motor speed and dexterity. Participants are required to depress two buttons with two fingers from the same hand as quickly as possible, alternating between the two buttons.	Ream (262) Shimoyama, Ninchoji (263)
	Grooved pegboard (dominant and non-dominant hand)	Measures manual/manipulative dexterity. Participants must insert pegs with a key along one side into a board with 25 holes with randomly orientated slots, by rotating them to line up with the slots. Speed and accuracy are measured.	Kløve (264), Bryden and Roy (265)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Motor performance			
	Pursuit aiming (1 and 2)	Measures hand-eye coordination. This test requires the subject to use a pencil to place one dot inside a circle, following a pattern given on a test sheet as quickly as possible for 60 seconds.	Anger, Liang (266), Guilford (267)
	Santa Ana dexterity	Measures manual dexterity. Participants are required to remove pegs from a plastic base plate, rotate them 180 degrees and replace them back in the same slot. They must turn as many pegs as possible in 30 s.	Melton (268), Seppalainen (183), Anger, Liang (266)
	Coin rotation (dominant and non-dominant hand)	Measures manual dexterity and motor speed. Participants are required to rotate a quarter dollar-sized coin 180 degrees between their thumb, index finger and middle finger as many times as possible in a given time frame (e.g. 20 seconds)	Mendoza, Apostolos (269), Mendoza, Apostolos (270)

Table 2.4. Continued - Neuropsychological tests and sub-tests

Functional Domain/ sub-domain	Test (subtests/test variables)	Description	Key References
Miscellaneous			
Visuospatial/construction	Block Design	Measures spatial visualisation ability and motor skill. The participant is required to rearrange blocks with different colour patterns on each side to match a provided pattern. Speed and accuracy are measured.	Kohs (271), Baker, Seppalainen (190)
Concept formation	Picture completion	Measures visual perception and recognition, attention and organisation. Participants are required to examine a picture with a key element missing and identify this within a defined time limit.	Healy (272),
Validation tests			
Baseline intelligence	National Adult Reading Test (NART)	Measures/is used to adjust the results of neuropsychological tests for pre-morbid intelligence. Participants are given a list of words which they much read and pronounce correctly.	Nelson and Willison (273), Crawford, Parker (274)
Malingering	Rey 15 item	Measures malingering or test effort. Participants are shown a picture of 15 easy to remember items (e.g. A B C, 1 2 3) laid out in a clear pattern for 10 seconds, and must recall them immediately upon having the card obscured from their view. The task is simple, therefore a low score is suggestive of insufficient effort, which may impact on the scores achieved for other tests applied.	Rey (275), Reznek (276)

In 1983, based on an international collaborative effort, the WHO recommended the Neurobehavioural Core Test Battery (NCTB) (266) for the clinical assessment of CSN, which consists of 7 core neurobehavioral tests/assessments covering the majority of functional domains shown in table 2.4. In the late 1980's the Neurological Evaluation Scale (NES), and its successors the NES 2 (277) and NES 3 (241) became the most widely used assessment tools. However, although appropriate for educated participants, NES 2 and NES 3 were less suitable for persons with a lower education status or who were computer illiterate. Second generation batteries were developed to address some of these issues, including the Behavioural Assessment and Research System (BARS), the Cambridge Neuropsychological Test Automated Battery (CANTAB) (278-280) and the Behavioural Evaluation for Epidemiology studies (BEES) (281). However, some of the above batteries can take well in excess of an hour to administer, which may not always be practical for assessment/screening of actively employed workers in an occupational setting.

The Repeatable Battery for the Assessment of Neurobehavioural Status, or RBANS (NCS Pearson Ltd, MN, USA) (260, 282) can be administered more quickly (under 25 minutes), and covers largely the same functional domains, including immediate memory, visuospatial and construction skills, language, attention and delayed memory. Immediate memory is assessed using a verbal serial list learning task (list of words) and recall of a short story; a shorter version of the Digit Span test is included to assess attention; a coding task similar to the Digit Symbol test is used to assess attention and processing speed; and a picture naming and semantic fluency exercise are included to assess language skills and fluid intelligence. Delayed memory is

assessed using a test involving the recall of words or figures from earlier sections of the battery after an intermission involving other, unrelated tasks, and a list recognition test is used to assess prompted delayed memory. It has proven efficacious in the detection of cognitive dysfunction amongst patients exposed to neurotoxic pharmaceuticals (283) and for the long-term monitoring of neuropsychological function after acute ethylene glycol poisoning (284). It has benefits over other batteries for use in epidemiological studies of actively employed workers, in that it is faster to administer and simpler in its design and the language used, and therefore appropriate for use in populations with lower educational status (192, 260, 285).

Acute intoxication

The influence of the intoxicative effects of acute solvent exposures (i.e. immediately after/within hours of having been exposed) on the neurobehavioural function of actively employed workers, particularly performance on objective tests, should be considered when assessing CSN (185-187, 286). Experimental studies have shown acute exposure to toluene and methyl ethyl ketone affect psychomotor function, both immediately after exposure and for some hours afterwards (286), and exposure to a mixture of aromatic hydrocarbons (including benzene, toluene and xylene) can affect visual perception and other CNS functions (186). In epidemiological studies, controlling for acute effects is usually achieved by arranging for testing to be conducted after an exposure-free period of sufficient duration for any transient effects to resolve. The biological half-life of most solvents used in industry is generally measured in hours (e.g. the half-life of toluene in the body has been estimated at

around 7.5 hours (287)). To account for this, researchers have often stipulated an exposure-free period prior to testing of 48 hours, or an exposure-free weekend, which usually includes abstinence from alcohol (18, 45, 288, 289). The acute intoxicative effects of solvents may also have an impact on a worker's ability to perform the often complex and hazardous tasks associated with collision repair work, potentially resulting in a higher likelihood of workplace accidents and injury, a reduced awareness of hazardous exposures an a general reduction in productivity (187, 290).

Neurobehavioural effects from other causes

When assessing workers for CSN, it is important to control for the effects of other conditions and exposures which may affect the nervous system, such as major depression, alcoholism, or drug abuse (2, 8, 10, 40, 191). This can be difficult, as many neurological and psychological disorders may present similarly to solvent-induced neurotoxicity. In particular, participants with a history of neurodegenerative (Parkinson's and Alzheimer's disease) and cerebrovascular disorders, inflammatory diseases or infections of the brain (e.g. meningitis) or major trauma should be identified and excluded from any statistical analyses (10). In addition, symptoms associated with depression and other psychiatric or mood disorders show many commonalities to those induced by solvent neurotoxicity, including reported problems with concentration and memory, fatigue and irritability (10, 291, 292), and may also affect cognitive performance (10, 292). The influence of age, premorbid intelligence, sleep disorders and other potential confounders should be taken into account, but not necessarily preclude solvent-induced effects (10, 71, 177, 291, 292).

Global incidence and prevalence of CSN

As mentioned above, differences in the criteria by which neurobehavioural outcomes are defined, and the lack of universally accepted diagnostic and assessment criteria makes it difficult to assess the global incidence and prevalence of CSN. However, some region-specific data on CSE prevalence have been reported previously, including in New Zealand.

In a Finnish study by Keski-Santti, Kaukiainen (10), 128 confirmed cases of CSE were diagnosed between 1995 and 2007, from a total population of about 5.2 million. Temporal trends showed a consistent decrease in the number of incident CSE cases over the study period from 8.6/million employed persons in 1995 to 1.2 in 2007. In a New Zealand study by Dryson and Ogden (12), 76 cases of CSE were diagnosed between 1993 and 1997, or 3.2 cases per million population per year (total of around 4.2 million). In a Review of CSE as an occupational disease in European countries by Triebig and Hallermann (11), occurrence of CSE in Austria, Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway Sweden and Switzerland was estimated at between 0.1 and 16.8 cases per million active members of the workforce per year. It is likely that the large variation in case numbers between countries is due to ongoing debate over the legitimacy of CSE as a disease associated with occupational exposure, and differences in reporting and diagnostic procedures (10). Nonetheless, it is clear that the incidence of CSE has declined steadily over the past 2 decades (11, 13); however, these statistics only relate to diagnosed cases, and do not provide an indication of the prevalence of borderline CSE, or lower-grade neurobehavioural dysfunction (293).

Occupations at risk

Diagnosed cases of CSE most commonly have a history of employment in industrial, automotive and metal painting and refinishing, particularly spray painting (10-12, 70). For example, in the New Zealand study by Dryson and Ogden (12), 39% of the verified cases were ex-spray painters. A similar proportion (38%) of cases in the Finnish study by Keski-Santti, Kaukiainen (10) were ex industrial, metal or car painters. Other common exposure-work reported by cases includes construction painting, work in the print-trade, floor laying and lacquering and fiberglass boat building (10, 12, 70). The class of solvents to which cases of CSE were most often exposed was aromatic hydrocarbons. For example, 78% of the Finnish cases were exposed to aromatics, particularly mixtures containing toluene and xylene (10). The majority of patients (92%) also reported exposure to solvent mixtures rather than individual solvents, which is consistent with surveys of the nature of solvent use in industrial settings(294).

Screening Programmes

A small number of studies have attempted to directly assess the incidence of CSE in workers occupationally exposed to solvents. In a large Dutch screening programme (295), over 20,000 painters from various industries were screened for CSE between 1997 and 2004 using the Neurotoxic Symptom Checklist-60 (NSC-60) (236). The survey yielded 719 painters with a positive score on the NSC-60 who were referred to the diagnosis team, 27 of whom were given a positive diagnosis of CSE. A routine referral

programme for suspected cases of CSE which ran alongside this programme over the same period identified 619 potential cases, 75 of which were diagnosed with CSE. For both programmes, a significantly higher proportion of cases were identified prior to 2002 than after, which the researchers suggested may be due to most cases having been successfully detected between 1997 and 2002 or, alternatively, a demonstration of the effectiveness of a ban on the use of solvent-based paints indoors and an associated reduction in worker exposures. Few other such screening programmes have been undertaken to assess the incidence of CSE in solvent-exposed working populations, but a number of epidemiological studies have assessed the prevalence of neurobehavioural effects in these workers. These are reviewed in the next section.

Epidemiological studies of solvent-exposed workers

From the 1970s through to the early 1990s, a number of international epidemiological studies demonstrated chronic health effects amongst workers with low-level, long-term exposures to solvent mixtures. Two reviews by Mikkelsen (70, 296) published in 1988 and 1997 identified at least 43 separate studies conducted between 1976 and 1997 of CNS effects associated with occupational mixed solvent exposure that included an assessment of neuropsychiatric disorders, symptoms of neurotoxicity and/or performance on objective neurobehavioural tests. A review published in 2000 by Gamble (297) identified about 100 studies of the effects of hydrocarbon exposures on the central and peripheral nervous system. Another comprehensive review of the evidence that long-term, low-level occupational exposure to solvents can result in neurobehavioural effects identified 45 separate and relevant epidemiological studies

published between 1976 and 1999 (293). A meta-analysis of the impact of solvent mixtures on neurobehavioural performance identified 46 separate studies of exposed workers published between 1975 and 2004 where neurobehavioural performance was assessed using standardised objective tests, and basic empirical test data were reported (16). These studies included workers from a variety of industry sectors, but despite being consistently over-represented amongst cases of CSE (10, 12), relatively few focused on industrial and vehicle collision repair spray painters (16). An additional literature search using similar search criteria to the above reviews/meta-analysis revealed 12 studies since 2008, none of which focused on the collision repair industry.

The key outcomes from these reviews (70, 293, 296, 297) and meta-analysis (16) are as follows:

1. Most studies reported at least some statistically significant effects of low-level, long-term solvent exposures on neurobehavioural or cognitive function.

2. “Unexpected” negative results in some studies of workers with higher exposures and positive results in workers with lower exposures may be at least in part due to methodological issues, particularly in earlier studies.

3. Some studies failed to properly adjust for potential confounders, particularly age (related to duration of exposure and test performance), primary intellectual ability (related to test performance) and use of alcohol and other drugs.

4. Some studies included large numbers of workers with negligible exposures (and therefore risk of neurotoxic effects) in 'exposed' groups, which is likely to have masked the true effect.

5. The inconsistency of methods used for exposure assessment and subjective and objective effect measures makes it difficult to compare results between studies.

6. A significant, but lesser, proportion of studies showed evidence of a dose-response relationship – where no trend was found a self or external selection towards healthier workers, e.g. a healthy worker survivor effect was often implicated.

7. Despite some inconsistencies, it seems unlikely that the findings of numerous studies from different occupational groups and from different countries are false-positive due to methodological issues or chance.

8. Effects have been consistently observed at exposures below relative workplace exposure standards, suggesting the need to reduce acceptable levels of exposure.

9. Where exposures were below workplace exposure standards, a positive association with symptoms/cognitive deficits was more likely to be observed when workers reported having experienced incidents of high level, acute exposure, i.e. peak exposures.

As it is beyond the scope of this thesis to review all studies of neurotoxic effects in solvent exposed workers, the following section will provide a summary of those focused on industrial and vehicle collision repair spray painters, beginning with

findings from subjective assessments of symptoms of neurotoxicity, with a focus on chronic symptoms, followed by results of objective testing of neuropsychological/cognitive function, and evidence of dose-response relationships. Studies in other occupationally exposed groups will be referenced where appropriate. These studies were included as they are particularly relevant to the studies described in the other chapters of this thesis.

Fourteen cross sectional studies conducted between 1976 and 2002 (188, 298) of car painters (17-20, 45, 72, 298) and industrial spray painters (188, 299-304) exposed to solvents were identified through a search of the literature. The characteristics of the groups studied and the methodologies used are presented in table 2.6. Their findings (specifically relating to subjective and objective neurotoxic effects) are reviewed briefly below.

Table 2.6 Studies of subjective and objective neurobehavioural effects in vehicle collision repair and industrial spray painters.

Study	Exposed workers/ referent group numbers	Internal/external referents	Exposed workers: Job title/workplace	Mean age of exposed/referents (yrs)	Duration of exposure (yrs)	Current exposure monitoring type	Average exposure level (ppm)	Exposure Index average*	Symptom questionnaire used	Associations observed (symptoms)	Objective test battery used	Associations observed (objective tests)
Hänninen, Eskelinen (72)	33/33	External	Spray painters - vehicle repair	N/A	7.4 ± 4.1	Personal	61	0.87	Bespoke	↑Memory/attention, fatigue, mood	Bespoke	↓Attention, memory, problem solving, manual dexterity
Elofsson, Gamberale (19)	80/80	External	Spray painters - Vehicle repair	N/A	N/A	Personal	62	0.47	Bespoke	↑Memory/attention, fatigue, acute CNS depression	Bespoke	↓Reaction time, manual dexterity, memory
Husman (18)	102/102	External	Spray painters - Vehicle repair	35/35	14.8 ± 25.2	Area/Ambient	61	0.32	Bespoke	↑Mood, fatigue memory, attention, CNS depression	N/A	N/A
Ng, Ong (300)	78/145	External	spray painters - Industrial, printers, Paint manufacturing workers	33/32	9.4 ± 10.1	Area/Ambient	N/A	0.39	Q16	↑Fatigue, memory, mood, sleep disturbance	WHO-NCTB based	↓Attention, reaction time,
Triebig, Barocka (20)	78/40	External	Spray painters - Industrial	44/41	26.0 ± 8.0	Area/Ambient	N/A	0.66	Q16	↕ Main functional domains (external) ↑ 'Features of depression' concentration, worrying (internal, high vs low exp.)	WHO-NCTB based	↕ All functional domains
Wang and Chen (188)	58/138	Internal	Spray painters - Industrial, paint manufacturing workers	41/30	17.6 ± 13.3	Area/Ambient	66	1.66	Q16	↑fatigue, mood, psychosomatic (high vs. low exp.)	N/A	N/A
Daniell, Stebbins (45)	39/43	Internal	Spray painters - Vehicle repair	29/38	8.6 ± 7.5	Personal and Area/Ambient	33	0.45	NES based	↑Fatigue, mood, attention (high vs. low exp.)	NES based	↓Manual dexterity, psychomotor perf., attention, memory processing speed
Böckelmann, Darius (17)	84/84	External	Spray painters - Vehicle repair	37/41	16 ± 10.7	Area/Ambient	46	N/A	Bespoke	↑Mood, psychosomatic, neurological ↕ Memory, concentration	WHO-NCTB based	↓ 'Cerebral insufficiency', attention, reaction time ↕ Some sub-tests
Nasterlack, Dietz (301)	360/189	External	Painters - various	42/45	25.7 ±10.3	N/A	N/A	2.96	Bespoke and Q16	↕ Individual symptoms ↑more than 6 symptoms (workers ≥28 yrs, high cumulative exp. group)	Bespoke	↕ All functional domains ↓most domains in 'high' vs. 'not high' exp. (internal)
Kishi, Harabuchi (302)	20/20	Internal	Spray painters - Industrial	40/40	14.2 ± 11.9	Area/Ambient	N/A	3.67	Bespoke and POMS	↑psychosomatic, mood, neurological, fatigue, concentration (high vs. low exp.)	Bespoke	↕ 6/7 tests ↓attention/processing speed
Chen, Dick (299)	260/539	External	Spray painters - Dockyard	N/A	N/A	N/A	N/A	N/A	Bespoke and Q16	↑19/22 individual symptoms, strongest for neurological	N/A	N/A
Cherry, Hutchins (303)	34/34	External	Spray painters - Dockyard	43/42	11.7	N/A	176	N/A	N/A	N/A	Bespoke	↓Attention, construction/psychomotor perf., memory, reaction time
Tripathi, Bhattacharya (304)	100/75	internal	Spray painters - Bus and Bus parts	33/33	10.4 ± 2.9	N/A	N/A	N/A	N/A	N/A	Bespoke	↓Memory, attention, processing speed.
Lee (298)	87/81	internal	Spray painters - vehicle	33/35	7.2 ± 5.9	Area/Ambient	N/A	N/A	N/A	N/A	WHO-NCTB based	↓Attention, memory, processing speed

*Exposure Indices - Calculated by dividing the concentration of each compound detected in the sample by its relevant exposure standard, and summing the resultant values together (values taken from the manuscripts for each study, therefore the method used to calculate the ALV varies between studies, e.g. due to changes in exposure standards over time). If this number exceeds 1, it is deemed that the exposure standard has been exceeded for the mixture.

'↑' = Higher prevalence of neurobehavioural symptoms in the functional domains listed was observed in exposed workers compared to unexposed or low-exposed workers (either external or internal comparison groups).

'↓' = Poorer cognitive test performance in the functional domains listed observed in exposed workers compared to unexposed/low-exposed workers.

'⇳' No difference in prevalence of neurobehavioural symptoms/cognitive test performance in the functional domains listed in exposed workers compared to unexposed/low-exposed workers.

Subjective symptoms of neurotoxicity

Despite the inherent subjectivity of questionnaires, they are essential tools in the assessment of neurobehavioural symptoms as they are able to evaluate certain neurobehavioural functions which would otherwise be difficult to measure, such as mood, feelings and emotions (224). In addition, standardised symptom assessment represents an important starting point for identifying populations "at risk" of effects associated with solvent exposure (7), and has proven effective for screening these populations for clinical and subclinical disease (6, 234). The following section will review the results of subjective assessments of neurobehavioural symptoms in the studies described above.

Collision repair workers

In a study of 100 Finnish car painters and an unexposed reference group of 101 railway workers (72), painters reported significantly more symptoms of memory and vigilance problems, fatigue, absent-mindedness and emotional lability than the reference group. In a similar Finnish study of 102 age-matched pairs of car painters and referents (locomotive engineers and assistants) (18), symptoms of fatigue, attention and memory problems occurred significantly more frequently in painters, as did acute effects indicative of CNS depression ("irritation" and intoxication-like symptoms). Elofsson, Gamberale (19) assessed neurobehavioural symptoms in a group of 80 Swedish car painters and two matched (by age, type of work, and education level) reference groups of unexposed industrial workers. Symptoms related to

disturbances in mood, fatigue, immediate memory and attention were more frequently experienced by painters. An excess of symptoms suggestive of CNS depression, peripheral neuropathy and cranial nerve dysfunction (e.g. changes in sense of smell and taste) were also reported more frequently amongst painters.

In a study of 84 German vehicle collision repair spray painters and 84 community controls (17), painters reported significantly more symptoms of neurotoxicity, specifically in the domains of mood lability, psychosomatic disturbances and neurological disturbances, however no differences were observed between groups in the number of memory and concentration symptoms reported. In contrast, another German study of 78 car spray painters and a group of 40 unexposed referents (20) showed no significant differences between exposed and unexposed workers in the occurrence of individual symptoms or the number reported overall. A high exposure group defined using a cumulative exposure index were, however, more likely to report symptoms associated with “special features of depression”, “loss of interest and concentration” and “worrying”. Daniell, Stebbins (45) studied 4 exposure groups (low never exposed, low current exposed, high previously exposed, high current exposed) identified from a sample of 123 U.S. collision repair workers. Compared to the low current exposure group, workers with high current exposure reported significantly more symptoms of neurotoxicity, particularly those indicative of fatigue, mood lability, and attention difficulties.

Industrial Spray painters and other solvent-exposed workers

In a study of 401 painters from a variety of industrial settings (spray painters, construction painters, etc.) and a reference group of 209 unexposed construction workers (301), no significant differences between exposure groups were observed for individual neurobehavioural symptom questions, but exposed workers over 28 years of age were at an increased risk of reporting 6 or more symptoms, as were those in the upper 20th percentile of a cumulative exposure index.

Ng, Ong (300) investigated neurobehavioural symptoms in 78 workers from 11 factories in Singapore, where spray painting and screen printing processes were used in the manufacture of electrical appliances. Exposed workers were at a significantly increased risk of symptoms associated with fatigue, memory problems, mood lability and sleep disturbances compared to the reference group. Wang and Chen (188) assessed symptoms of neurotoxicity in 196 Taiwanese workers from two paint manufacturing factories and 25 factories where spray painting with organic solvents took place. Workers were divided into three exposure categories using an exposure index based on their exposure characteristics (e.g. time spent on high-exposure tasks) and the results of the exposure sampling. Only workers in the high exposure group were at a significantly increased risk of reporting chronic symptoms, namely fatigue, mood lability and psychosomatic disturbances.

In a similar study of 81 Japanese railway plant repair painters and a matched group of unexposed referents from the same work sites (302), exposed workers were at a significantly increased risk of chronic neurobehavioural symptoms, including psychosomatic disturbances, mood lability, neurological disturbances, fatigue and

concentration problems. However, when adjusted for differences in verbal intelligence (vocabulary), results were only significant for some symptom domains (e.g. "confusion"). Chen, Dick (299) compared neurobehavioural symptoms amongst 260 Scottish dockyard spray painters, both currently employed and retired, with a reference group of 539 controls randomly selected from the local population. Painters were significantly more likely to report all but three of the 22 neurobehavioural symptoms, with the strongest effect seen for neurological symptoms. Also, painters were significantly more likely to report more than 12 symptoms overall.

Objectively assessed neuropsychological performance

As discussed above, questionnaires assessing symptoms of neurotoxicity are limited by their inherent subjectivity, and the ubiquity of many of the symptoms amongst the general population (e.g. headaches, irritability) (224). As a result, Objective tests of neuropsychological and neurological function are seen as the gold standard for assessing causation and severity of neurobehavioural effects, as they provide a quantitative measure of functional deficits (6-8, 16). The results of neurobehavioural testing in studies of spray painters and other solvent exposed workers are reviewed briefly below.

Collision repair workers

In the study of car painters by Hänninen, Eskelinen (72), spray painters performed significantly more poorly on almost all neuropsychological tests, particularly tests of attention, immediate memory and fluid intelligence (problem solving). Decrements in psychomotor performance were also observed, the largest of which were for the Santa Ana manual dexterity test (183, 268). The authors concluded that impairment of memory and concentration seemed to be central features of solvent-related neurobehavioural effects. Elofsson, Gamberale (19) also observed decrements in reaction capability, manual dexterity, perceptual speed and memory amongst exposed Swedish car painters. They showed that age had a significant influence on test performance, and highlighted the importance of controlling for differences in age between exposure groups. Lee (298) observed significantly poorer test performance (visual perception/immediate memory, attention/processing speed) in Korean car painters and printers exposed to both 'low' and 'high' levels of mixed solvents compared to an unexposed control group selected from the same factories (security, administrative and manual workers). Controlling for age and premorbid intelligence reduced the magnitude of the effect, but differences in performance on the Benton visual retention (immediate memory) and digit symbol (attention/processing speed) remained significant/borderline significant. Böckelmann, Darius (17) found that collision repair spray painters performed more poorly on a test of 'cerebral insufficiency', the D2 and digit span tests (attention) and the simple choice reaction time test, but not on all sub-tests.

In the study of car painters by Daniell, Stebbins (45), crude neuropsychological test scores were significantly poorer for exposed workers (compared to unexposed referents) for finger tapping, hand-eye coordination (psychomotor performance), digit symbol, pattern recognition, digit span (processing speed, attention, immediate memory), pattern memory and the paired associate test (attention, immediate memory). However, when adjusted for age and premorbid intelligence, the difference between groups was no longer statistically significant for many tests, but digit span difference (attention) and pattern recognition response time (attention/reaction time) remained borderline significant. In contrast, Triebig, Barocka (20), observed no significant differences in neuropsychological test performance between spray painters and an unexposed reference group. However, as discussed above, scores on some tests were lower amongst exposed workers, but the authors believed this to be entirely due to the older age and lower premorbid intelligence. Results were similar in the study of industrial painters by Kishi, Harabuchi (302), in which, according to the authors, the painters performed poorer than unexposed referents in only one of the 7 tests applied (digit symbol test of attention/processing speed). The painters scored lower on 6 of the 10 test variables, but the differences failed to reach statistical significance.

Industrial Spray painters and other solvent-exposed workers

Cherry, Hutchins (303) applied an 8-test battery to a group of 42 British dockyard spray painters and an age matched comparison group of unexposed joiners and carpenters. Painters took longer to complete the Trail Making B test (switching

attention), visual search (attention), block design (visuospatial/construction, psychomotor performance), grooved pegboard (manual dexterity/psychomotor performance), immediate memory and simple reaction time tests. While the painters did score lower on a premorbid intelligence test (verbal intelligence), the observed effects remained even after careful control for this (and age). Ng, Ong (300) also observed poorer digit span and choice reaction time test performance in exposed workers (industrial spray painters), concluding that the effects observed were consistent with the WHO's definition of 'mild toxic encephalopathy' (266).

Tripathi, Bhattacharya (304) used a battery of 5 tests to assess cognitive performance in a group of 100 Indian spray painters exposed to solvent mixtures, and a reference group of 75 unexposed security workers from the same large bus painting factory. The spray painters performed significantly more poorly than the reference group on tests of immediate memory and attention and processing speed. In contrast, Nasterlack, Dietz (301) reported no significant differences in neuropsychological test performance between exposed (industrial painters, including some construction painters) and unexposed workers. In fact, exposed workers performed better on the Benton visual retention (memory) and D2 tests (attention). However, when exposed workers were stratified into 'not high' and 'high' exposure groups, those with 'high' exposure performed more poorly on most tests compared to the 'not high' group.

A number of other cross-sectional studies have been conducted in industrial settings were workers are exposed to mixed solvents, including vehicle mechanical repair, (288) rubber and rubber product manufacturing (130), printing and publishing ((67,

305, 306), floor laying and finishing (307) and paint manufacturing (308, 309). In general, similar patterns of subjective and objective effects were observed.

Dose-response relationships

The majority of epidemiological studies in solvent-exposed workers have also explored the effect of various exposure parameters related to dose on neurobehavioural effect sizes (16, 70, 191), as a dose-response relationship is often considered a requirement for causal inference (310). As discussed in chapter 4, dose-response associations have in general been the least consistent finding in studies of solvent exposed workers. Dose-response relationships have been observed for a number of outcomes in workers with relatively low exposures (296, 311), whereas no such association has been reported in workers with much higher cumulative exposures (309). Longer durations of exposure have been repeatedly associated with reduced risk estimates (22, 23, 302) and this has been observed across a range of industrial groups (19, 20, 23, 162, 172, 289, 312). A 'healthy worker survivor' selection bias (described above) is likely to explain this finding, in addition to exposure error, methodological issues and insufficient adjustment for important confounders (e.g. age and premorbid intelligence) in some studies (discussed in detail later on in this thesis) (16, 23, 70, 296, 302, 311, 313).

Despite these inconsistencies, most studies suggest spray painters and other solvent-exposed workers are at greater risk of neurobehavioural effects compared to unexposed workers. This is supported by the results of a 2008 meta-analysis by Meyer-Baron, Blaszkewicz (16), in which findings consistent with adverse effects on neuropsychological function were found for 43 of the 48 tests used in the 46 studies analysed (discussed in more detail in chapter 5).

This review also highlights the relatively small number of adequately designed studies of what is a well-recognised occupational hazard. Furthermore, only 14 of these focused on solvent exposures and neurotoxicity in spray painters, despite this group being consistently over-represented amongst cases of CSE (10, 12). None of these were conducted in the past decade, which may reflect the feeling amongst some researchers that solvent exposures in these industries are no longer a significant hazard (297).

2.4 Exposure controls to reduce morbidity

As discussed in chapter 6, studies have shown that use of PPE can reduce both airborne and dermal solvent exposures and subsequent total body-burden in workers performing a range of industrial tasks (31-34), including spray painters (29, 30, 36). For example, in a Swedish study of spray coating and laminating workers in a boat factory (31), the use of respiratory PPE reduced airborne styrene exposure by between 56% and 92%. In a similar, more recent Taiwanese study (30), use of a respirator was shown to reduce airborne xylene exposures amongst 15 male shipyard spray painters by up to 96%. The results of biological monitoring were highly correlated with airborne exposures in both studies, and reductions in urinary solvent metabolite levels of between 30% and 99% were observed when respirators were used. The authors of the Swedish study suggested that variations in the correlation between airborne exposures outside the mask and levels of metabolites excreted in urine were due to differences in how often masks were worn, levels of background exposure (when mask weren't worn) and leakage through the respirator or past the face shield (due to poor fit). In contrast the authors of the Taiwanese study concluded that when participants wore their mask during high exposure tasks (e.g. spray painting), the majority of the body burden of solvents 'unaccounted' for (up to 65%) was contributed by dermal exposures. Others have made similar suggestions (25, 26, 314). The effectiveness of gloves and protective clothing at reducing dermal exposures was demonstrated in a similar report from the same study (36); When workers exposed to ethyl benzene and xylene wore gloves and chemical suits, mean urinary mandelic acid (metabolite of ethyl benzene) and methyl Hippuric acid (xylene) concentrations were

reduced by 69% and 49% respectively compared to they were not worn (by the same workers).

The efficiency of respiratory and dermal protective equipment may also be dependent upon type, quality and maintenance level (30, 36, 315). Various types of respiratory protection are available, but most commonly either a 'full-face' (visor covering the face from hairline to chin, with or without a hood to cover the top of the head and neck) or 'half-face' (covering the nose and mouth only) respirator, fitted with either disposable absorbent cartridges (usually activated carbon) to filter inhaled air, or a positive-pressure, 'supplied air' feed is used. (30, 31). Full-mask, supplied air respirators are seen as the gold standard (316), and have proven superior in field tests, including in relation to body burden of solvents; for example, in a field comparison of a number of respirator types conducted by Triebig, Werner (34), use of an air-fed respirator reduced styrene body burden (urinary mandelic acid) levels in exposed workers by an average of 83%, compared to a reduction of only 26% with half-mask, active carbon cartridge respirators.

The regularity with which respirators are maintained may also affect their performance, particularly half masks fitted with absorbent cartridges. This was shown in an evaluation of the efficiency of respirators in 5 Japanese reinforced fiberglass factories, where workers were exposed to styrene (32). In one of the 5 factories included in the study, respirator cartridges were changed twice daily while in the other 4 they were changed on average once a month, and the average protective efficiency of the masks were 84% and 47% respectively. Respirator fit quality may also affect a workers' exposure (135, 315, 316), as a poor fit may allow solvent vapour to

be drawn past the seal between the face piece and the workers face, and the quality of seal may also be compromised be facial hair (315). However, this only applies to negative pressure respirators, not positive pressure/supplied air respirators, which may contribute to their superior performance (described above (34)). The consistency of PPE use can also vary greatly between workplaces and workers, as observed in surveys of PPE use and workplace practices in various industrial settings, including the collision repair industry (29, 122, 135, 317, 318). For example, in a study of isocyanate exposures (hardeners used in many paint formulations and a known cause of occupational asthma (15, 134, 319, 320)) in 37 US collision repair workshops (136), supplied air respirator systems were available in 54% of workshops, but were used in only 30%.

As with lower airborne and dermal exposures (16, 70, 296), a lower body burden of solvents has also been associated with a reduced risk of neurobehavioural effects (29, 286). This was shown in a study of 645 shipyard spray painters and other workers(29), where a decreasing level of cumulative biological exposure to mixed solvents was associated with a lower risk of abnormal neuropsychological function. However, few studies have directly assessed the impact of PPE use on the risk of neurotoxic effects. A study of 100 Thai workers from two paint manufacturing plants (321) showed inconsistent PPE use was associated with an increased risk of neurobehavioural symptoms, but details of the PPE used were not reported. A small number of studies in the collision repair industry have included surveys of PPE use (14, 135, 136), but most have been focused on factors affecting isocyanate rather than solvent exposures, and have not included health assessments. In addition, to the author's knowledge no

studies of solvent-exposed workers have assessed the effects of workplace hygiene practices (e.g. washing hands in solvents) on the risk of neurobehavioural symptoms.

Interventions to reduce exposures and occupational disease

To date, Interventions to reduce the burden of occupational disease are extremely rare. Of those implemented, most are limited to promoting national awareness of a particular hazard, which is often ineffective (322), or banning specific products or chemicals, which is not always possible. Also, many studies evaluating occupational interventions have been of poor quality, and few were focused on chronic health outcomes (323, 324). Although several studies have assessed health and safety practices (137, 141, 143, 325), only one intervention study has been conducted in the collision repair industry (38) and the intervention package used was focused on health and safety training, and specific instruction in the use and importance of PPE. The results showed improvement in access to training and increased use of some PPE, but neither exposure levels nor health effects were assessed. As a result, the evidence base for the development of more effective interventions specific to this industry is limited.

2.5 Summary

Occupational solvent exposures have generally declined over the past half century globally, most likely due to improvements in workplace conditions, technology and health and safety practices. However, due to a lack of studies in the past decade, little is known about solvent exposures and their determinants in contemporary vehicle collision repair workshops. This is particularly true in New Zealand, where no such studies have been conducted. As a result, it is unclear whether collision repair workers are at risk of elevated solvent exposures (and associated neurotoxicity), and, if this is the case, there is currently no contemporary evidence base for developing interventions to reduce these exposures.

Although acknowledged as early as the 1850s, the associations between occupational solvent exposures and CSN are still not fully understood. Also, data on the incidence and prevalence of occupational CSN, especially sub-clinical neurobehavioural effects, is limited, particularly outside of Europe (where the majority of studies and surveys have been conducted). Several epidemiological studies since the 1970s have shown symptoms of neurotoxicity and deficits in cognitive performance in spray painters and other solvent-exposed workers (18, 19, 45, 72, 326), but findings have not always been consistent (20, 69, 162). Dose-response associations have often been weak, possibly due to a healthy worker survivor effect (16). Also, due to the lack of studies in the past decade, it is unclear if workers in contemporary collision repair workshops are at risk of CSN, and if so how severe these effects may be.

PPE use and good workplace hygiene practices have been associated with reduced airborne and dermal solvent exposures and body burden in spray painters (29, 30, 36) and other solvent exposed workers (31-34). However, few studies have assessed whether they are protective against neurobehavioural effects, or the factors that influence their effectiveness. Also, as PPE use is generally seen as the last line of defence in the prevention of exposure, application of higher level controls based on an assessment of the underlying determinants of exposure is preferable (30, 123, 135, 316, 327-329). On the basis of this data, interventions to reduce solvent exposures which are focused on the workplace conditions and behaviours which contribute most to exposure can be developed and implemented.

3 Determinants of airborne solvent exposure in the collision repair industry

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Objectives: To assess the determinants of airborne solvent exposures in contemporary vehicle collision repair workplaces.

Methods: Personal, full-shift airborne solvent exposures (n=97) were assessed in 85 vehicle collision repair workers from 18 workshops. Peak exposures were assessed using a small number of video exposure monitoring (VEM) measurements.

Results: Solvent exposures were highest in spray painters (2.7 ppm) followed by panel beaters (0.5ppm), but were well below workplace exposure standards. The lowest exposure levels were observed for mixing room extraction located away from the mixing bench (Exposure Ratio (ER) 0.51, 0.30-0.87). Time spent mixing paint was associated with higher exposures (ER for every 10 minute increase 1.14, 1.05-1.24), as was time spent cleaning equipment with solvents (ER 1.11, 0.88-1.39), spraying primer (ER 1.10, 0.96-1.27) and spraying clear coat paint (ER 1.07, 1.00-1.15). Overall, the combined non-spray painting tasks (mixing paint, degreasing and cleaning equipment) were more strongly associated with exposure (ER 1.10, 1.03-1.18) than the combined spray painting tasks (ER 1.03, 1.00-1.05). Peak exposures ranged from 10-1100ppm with the strongest and most frequent peaks occurring during paint mixing, decanting of solvents, cleaning of equipment and painting in a cross-draft spray booth.

Conclusions: Airborne solvent exposures in the collision repair industry were associated with job title, the design and location of exhaust ventilation and emission sources, and time spent on specific tasks, with highest average and peak exposures shown for non-spray painting tasks. These findings provide a contemporary basis for intervention programmes to reduce airborne solvent exposures in this industry.

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3.1 Introduction

Numerous studies across a range of industries, including the vehicle collision repair industry, (17, 18, 21, 45, 69, 72, 298) have shown evidence of solvent-related neurotoxicity symptoms, cognitive deficits and psychiatric effects amongst exposed workers (67, 166, 188, 291, 302, 330). We recently showed that vehicle spray painters and panel beaters (or auto-body repair workers) in New Zealand had significantly increased risks of neurobehavioural symptoms (331) and deficits in neuropsychological performance (332), despite airborne solvent exposures being below workplace exposure standards. The greatest effects were observed in workers who did not consistently use personal protective equipment including respirators and gloves (333), highlighting the importance of airborne and dermal exposure.

Although generic determinants (e.g. job tasks, environmental conditions, workplace practices and equipment characteristics) for some airborne occupational exposures have been reported (123), most are unique to specific industries and sometimes individual workplaces (124-131). Exposure determinants for isocyanates and other health hazards in the collision repair industry have been studied previously (14, 15, 100, 122, 134-143, 334), but only a few contemporary studies have focused on solvents, and/or included quantitative exposure assessment (335). Solvent exposures in this industry have likely declined over the past decades internationally, at least in part due to changes in paint formulations, health and safety practices and improved exposure control technologies (13). As a result, exposure determinants in this industry may have changed and results from previous studies (14, 123, 135, 136, 336) may be less applicable to current collision repair workshops, hampering the development and

implementation of effective evidence-based interventions to further reduce airborne solvent exposures.

The collision repair industry in New Zealand, as in many other countries, is comprised primarily of small-to-medium sized enterprises where health and safety is likely to be managed less effectively than in larger establishments (45, 46). In view of this and the continued high burden of solvent-related morbidity in collision repair workers (331, 332), targeted, cost-effective and easy to implement interventions based on current and industry-specific evidence are urgently needed.

In this study, as part of a larger study of solvent exposures and neurotoxicity in vehicle collision repair workers (331), we assessed determinants of personal airborne solvent exposure in 85 vehicle collision repair workers from 18 workshops in New Zealand.

3.2 Methods

Participant recruitment

Study participants were recruited from 370 collision repair workers (vehicle spray painters and panel beaters or auto body repair workers) who took part in a previous questionnaire survey conducted between 2011 and 2014, the methods and results of which are described in detail elsewhere (331). In total, 46 spray painters and 29 panel beaters from 18 randomly selected collision repair workshops were recruited for exposure monitoring. We also recruited a small group of office workers (n=10) from the same workshops with no history of spray painting or panel beating. Most workshops employed between 2 and 15 workers including 2-6 spray painters, which is representative of the sector in New Zealand.

Work tasks

As workshops were small to medium in size, the majority of spray painters performed a wide range of tasks, including: sanding; degreasing; masking; mixing of paint; spray painting primer, colour and clear-coat (top-coat) paints; and cleaning spray equipment. The majority of painting was conducted inside spray booths, most of which were commercially produced single vehicle capacity units with downdraft extraction systems (ceiling to floor air flow), built to similar specifications. The remainder were cross-draft booths, a small number of which were owner-built.

The main job tasks performed by panel beaters were disassembly and replacement or repair of damaged parts (including chassis realignment and cutting, welding and grinding of steel/aluminium/plastic), planishing to restore (steel or aluminium) panels, degreasing of panels/parts (usually with heavy duty solvent-based degreasers), filling of damaged panels with polyester resin, and sanding of repaired areas. They also occasionally applied primer paint in small quantities from an aerosol can (outside the spray booth).

Spray painting and panel beating were generally performed in designated areas, usually without physical barriers between them. However, some shops had separate panel beating and spray painting 'shops', although usually with open internal access for moving vehicles between areas. In those shops, panel beating and painting preparation were done in the main workshop(s), where ventilation was restricted to open roller doors and windows, or occasionally general mechanical ventilation (roof-mounted extractor fans).

Workplace characteristics and practices

Work place characteristics and practices were assessed through a hygiene survey and/or post-sampling questionnaire (see below). The use of 'Water-based' paints (typically 10% w/w solvents, 70% water, 20% paint solids (337)) was assessed by questionnaire and refers to the use of water-based colour paint only, as at the time of the study, the primer and clear-coat/top-coat paints used were almost exclusively solvent-based formulations (up to 85% w/w solvents and the remainder solids (337)).

The mixing room was identified as a dedicated space for preparing paint and spraying equipment, with or without direct access to one or more of the spray booths. It is also used for storing paint, paint tints and raw solvents for thinning paint, degreasing and cleaning. Paint mixing in each workshop was conducted almost exclusively at a single main mixing bench with extraction in the form of built-in vents located either above or at floor level under the front edge of the bench, or at the same heights but on an adjacent wall. The spray equipment washer ('gun washer') used by most workshops consisted of a purpose-built cabinet that can be open-sided or enclosed, sometimes with dedicated local exhaust ventilation (LEV), and was located either inside the mixing room or the general workshop. Other workplace factors recorded include the number of employees, the number of spray painters, and the cubic volume of the workshop estimated from floor area and ceiling heights.

Full-shift airborne exposure monitoring

The current study focused primarily on tasks which were likely to contribute most to airborne solvent exposure, as shown in previous studies (14, 100, 331), including: mixing paint, spray painting, degreasing panels and cleaning spray painting equipment. These tasks represented a sizeable proportion of the vehicle repair workload and varied little between workshops, as vehicle refinishing generally follows a uniform process.

Full-shift airborne personal exposure measurements were conducted in 85 workers throughout the working week. Repeat measurements were collected for 5 spray

painters and 7 panel beaters, resulting in 97 exposure measurements. Samples were collected using a whole-air method (64), which involved 2mm internal diameter teflon tubing running from the workers breathing zone connected to a 400cc stainless steel sampling canister (Restek Corporation, PA, USA) negatively pressurised to near full vacuum (-30 mmHg). A flow controller (Restek Corporation, PA, USA) was used to maintain a flow rate of 0.9 ml/min. In order to ensure consistent flow rate throughout the sampling period, sampling was stopped when air pressure in the canisters reached between -5 and -3 mmHg. The internal surfaces of the canister, connecting stainless steel hardware and flow controller were Siltek™ treated, a silica-based inert coating designed to maximise sample stability (Restek Corporation, PA, USA).

Samples were analysed within 48 hours by an external laboratory using Selected Ion Flow Tube Mass Spectrometry (SIFT-MS; Syft Technologies, Christchurch, NZ) for toluene, xylene, styrene, acetone, butyl and propyl acetate, tri-methylbenzene, n-hexane, methyl ethyl ketone (MEK), methyl isobutyl ketone (MIK), ethanol, butanols, propanols and di-methoxyethane. The general and compound-specific methods are described in detail elsewhere (59, 104, 106-108, 338, 339). In brief, data on reaction rate coefficients and ratios of products for the target compounds is held in a library on board the SYFT-MS instrument (collated from the results of compound-specific validation studies: Smith and Španěl (105), Španěl, Ji (106), Španěl and Smith (107), Španěl and Smith (108), Španěl and Smith (338), Syft Technologies Limited (340), Syft Technologies Limited (341), Syft Technologies Limited (342), Syft Technologies Limited (343). Before sample analysis, a certified gas standard was used to confirm that the instrument-based parameters were standardised (including for reaction time and ion

transmission) and that the instrument was measuring the compounds in the certified standard correctly (59, 104). The compound-specific data library was then used to detect and quantify the target compounds in the sample.

Although every effort was made to maintain consistent sampling times, they inevitably varied to some degree. This resulted in variable canister pressures and subsequent sample flows into the SYFT- MS instrument. Variable correction factors to calculate the original atmospheric concentration were therefore required. As a consequence, it was not possible to report one LOQ/LOD for each compound. Instead, a conservative LOQ/LOD estimate of 5ppb was calculated (according to the method described by Milligan, Francis (104)) and used for all compounds. Samples below this limit (42% for di-methoxyethane, 2% for tri-methylbenzene, 13% for butanols, 26% for propanols, 13% for acetone, 16% for MEK, 3% for butyl acetate, 15% for ethanol, 7% for n-hexane, 37% for MIK, 0% for xylenes, 12% for propyl acetate, 23% for styrene and 0% for toluene) were assigned a value of 2.5 ppb. Solvent levels are presented both for each compound individually and as aggregated total levels by summing the concentrations of the individual compounds (figure 3.1).

A short post-sampling questionnaire was administered to each participant covering work tasks performed, time spent on each task during the sampling period, and paint and product types used. Work tasks of particular interest were: spraying primer paint, solvent-based colour paint, water-based colour paint, clear-coat (top-coat) paint; mixing paint; degreasing panels; and cleaning spray equipment. Workers were asked to recall how long they had spent on each task in 5 minute blocks. In addition, we

conducted an on-site workplace hygiene survey in all 18 workshops; the workplace practices assessed are summarised in table 3.1.

Video Exposure Monitoring

In addition to full-shift exposure monitoring, a small number of Video Exposure Monitoring (VEM) measurements were conducted in spray painters randomly selected from those who took part in the full-shift monitoring, to obtain information on peak exposures and associated tasks (78). A Velocicalc 9565-P/985 photoionisation detector (TSI Inc., MN, USA) fitted with a 10.6 electron-volt lamp (Ion Science LTD., Cambridge, UK), with a working limit of 0.1 ppm, was worn by each worker with the sensor placed in their breathing zone. Wireless video cameras (D-LINK®, Taipei, TW) were used to record the participants' activities. Data feeds from the PID and cameras were wirelessly transmitted in real-time to a software package on a laptop computer developed by VEM Systems™ LLC and Purdue University (81).

The VEM observations covered a range of spray painting tasks conducted by three spray painters from different workshops. The first of the three observations (figure 2a) took place during a typical spray painting operation, involving repeated cycles of mixing paint, decanting thinners and spray painting. The spray booth used was equipped with downdraft ventilation. Extraction in the mixing room was located above the height of the mixing bench on an adjacent wall, and the gun washer was located outside in the main workshop. The second observation (figure 2b) included two spray painting cycles in a cross-draft spray booth and a period of spray gun and equipment cleaning in a mixing room. Extraction in the mixing room was located at

floor level next to the main mixing bench and a smaller, separate bench in the middle of the room was used for equipment cleaning, where the enclosed gun washer with dedicated LEV was located. The final observation (figure 2c) captured exposures during 2 painting cycles and a period of spray gun and equipment cleaning. Painting was conducted in a downdraft booth, with ventilation in the mixing room at floor level next to the mixing bench. The gun washer had dedicated LEV and was located in the mixing room, but was of an older design with open sides and a manually activated spray jet for applying solvent when cleaning equipment.

Statistical Analyses

Analyses were conducted using Stata version 13.1 (StataCorp LP, Texas, USA). As exposure data approximated a log-normal distribution they were log-transformed prior to analysis and geometric mean concentrations were presented for each of the collision repair groups (office staff, spray painters and panel beaters). Due to repeat measures (n=12) in the same workers and multiple workers from the same workshops, we used multi-level mixed-effect linear regression, with worker and workshop specified as random effects. Due to log-transformation, outcomes are presented as exposure ratios (ER) (the proportional difference in total solvent level relative to the reference category for the determinant variable, identified as '(REF)' in the tables) with 95% confidence intervals.

Initially, univariate analyses were undertaken for each potential exposure determinant separately (table 3.1). In addition to being analysed continuously, variables relating to

workshop size were also categorised (number of employees overall: <6, 6-10, and >10; number of spray painters: 2, 3 or ≥ 4; and estimated volume of the workshop: < 1000 m^3, 1001-2000 m^3 and ≥2000 m^3). We then repeated the analyses mutually adjusting for all potential exposure determinants; this showed similar trends for most outcomes, but there was some evidence of colinearity ('adjusted exposure ratio', table 3.1) (344). Further analyses showed correlations between some mixing room extraction and gun washer extraction factors (Pearson's r^2, 0.22-0.42), paint type and paint brands (r^2, 0.23-0.79), number of employees overall and number of painters (r^2, 0.68), and between measures of work task duration (r^2, 0.32-0.65). To address this we combined the mixing room extraction and gun washer extraction variables as follows: height of mixing room extraction and location of mixing room extraction, and location of gun washer extraction and gun washer LEV status. We also included only paint brand (rather than paint type) and number of painters (rather than number of employees) in the model. Finally, we used an overall measure of time spent on all spray painting and all non-spray painting tasks ('all tasks combined') rather than time spent on specific tasks. We then repeated the multivariate analyses including only spray painters (table 3.1), as some job tasks and workplace factors were less relevant to office work and panel beating (e.g. gun washer extraction, time spent spraying colour paint).

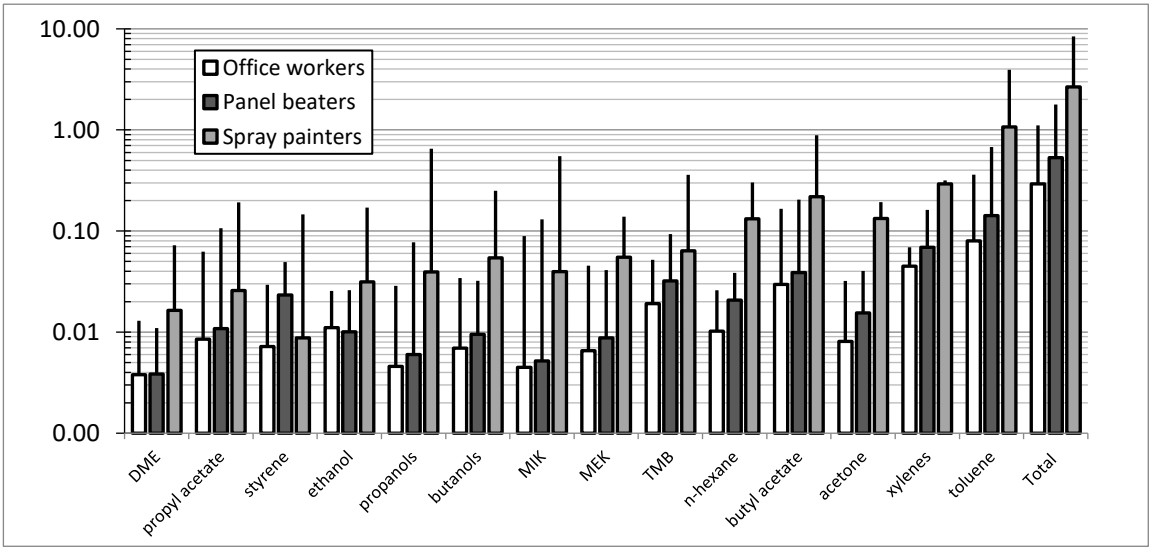
In a separate analysis we assessed the effect of time spent on each individual task (table 3.2). We initially analysed each specific task individually with and without adjusting for all other co-variables included in the previous analysis ('unadjusted' and 'adjusted' exposure ratios). Due to multicolinearity we were not able to conduct the

same analysis whilst mutually adjusting for time spent on other individual tasks. Instead we created two new variables representing the combined duration of all tasks related to spray painting and the combined duration of all other (non-spray painting) tasks. We first assessed the effect of each of these variables separately in univariate analyses ('Combined tasks', unadjusted) and then repeated the analyses including all other co-variables ('Combined tasks', adjusted). We then repeated the analyses including both combined variables ('Combined tasks – Mutually adjusted', unadjusted) and then both combined variables and all other co-variables ('Combined tasks – Mutually adjusted', adjusted; table 3.2). Finally, we repeated all analyses including only the spray painters ('Spray painters only', table 3.2).

3.3 Results

Personal total solvent exposures ranged from 0.04 – 16.5 ppm, with an overall geometric mean (GM) of 1.2 ppm. All levels were below New Zealand and international occupational exposure limits (110, 113). Exposures were highest for spray painters (GM, 2.7 ppm), followed by panel beaters (0.5 ppm) and office workers (0.3 ppm) (Figure 3.1). The highest levels were measured for toluene, xylenes, butyl acetate, n-hexane and acetone, which showed a similar exposure pattern by job title as total solvents, apart from styrene, which was highest amongst panel beaters (Figure 3.1).

Figure 3.1. Full shift geometric mean airborne specific and total solvent concentrations



DME – Dimethoxyethane, MIK – methyl isobutyl ketone, MEK – methyl ethyl ketone, TMB – trimethylbenzene
Error bars on columns indicate geometric standard deviation

Multivariate analyses showed that job title was the strongest predictor of exposure, with an ER of 5.02 (95% CI 3.11-8.10) for spray painters compared to office workers

(table 3.1). Extraction in the mixing room at the same height as the mixing bench was associated with twice the exposure compared to extraction at floor level (ER 1.89, 1.07-3.38); extraction located away from the mixing bench (i.e. on an opposite or adjacent wall) was associated with the lowest exposure levels (ER 0.51, 0.30-0.87). Exposure levels varied by paint brand used, but in general no clear trends were observed, except that “de-Beer” paints were associated with a 70% reduction in exposure levels (ER 0.27, 0.09-0.86). More time spent on all work tasks was associated with higher exposures (ER 1.03, 1.00-1.05 for every 10 minute increase, table 3.1). The analyses including only spray painters showed similar trends for all analyses.

Table 3.1. Determinants of airborne total solvent exposure

Determinant	Number of samples (%)	All collision repair workers (n=97) Unadjusted exposure ratio (95%CI) [1]	All collision repair workers (n=97) Adjusted exposure ratio (95%CI) [1, 2]	Spray painters only (n=53) Adjusted exposure ratio (95%CI) [1, 2]
Job title				
Office staff (REF)	10 (10.3)			
Panel beater	33 (34.0)	**1.60 (0.98-2.61)^**	1.33 (0.82-2.15)	-
Spray painter	54 (55.7)	**7.09 (4.44-11.32)****	**5.02 (3.11-8.10)****	-
No. employees				
<6 (REF)	17 (17.5)			
6-10	48 (49.5)	0.95 (0.34-2.66)	-	-
>10	32 (33.0)	0.82 (0.24-2.79)	-	-
Continuous	-	0.98 (0.90-1.06)	-	-
No. painters				
2 (REF)	47 (48.5)			
3	26 (26.8)	0.86 (0.38-1.96)	**0.51 (0.26-1.03)***	0.53 (0.23-1.19)^
>=4	24 (24.7)	2.08 (0.84-5.16)	1.07 (0.66-1.71)	1.22 (0.75-1.98)
Continuous	-	**1.29 (0.97-1.72)^**	1.02 (0.88-1.18)	1.1 (1.0-1.3)
Workshop volume (cubic metres)				
<1000 (REF)	27 (27.8)			
1001 - 2000	33 (34.0)	1.98 (0.93-4.23)	1.60 (0.86-2.98)	0.89 (0.44-1.82)
>2000	37 (38.1)	0.73 (0.33-1.59)	1.72 (0.88-3.37)	1.45 (0.64-3.32)
Continuous	-	1.00 (1.00-1.00)	1.0 (0.8-1.4)	1.0 (1.0-1.0)
Paint brand				
Dupont (REF)	26 (28.9)			
De Beer	5 (5.6)	0.91 (0.26-3.16)	**0.27 (0.09-0.86)***	**0.23 (0.06-0.87)***
PPG solvent-based	27 (30.0)	**2.90 (1.40-6.23)****	**1.56 (0.96-2.52)^**	1.10 (0.62-1.96)
PPG water-based	28 (31.1)	1.29 (0.61-2.74)	1.20 (0.68-2.13)	1.03 (0.48-2.21)
Spies Hecker	4 (4.4)	0.89 (0.24-3.36)	1.39 (0.0.68-2.84)	1.00 (0.42-2.39)
Paint type				
Water-based paint system (REF)	28 (28.9)			
Solvent-based paint system	69 (71.1)	1.06 (0.45-2.52)	-	-
Booth extraction				
Downdraft booth (REF)	91 (93.8)			
Non-downdraft booth	6 (6.2)	1.07 (0.30-3.80)	1.62 (0.60-4.38)	0.65 (0.22-1.92)
Mixing room extraction				
Floor level next to mixing bench (REF)	56 (58.3)			
Extraction above and next to mixing bench	16 (16.7)	1.86 (0.71-4.86)	-	-
Floor level away from mixing bench	19 (98.8)	1.28 (0.44-3.68)	-	-
Extraction above and away from mixing bench	5 (5.2)	0.63 (0.14-2.94)	-	-
Height of mixing room extraction (from floor level)				
at floor level (REF)	75 (78.1)			
Above main mixing bench	21 (21.9)	1.42 (0.60 -3.39)	**1.89 (1.07-3.38)***	**2.31 (1.17-4.55)***
Location of mixing room extraction				
Next to main mixing bench (REF)	72 (75.0)			
Away from main mixing bench	24 (25.0)	0.96 (0.37-2.48)	**0.51 (0.30-0.87)***	**0.45 (0.26-0.77)****
Gun washer extraction [3]				
In mixing room with LEV (REF)	30 (32.6)			
In mixing room without LEV	18 (19.6)	0.96 (0.41-2.24)	-	-
In workshop with LEV	25 (27.2)	1.13 (0.50-2.56)	-	-
In workshop without LEV	19 (20.7)	**2.17 (0.90-5.25)^**	-	-
Location of gun washer				
In mixing room (REF)	48 (52.2)			
In general workshop	44 (47.8)	1.38 (0.90-2.14)	1.22 (0.85-1.74)	1.42 (0.96-2.10)
Gun washer LEV status				
Dedicated LEV (REF)	55 (59.8)			
Without dedicated LEV	37 (40.2)	1.05 (0.66 – 1.68)	1.24 (0.85-1.82)	1.28 (0.87-1.89)
Measures of task duration [4]				
All tasks combined (mean 59.4 mins, range 0 – 435)	-	**1.10 (1.06-1.13)****	**1.03 (1.00-1.05)***	**1.03 (1.01-1.06)****

^ = p<0.1,* = p<0.05, ** = p<0.01,

[1] Workshop and Participant identifiers specified as random effects

[2] Adjusted for number of spray painters, workshop volume, booth extraction, paint brand, height & location of mixing room extraction, location of gun washer, gun washer LEV status and time spent on all tasks.

[3] Multiple responses possible – e.g. one workshop had two gun washers in different locations (one in workshop, one in mixing room)

[4] ERs represent difference in exposure level with every 10 minute increase in time spent on task

"-"Not applicable or not included in the multivariate analyses

Further analyses assessing the effect of each work task separately showed the strongest effects for mixing paint (ER 1.14, 1.05-1.24), spraying clear coat (ER 1.07, 1.00-1.15), spraying primer paint (ER 1.10, 0.96-1.27) and washing spray guns/equipment (ER 1.11, 0.88-1.39; table 3.2). For the combined measures of task duration, the strongest effect was observed for time spent on non-spraying tasks (ER 1.10, 1.03 – 1.18) compared to all spray painting (ER 1.03, 1.00 – 1.05). The analyses including only spray painters showed similar trends, except for those involving mutual adjustment for both combined tasks, which resulted in a weaker and non-statistically significant association for all non-spray painting tasks (1.04, 0.97-1.12).

Table 3.2. Task duration and airborne total solvent exposure

	All collision repair workers (n=97)			Spray painters only (n=53)
Task duration	**Mean minutes (range)**	**Unadjusted exposure ratio (95%CI) [1]**	**Adjusted exposure ratio (95%CI) [1, 2, 3]**	**Adjusted exposure ratio (95%CI) [1, 2, 3]**
Individual tasks [4]				
Spraying primer	6.4 (0-45)	**1.39 (1.17-1.65)****	1.10 (0.96-1.27)	1.10 (0.97-1.25)
Spraying colour (solvent)	14.7 (0-240)	**1.12 (1.05-1.18)****	**1.04 (1.00-1.08)^**	**1.05 (1.01-1.08)****
Spraying colour (water)	4.6 (0-90)	**1.22 (1.06-1.40)****	1.03 (0.94-1.13)	1.02 (0.92-1.14)
Spraying clear coat	9.3 (0-90)	**1.25 (1.14-1.38)****	**1.07 (1.00-1.15)^**	**1.06 (1.00-1.14)^**
Mixing paint	9.6 (0-90)	**1.38 (1.38-1.53)****	**1.14 (1.05-1.24)****	**1.11 (1.04-1.20)****
Gun washing	4.1 (0-30)	**1.93 (1.52-2.47)****	1.11 (0.88-1.39)	1.01 (0.81-1.28)
Degreasing panels	10.6 (0-60)	**1.46 (1.28-1.65)****	1.01 (0.89-1.15)	0.96 (0.86-1.08)
Combined tasks [4]				
All Spray painting combined	35.0 (0-345)	**1.10 (1.06-1.13)****	**1.03 (1.00-1.05)***	**1.03 (1.01-1.06)****
All non-spray painting tasks combined	24.4 (0-115)	**1.26 (1.20-1.33)****	**1.10 (1.03-1.18)****	**1.08 (1.02-1.15)***
Combined tasks – mutually adjusted [5]				
All Spray painting combined	35.0 (0-345)	1.01 (0.97-1.05)	1.01 (0.98-1.04)	**1.03 (1.00-1.05)^**
All non-spray painting tasks combined	24.4 (0-115)	**1.25 (1.16-1.33)****	**1.08 (1.00-1.17)***	1.04 (0.97-1.12)

^ = p<0.1,* = p<0.05, ** = p<0.01

[1] Workshop and Participant identifiers specified as random effects

[2] ERs represent difference in exposure level with every 10 minute increase in time spent on task

[3] Adjusted for number of spray painters, workshop volume, booth extraction, paint brand, height & location of mixing room extraction, location of gun washer and gun washer LEV status.

[4] Each task duration measure was analysed separately i.e. no mutual adjustment for other tasks was conducted

[5] Analyses mutually adjusted for the other combined task variable

Video Exposure Monitoring

The first VEM observation (figure 3.2) showed repeated and sustained peaks in solvent levels of 10-60 ppm during paint mixing, with infrequent peaks of 80-160 ppm. Exposures during painting in the downdraft booth were below the PID's limit of detection (0.1 ppm). The highest peak (around 270 ppm) was observed during decanting of paint thinners from a larger drum into a mixing vessel. For the second observation (figure 3.3), the subject was required to stand directly between the vehicle being painted and the wall-mounted extraction source, thus spraying against the direction of air flow. This resulted in brief peaks of around 300ppm. A series of peaks of 10-100 ppm were also observed during spray gun and equipment cleaning involving both the gun washer and hand cleaning. The third VEM observation (figure 3.4) showed peak exposures of up to 900-1150 ppm associated with gun cleaning.

Figure 3.2. VEM observation 1 – Mixing and decanting paint and thinners and spray-painting in a downdraft spray booth

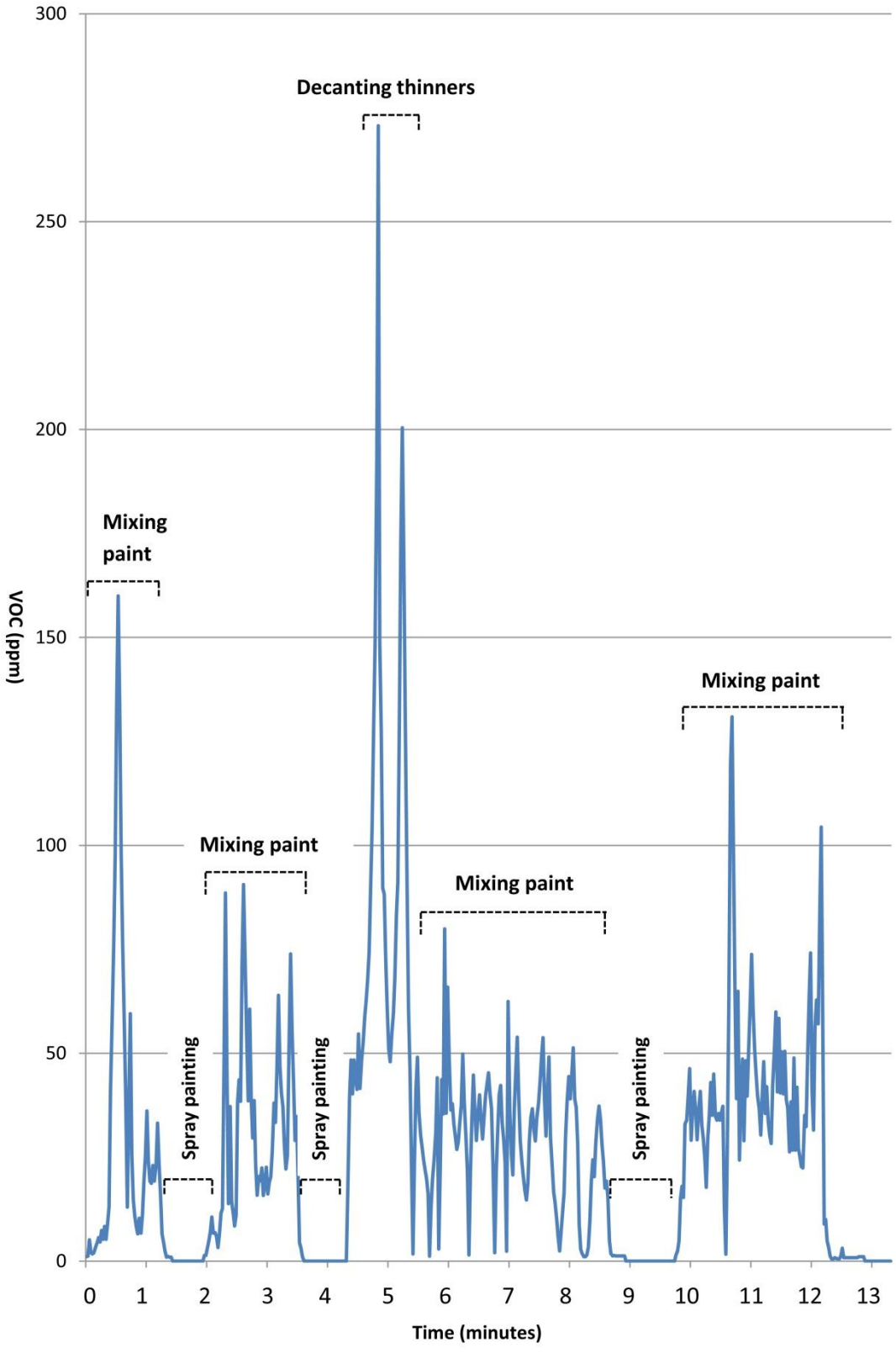


Figure 3.3. VEM observation 2 – Spray painting in a cross-draft booth and cleaning spray equipment in a gun washer with dedicated LEV

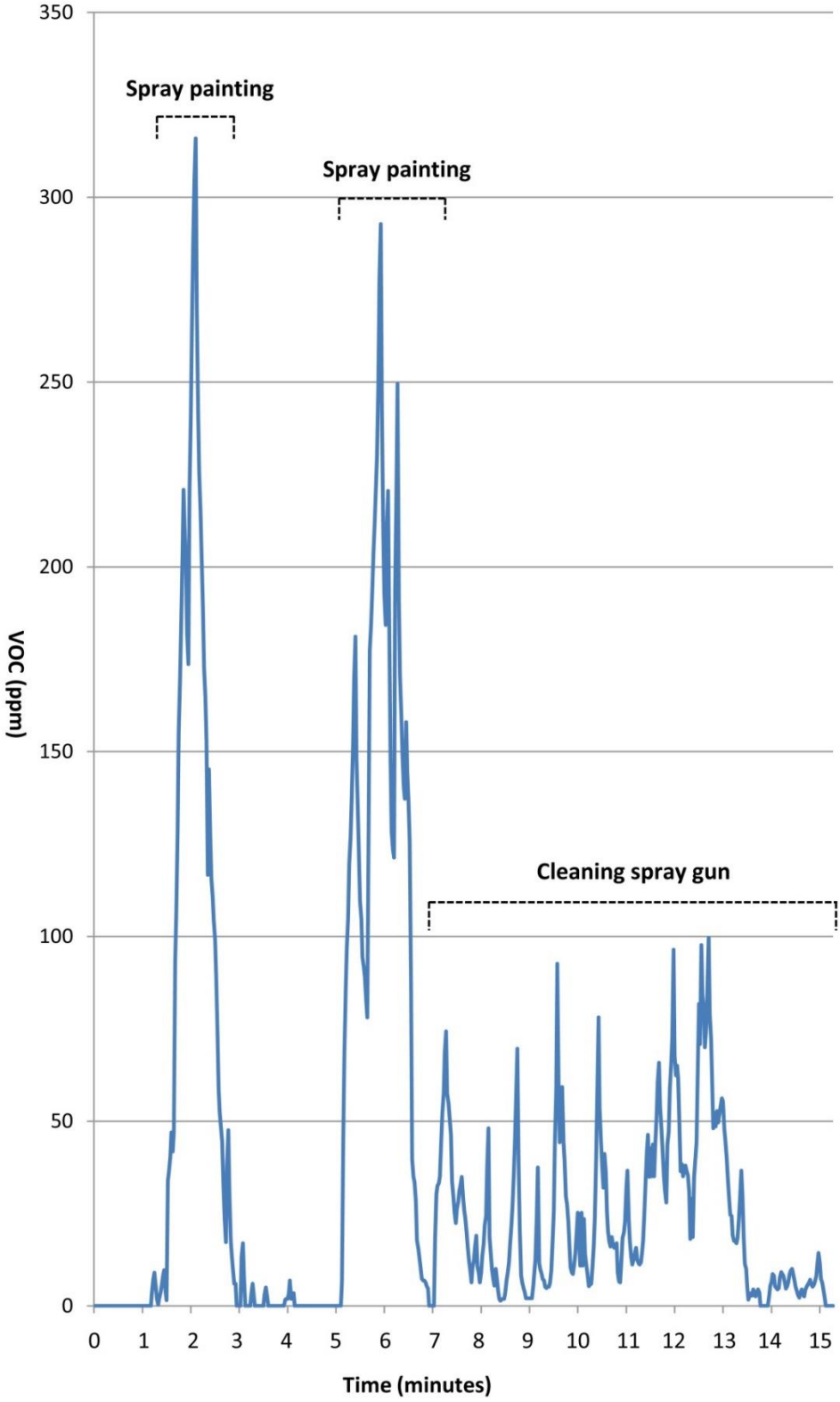
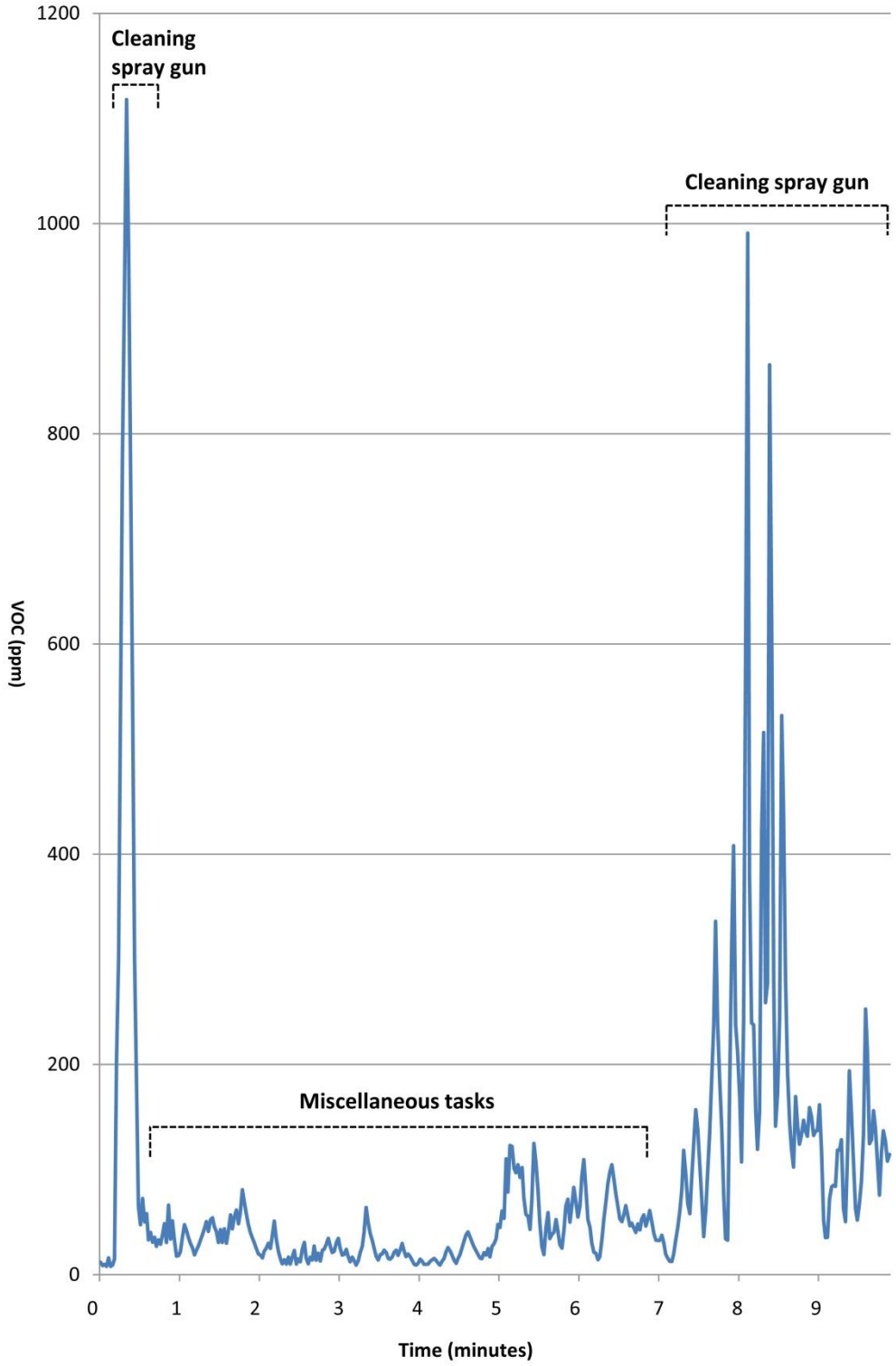


Figure 3.4. VEM observation 3 – Cleaning spray equipment in an open-sided gun washer with dedicated LEV and performing other miscellaneous tasks in a paint mixing room



3.4 Discussion

Although airborne solvent levels were generally low, significant differences were found between job titles and workshop characteristics. In particular, as expected, working as a spray painter was associated with the highest exposure. Other factors, such as the brand of paint used, type and positioning of exhaust ventilation, the use of gun washing equipment, and time spent conducting preparatory and cleaning tasks also affected exposure levels. VEM observations showed peak exposures for paint mixing, decanting of solvents, cleaning of spray equipment and spray painting in a cross-draft booth.

Average airborne solvent exposures were comparable to those observed in other more recent studies (100), and well below both New Zealand and international workplace exposure standards (110), although peaks of 30-1100ppm during certain tasks were measured (Figures 3.2-3.4). Nonetheless, despite low average airborne exposures, we have previously shown significantly increased risks of neurotoxicity in this group of workers (331, 332). This may be because dermal exposures, which we were unable to measure, may be of particular importance (26). Also, although peak exposures are intermittent and contribute little to full-shift average exposures, they may act as a "tipping point" in the development of neurotoxicity and may be stronger predictors of the risk of short and long-term health effects than cumulative mean exposures (28).

Solvent exposure patterns by job title were similar for all individual solvents (with highest levels in spray painters followed by panel beaters and office workers), except

for styrene, which was on average higher for panel beaters. This is likely related to panel beaters regularly using polyester-based resins (for repairing damaged bodywork), which contain 10-20% (w/w) of styrene.

A larger shop volume was associated with higher exposures (not statistically significant). This differs from previous studies, which showed lower exposures in larger workshops where agents may be less likely to concentrate and equipment may be newer and/or better maintained (14, 136). In these studies crowding was also positively associated with solvent levels. We conducted the same analysis, but were unable to replicate this finding (data not shown).

Several studies have shown that cross-draft booths may be inferior in reducing solvent exposure compared to downdraft booths (14, 136, 139). We found the same, but our finding was not statistically significant (p=0.29). VEM showed that cross-draft booths required workers, at times, to stand between the object being painted and the extraction source (figure 2b) which may explain the inferior performance observed in other studies (14).

Extraction located above the height of the main mixing bench was associated with higher exposure (ER 1.89, 95% CI 1.07-3.38), and extraction at the opposite or adjacent wall from the bench with lower exposure (ER 0.51, 0.30-0.87; table 3.1). Previous studies in other industries have also shown that the arrangement of exhaust ventilation may have considerable effects on exposure (125, 345).

As expected, and shown by others (14, 100, 127), more time spent on work tasks such as spray painting and mixing paint was associated with higher airborne solvent

exposures. However, associations were generally stronger for non-spraying tasks (mixing paint, degreasing, cleaning equipment) (table 3.2). This is consistent with results from a Finnish study (100), which showed tasks conducted outside the spray booth may contribute more to the overall solvent exposure. Our VEM observations also showed that the highest and most frequent peaks occurred during paint mixing and gun cleaning (figure 2a and figure 2c) rather than spray painting. However, when analyses of full shift exposure levels were restricted to only spray painters, the effect for time spent on non-spray painting tasks was no longer significant. Non-spray painting tasks may therefore particularly contribute to 'bystander' exposures in panel beaters and office staff and less to exposure of spray painters.

No significant difference in exposure was observed between shops equipped with water-based paint systems and solvent-only systems. This differs from a Finnish study (100), which showed that use of solvent-based paints was associated with levels three-times higher than water-based paints. It is unclear why our findings differ, but it may reflect the small sample size and the fact that spray painting in general seemed to contribute less to exposure levels than non-spraying tasks.

Total summed solvent concentrations as used in our analyses do not account for variations in the relative toxicity of the individual compounds. We therefore repeated the analyses using 'Additive Limit Values' (ALV), which use a weighted sum approach based on each components' relative toxicity as reflected by its workplace exposure standard (110). This did not significantly alter the results (supplementary tables 3.3 and 3.4). Conclusions therefore equally apply to ALV solvent concentrations.

Limitations

We observed significant collinearity between some tasks and/or workshop characteristics. To control for this we aggregated some variables, which meant we were not able to assess the effects for each independently. Exposure assessment for each worker was generally conducted on a single work day and as a result the solvent levels measured may not be entirely representative. However, exposure monitoring was conducted randomly throughout the working week (Monday-Friday) for 8 months, so likely covered most work conditions.

Personal exposures were not measured inside respiratory protection; the levels reported are therefore likely to be an over estimation (100). However, our field observations suggest that respirators were usually only worn when spray painting inside the booth, where airborne solvent levels were low, as shown in the VEM observations. The degree of overestimation is therefore likely to be low, particularly as spray painters only spent an average of 7% of their work shift spray painting inside the booth.

The SYFT-MS method used for analysis was not accredited; however, the instrument and analytical techniques used have been validated and published widely in the literature (105-108, 338).

We did not collect data on the quantity of paint used during the sampling period or on individual painting jobs, which is likely to be an important exposure determinant (14, 136). However, previous studies have shown that assessment of the time spent on tasks is a valid indicator of work load and therefore paint/product use (14).

There are also limitations to the VEM method. Prior emissions can obscure the relationship between current task and exposure, as can activities being conducted nearby which are not being observed (123). Also, PIDs are not compound-specific and may provide different readings for different solvents, although, average concentrations of solvent mixtures obtained from PIDs often correlate highly (r^2=0.95) with those using traditional methods (86). Furthermore, VEM was only available for a small number of observations, and some peaks may therefore have been missed.

Finally, we were unable to take into account other potential determinants, such as variations in equipment design (e.g. spray guns), application of administrative controls, worker training, or economic and workload factors, all of which may affect worker exposures (14, 136). However, the analyses were adjusted for workshop ID, taking into account potential variations in these factors between workshops.

In conclusion, the current study showed that personal airborne solvent exposures in the collision repair industry were associated with job title, the location of exhaust ventilation and emission sources, the paint products used and time spent on tasks where exposures are likely to occur, particularly non-spray painting tasks such as paint mixing and washing equipment with solvents. These findings provide a contemporary basis for future intervention, but further investigation, particularly of dermal exposure, is required to maximise their efficacy.

Acknowledgements

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3.5 Supplementary material

Table 3.3. Supplementary table. Determinants of airborne total solvent exposure – Additive Limit Value concentrations of all solvents detected

		All collision repair workers (n=97)		Spray painters only (n=53)
Determinant	Number of samples (%)	Unadjusted exposure ratio (95%CI) [1]	Adjusted exposure ratio (95%CI) [1, 2]	Adjusted exposure ratio (95%CI) [1, 2]
Job title				
Office staff (REF)	10 (10.3)			
Panel beater	33 (34.0)	**1.70 (0.98-2.60)^**	1.42 (0.84-2.40)	-
Spray painter	54 (55.7)	**7.22 (4.31-12.09)****	**4.67 (2.69-8.09)****	-
No. employees				
<6 (REF)	17 (17.5)			
6-10	48 (49.5)	0.88 (0.30-2.58)	-	-
>10	32 (33.0)	0.77 (0.21-2.82)	-	-
Continuous	-	0.97 (0.89-1.06)	-	-
No. painters				
2 (REF)	47 (48.5)			
3	26 (26.8)	0.83 (0.34-1.99)	**0.48 (0.22-1.01)^**	**0.36 (0.15-0.89)***
>=4	24 (24.7)	2.19 (0.83-5.75)	1.14 (0.68-1.93)	1.29 (0.75-2.19)
Continuous	-	**1.31 (0.97-1.79)^**	1.09 (0.90-1.34)	1.13 (0.96-1.33)
Workshop volume (cubic metres)				
<1000 (REF)	27 (27.8)			
1001 - 2000	33 (34.0)	1.94 (0.86-4.38)	1.53 (0.78-3.01)	1.03 (0.48-2.20)
>2000	37 (38.1)	0.68 (0.29-1.59)	1.62 (0.78-3.37)	1.91 (0.79-4.65)
Continuous	-	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Paint brand				
Dupont (REF)	26 (28.9)			
De Beer	5 (5.6)	0.74 (0.20-2.75)	**0.18 (0.05-0.65)****	**0.11 (0.02-0.45)****
PPG solvent-based	27 (30.0)	**3.36 (1.53-7.37)****	**1.86 (1.10-3.16)***	1.21 (0.66-2.23)
PPG water-based	28 (31.1)	1.39 (0.63-3.09)	1.27 (0.67-2.40)	0.92 (0.40-2.12)
Spies Hecker	4 (4.4)	0.84 (0.21-3.38)	1.46 (0.66-3.20)	0.99 (0.38-2.59)
Paint type				
Water-based paint system (REF)	28 (28.9)			
Solvent-based paint system	69 (71.1)	1.04 (0.41-2.61)	-	-
Booth extraction				
Downdraft booth (REF)	91 (93.8)			
Non-downdraft booth	6 (6.2)	1.04 (0.27-3.96)	1.30 (0.44-3.90)	0.44 (0.13-1.45)
Mixing room extraction				
Floor level next to mixing bench (REF)	56 (58.3)			
Extraction above and next to mixing bench	16 (16.7)	1.79 (0.63-5.03)	-	-
Floor level away from mixing bench	19 (98.8)	1.26 (0.40-4.00)	-	-
Extraction above and away from mixing bench	5 (5.2)	0.74 (0.14-3.90)	-	-
Height of mixing room extraction (from floor level)				
at floor level (REF)	75 (78.1)			
Above main mixing bench	21 (21.9)	1.43 (0.57-3.62)	**2.28 (1.21-4.29)***	**3.57 (1.73-7.37)****
Location of mixing room extraction				
Next to main mixing bench (REF)	72 (75.0)			
Away from main mixing bench	24 (25.0)	1.00 (0.36-2.76)	**0.47 (0.27-0.84)***	**0.39 (0.22-0.69)****
Gun washer extraction [3]				
In mixing room with LEV (REF)	30 (32.6)			
In mixing room without LEV	18 (19.6)	0.97 (0.39-2.41)	-	-
In workshop with LEV	25 (27.2)	1.19 (0.49-2.88)	-	-
In workshop without LEV	19 (20.7)	**2.23 (0.86-5.79)^**	-	-
Location of gun washer				
In mixing room (REF)	48 (52.2)			
In general workshop	44 (47.8)	1.40 (0.91-2.17)	1.20 (0.82-1.78)	1.31 (0.84-2.05)
Gun washer LEV status				
Dedicated LEV (REF)	55 (59.8)			
Without dedicated LEV	37 (40.2)	1.00 (0.62-1.59)	1.27 (0.84-1.93)	1.38 (0.88-2.14)
Measures of task duration [4]				
All tasks combined (mean 59.4 mins, range 0 – 435)	-	**1.09 (1.05-1.13)****	**1.02 (1.00-1.05)***	**1.02 (1.00-1.04)***

^ = p<0.1,* = p<0.05, ** = p<0.01,

[1] Workshop and Participant identifiers specified as random effects

[2] Adjusted for number of spray painters, workshop volume, booth extraction, paint brand, height & location of mixing room extraction, location of gun washer, gun washer LEV status and time spent on all tasks.

[3] Multiple responses possible – e.g. one workshop had two gun washers in different locations (one in workshop, one in mixing room)

[4] ERs represent difference in exposure level with every 10 minute increase in time spent on task

"-"Not applicable or not included in the multivariate analyses

Table 3.4. Supplementary table - Task duration and airborne total solvent exposure expressed as Additive Limit Values

		All collision repair workers (n=97)		Spray painters only (n=53)
Task duration	**Mean minutes (range)**	**Unadjusted exposure ratio (95%CI) [1]**	**Adjusted exposure ratio (95%CI) [1, 2, 3]**	**Adjusted exposure ratio (95%CI) [1, 2, 3]**
Individual tasks [4]				
Spraying primer	6.4 (0-45)	**1.37 (1.14-1.64)****	1.09 (0.94-1.27)	1.09 (0.95-1.26)
Spraying colour (solvent)	14.7 (0-240)	**1.11 (1.04-1.18)****	1.03 (0.98-1.07)	**1.04 (1.00-1.08)***
Spraying colour (water)	4.6 (0-90)	**1.21 (1.05-1.39)****	1.03(0.92-1.14)	1.00 (0.88-1.12)
Spraying clear coat	9.3 (0-90)	**1.23 (1.12-1.37)****	1.05 (0.98-1.14)	**1.04 (0.97 -1.12)***
Mixing paint	9.6 (0-90)	**1.36 (1.23-1.51)****	**1.13 (1.03-1.23)***	**1.09 (1.01-1.18)***
Gun washing	4.1 (0-30)	**1.86 (1.44-2.41)****	1.07 (0.83-1.37)	0.99 (0.77-1.27)
Degreasing panels	10.6 (0-60)	**1.44 (1.26-1.65)****	1.01 (0.88-1.16)	0.94 (0.84-1.06)
Combined tasks [4]				
All Spray painting combined	35.0 (0-345)	**1.09 (1.05-1.13)****	1.02 (0.99-1.05)	**1.02 (1.00-1.05)^**
All non-spray painting tasks combined	24.4 (0-115)	**1.25 (1.18-1.32)****	**1.09 (1.01-1.17)***	**1.06 (0.99-1.13)^**
Combined tasks – mutually adjusted [5]				
All Spray painting combined	35.0 (0-345)	1.01 (0.97-1.05)	1.01 (0.98-1.04)	1.02 (0.99-1.05)
All non-spray painting tasks combined	24.4 (0-115)	**1.24 (1.15-1.33)****	**1.08 (0.99-1.17)^**	1.03 (0.96-1.11)

^ = p<0.1,* = p<0.05, ** = p<0.01

[1] Workshop and Participant identifiers specified as random effects

[2] ERs represent difference in exposure level with every 10 minute increase in time spent on task

[3] Adjusted for number of spray painters, workshop volume, booth extraction, paint brand, height & location of mixing room extraction, location of gun washer and gun washer LEV status.

[4] Each task duration measure was analysed separately i.e. no mutual adjustment for other tasks was conducted

[5] Analyses mutually adjusted for the other combined task variable

4 Solvent neurotoxicity in vehicle collision repair workers in New Zealand

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Objectives: To assess whether solvent use and workplace practices in the vehicle collision repair industry are associated with symptoms of neurotoxicity in spray painters and panel beaters (auto body repair workers).

Methods: Neurobehavioural symptoms were assessed using a cross-sectional study design in 370 vehicle collision repair and 211 reference workers using the EUROQUEST questionnaire. Full-shift airborne solvent levels were measured in a subset (n=92) of collision repair workers.

Results: Solvent exposures were higher in spray painters than in panel beaters, but levels were below current international exposure standards. Collision repair workers were more likely to report symptoms of neurotoxicity than reference workers with ORs of 2.0, 2.4 and 6.4 (all $p<0.05$) for reporting ≥ 5, ≥ 10 and ≥ 15 symptoms respectively. This trend was generally strongest for panel beaters (ORs of 2.1, 3.3 and 8.2 for ≥ 5, ≥ 10 and ≥ 15 symptoms respectively). Associations with specific symptom domains showed increased risks for neurological (OR 4.2), psychosomatic (OR 3.2), mood (OR 2.1), memory (OR 2.9) and memory and concentration symptoms combined (OR 2.4; all $p<0.05$). Workers who had worked for 10-19 years or 20+ years in the collision repair industry reported consistently more symptoms than those who had only worked less than 10 years even after adjusting for age. However, those who worked more than 20 years generally reported fewer symptoms than those who worked 10-19 years, suggesting a possible healthy worker survivor bias.

Conclusions: Despite low airborne solvent exposures, vehicle collision repair spray painters and panel beaters continue to be at risk of symptoms of neurotoxicity.

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4.1 Introduction

Acute health effects of occupational exposure to solvents (e.g. headaches, nausea and light-headedness) have long been recognised, with high exposures associated with intoxication, unconsciousness and in some cases death (39). Chronic effects such as sustained changes in mood, memory, concentration and cognitive deficits have also been documented, in some cases leading to a diagnosis of Chronic Solvent Neurotoxicity (CSN) or Chronic Toxic Encephalopathy (CTE) (2, 7, 12, 39, 172). Among those with CSN, industrial and automotive repair spray painters are consistently over-represented (10). Spray painting involves the use of large quantities of solvent mixes for preparation work, cleaning of refurbished panels, and thinning of paint. This and the subsequent spraying of solvent-containing paints may result in elevated solvent exposure through both inhalation and dermal absorption (39).

Several cross-sectional studies since the 1970s have shown symptoms of neurotoxicity in spray painters and other solvent-exposed workers (18, 19, 45, 72, 326), but findings have not always been consistent (20, 69, 162). Dose-response associations have been reported (346) but are often weak, possibly due to the 'healthy worker survivor bias' (16). Also, previous studies have often been conducted in larger enterprises where workplace hygiene and hazards are likely to be managed more effectively (45, 46) and studies were not always adequately controlled for potential confounders (16, 70, 297).

Significant changes in paint formulations, solvent use and workplace practices have occurred in this industry in the past few decades which, as suggested recently (13), may have resulted in a significant decline in workplace solvent exposures. However,

little research has been conducted to confirm this and it is also unclear whether this has contributed to a significantly reduced risk of neurotoxicity in collision repair workers. In the current study, collision repair industry workers (n=370) from small to medium workshops, and a reference group of construction industry workers (n=211) in New Zealand were recruited to assess contemporary solvent exposures and associated neurotoxicity risks.

4.2 Methods

Study Population

The study population was recruited from collision repair workshops throughout the North Island of New Zealand, with a focus on the main centres (Wellington and Auckland). Workshops were identified from the Yellow Pages and internet searches and approached on an ongoing basis until the desired sample size was reached. This figure (400 collision repair workers, 200 reference workers) was derived from an estimation based on previous studies that around 15-20% of the collision repair workforce was likely to have neurobehavioural symptoms compared with less than 5% of the comparison group. This gave the study a 90-99% power to detect a two to three-fold difference (i.e. 10-15% vs 5%). In total 175 workshops each employing between 2 and 15 staff were recruited.

All staff aged between 17-70 years were invited to take part, including spray painters, panel beaters (or auto body repair workers) and office staff with a history of work as a spray painter or panel beater. This last group were all ex-tradesmen and were recoded as a spray painter or panel beater accordingly, which more accurately reflected their working life exposure. Exclusion criteria were no history of work involving solvent exposure or any history of major head injury or neurological/neurodegenerative disease, including meningitis, major depression or epilepsy. Collision repair workers who declined participation were invited to complete a short questionnaire assessing key demographic factors. A reference group of construction workers from various trades (scaffolders, carpenters, electricians, builders and building labourers, fire safety

system installers, plumbers and associated management staff) with negligible/no exposure to solvents was recruited in the same regions using a similar strategy and exclusion criteria.

Questionnaire

Information on demographics, work characteristics, use of solvents and solvent-based products and potential confounders was obtained for all participants by questionnaire. Current (i.e. in the past 3 months) symptoms of neurotoxicity were measured using an adapted version of the EUROQUEST (232) questionnaire, administered face-to-face. The questionnaire consists of 59 core items, which cover the following symptom domains: neurological (e.g. numbness and tingling in extremities, balance problems), psychosomatic (e.g. headaches, nausea, tinnitus), mood, memory, concentration, fatigue and sleep quality. EUROQUEST also includes questions on symptoms of acute exposure (irritation of the mucosal membranes and intoxication, 6 items). Symptom frequency for these and the 59 core symptoms in recent months was reported on a 4-point scale, "seldom or never", "sometimes", "often" or "very often". Questions regarding sensitivity to environmental conditions (6 items, e.g., *"Are you sensitive to bright lights?"*) and anxiety (6 items, e.g., *"Are you generally a nervous person?"*) were also included and rated on a different 4-point scale ("strongly disagree", "disagree", "agree" or "strongly agree"). The final section of the EUROQUEST assesses perceived general health (4 items), where participants are asked to rate different aspects of their general health and wellness as "very good" "good", "poor" or "very poor". For the purpose of subsequent analyses we dichotomised symptoms, with "strongly disagree"

or “disagree”, “seldom or never” or “sometimes”, and “poor” or “very poor” constituting a negative response and “agree” or “strongly agree”, “often” or “very often”, “very good” and “good” constituting a positive response (175). Anxiety (6 items, e.g., “*Are you generally a nervous person?”)* and perceived general health (4 items, e.g., *“how good is your health?”)* were included to enable us to control the analyses for individual personality traits which have been found to lead participants to under or over report their symptoms (175). Responses to these questions were aggregated to produce a total ‘score’ for each domain.

Exposure assessment

Full-shift airborne personal exposure measurements were conducted with a random sample of workers from 17 collision repair workshops representative of the 175 involved using a whole-air method (64); these included 50 spray painters and 36 panel beaters. We also included a small group of office workers (n=6) with no history of spray painting or panel beating (these workers were not included in the questionnaire survey). Teflon tubing running from the workers breathing zone was connected to a 400cc stainless steel sampling canister (Restek Corporation, PA, USA) negatively pressurised to near full vacuum (-30 mmHg). A flow controller (Restek Corporation, PA, USA) was used to maintain a flow rate of 0.9 ml/min and sampling was stopped when air pressure in the canisters reached between -5 and -3 mmHg. Samples were analysed using Selected Ion Flow Tube Mass Spectrometry, or SIFT-MS (Syft Technologies, Christchurch, NZ) for toluene, xylene, styrene, acetone, methyl and ethyl-acetates, butanols and propanols, benzenes, hexanes, methyl ethyl ketone and

ethanol, the method of which has been described in detail elsewhere (59). The limit of detection was 5 parts per billion (ppb) and samples below this limit were assigned a value of 2.5 ppb. Exposure measurements were analysed by aggregating the concentrations of the individual compounds detected. In addition, the additive limit value (ALV) was calculated by assigning a weight to each individual compound detected, based upon its relative workplace exposure standard (American Governmental Conference of Industrial Hygienists' Threshold Limit Values (110)), and summing these values together. Where the ALV was >1, it was deemed that the exposure standard for that combination of compounds had been exceeded (110).

Statistical analyses

All statistical analyses were conducted using Stata version 13.1 (StataCorp LP, Texas, USA). As exposure data were not normally distributed we used geometric mean concentrations and standard deviations to summarise exposures for each of the collision repair groups (office staff, spray painters and panel beaters). Symptoms of neurotoxicity were initially grouped on the basis of the total number of positive symptoms reported, i.e. ≥5, ≥10, or ≥15. For symptoms clustered in specific domains (described above) we used a cut-point of ≥3 positive symptoms, which is an approach previously shown to be highly sensitive and specific in the classification of CSN patients (175). Also, an additional domain of memory and concentration symptoms combined was created for the same reason.

Prevalence ORs comparing symptoms between collision repair workers and the reference population were calculated using logistic regression. All analyses were adjusted for age, ethnicity, smoking, alcohol consumption, education status and personality trait score (175). Other potential confounders including sleep quality, chronic diseases (e.g., diabetes), head injuries, concussion, chronic fatigue, prescription drug use and pre-existing health issues were also considered, but these did not appreciably affect the observed associations. Sensitivity analyses were conducted excluding reference workers who reported some exposure to solvents.

The effect of work duration was assessed by dividing collision repair workers into tertiles, and these were then 'rounded off' to the nearest unit of work duration i.e. those who had worked in the industry for less than 10 years (average of 5.4 years; range 0.3 – 10.4), 10-19 years (average 14.8 years (10.4 – 21.0)), and more than 20 years (average 31.3 years (21.0 – 50.0)). Due to the high correlation of age with employment duration (Spearman's correlation coefficient = 0.89) and the resulting potential for multicolinearity, a second regression model was produced which controlled for all confounders except age, in order to assess any effect this may have had on the risk estimates (supplementary table 4.8).

4.3 Results

The response rates for the collision repair workers and the reference population were 69% and 64% respectively. Of the 399 collision repair workers who agreed to participate, seven fulfilled the exclusion criteria. Three of the 223 reference workers were excluded for previously working as spray painters. Additionally, 20 collision repair workers and four reference group workers were unable to complete the interview. Seven current panel beaters reported having previously worked for extended periods as a spray painter, so were recoded as such, as this more accurately reflected their working life exposure. Women (two spray painters and one reference worker) were also excluded due to low numbers. Also, age data was missing for 4 reference workers. Complete data was therefore available for 370 collision repair workers (234 spray painters, 90 panel beaters and 46 office workers who were previously employed in either role) and 211 reference workers.

Fifty-three collision repair workers who declined to participate completed the non-respondent questionnaire. No appreciable differences were found between those who participated and those who declined in general population characteristics including age (38.6 yrs vs 36.7 yrs), ethnicity (Māori, 13.2%; Pacific, 13.2%; Other, 73.6% vs 13.5%; 8.1%; and 78.4%, respectively) smoking habits (non-smokers, 41.5%; ex-smokers, 26.4%; current smokers, 32.1% vs 41.2%; 21.8%; and 37.0%, respectively).

Collision repair workers included a higher proportion of Māori, were marginally older, smoked less, and consumed less alcohol than the reference group. Fewer had completed a tertiary degree than the reference group, and they also scored higher on

the personality trait scales (table 4.1). All analyses therefore controlled for these factors. Within the collision repair group, panel beaters were slightly older and had a higher proportion of Pacific people than spray painters (table 4.1).

Table 4.1. Demographic and work characteristics of study participants

	Reference workers (n=211)		All Collision repair (n=370)		Panel beaters (n=103)		Spray painters (n=267)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ethnicity								
Maori	68	32.2	50	13.5	13	12.6	37	13.9
Pacific	23	10.9	30	8.1	13	12.6	17	6.4
Other (incl. NZ European)	120	56.9	290	78.4	77	74.7	213	80.8
Smoking Status								
Non-smoker	87	41.2	151	40.8	39	37.9	112	42.0
Ex-smoker	46	21.8	109	29.5	34	33.0	76	28.5
Current smoker	78	37.0	110	29.7	30	29.1	79	29.6
Education level								
primary	4	1.9	10	2.7	5	4.8	5	1.9
secondary	141	66.8	261	70.5	67	65.0	194	72.7
trade cert.	50	23.7	85	22.9	27	26.2	58	21.7
Tertiary	16	7.6	14	3.7	4	3.9	10	3.7
	Mean	**Range**	**Mean**	**Range**	**Mean**	**Range**	**Mean**	**Range**
Age	36.3	17-66	36.7	17-64	38.5	20-63	36.0	17-64
Alcohol (Mean drinks per week)	15.7	0-120	13.5	0-140	13.9	0-106	13.4	0-140
Duration of employment (Years)	-	-	17.0	0.3 - 50	18.1	1 - 47.4	16.6	0.3 - 50
EUROQUEST personality score	0.69	(0 – 5)	0.79	(0 – 6)	0.77	(0 – 6)	0.80	(0 – 6)

The majority of exposure measurements showed detectable levels of toluene, xylene, acetone and butyl acetate, with a smaller proportion also indicating the presence of hexane, methyl ethyl ketone, and methyl isobutyl ketone (data not shown). Overall, airborne solvent concentrations were low and below the American Conference of Governmental and Industrial Hygienists' TLVs (ACGIH, TLVs) (110). Solvent levels were highest in spray painters (geometric mean combined solvent level of 2.26 ppm) followed by panel beaters (0.57 ppm) and office staff (0.19 ppm; table 4.2). The additive limit values for the solvent mixtures were also generally low (table 4.2).

Table 4.2. Full shift whole-air concentrations of all solvents detected combined (geometric means), including Additive Limit Value (ALV) calculation

	Office workers (n=6)	**Panel Beaters (n=36)**	**Spray Painters (n=50)**
Total Hydrocarbons (ppm)	Mean (SD)	Mean (SD)	Mean (SD)
Geometric Mean (Geometric SD)	0.19 (2.1)	0.57 (2.4)	2.26 (2.6)
Range	0.1 - 0.6	0.1 - 2.5	0.1 - 16.6
ALV calculated from ACGIH TLV's			
Mean (SD)	0.04 (0.01)	0.06 (0.03)	0.15 (0.12)
Range	0.03 - 0.06	0.04 - 0.13	0.03 - 0.70

Collision repair workers reported significantly more symptoms of neurotoxicity than reference workers with ORs of 2.0 (95% CI, 1.3 – 3.3), 2.4 (1.2 – 4.8) and 6.4 (1.8 – 23.0) for reporting ≥5, ≥10 and ≥15 symptoms respectively (table 4.3). Associations with specific symptom domains (using cut-points of ≥ 3 positive symptoms) showed increased risks for neurological (OR 4.2, 95% CI, 1.2 – 15.3), psychosomatic (OR 3.2, 1.2 – 9.1), mood (OR 2.1, 1.0 – 4.3), memory symptoms (OR 2.9, 1.2 – 7.0), and combined memory and concentration symptoms (OR 2.4, 1.2 – 4.8, table 4.3). Generally, the strongest associations were observed in panel beaters. Highly comparable results were found when different cut-offs were used (e.g., ≥2 or ≥4 symptoms; supplementary table 4.7). The analyses by employment duration were based on small numbers in some strata but showed that workers with medium employment duration reported the greatest number of symptoms followed by those with the longest employment duration. Those with the shortest employment duration had the least number of symptoms, but they still reported more symptoms than the reference population (table 4.4). Using alternative stratifications (i.e., using quartiles, quintiles) did not significantly alter the results (supplementary table 4.6).

Adjusting for age altered the standard error for some outcomes, but the effect on risk estimates and trends was negligible when compared to the model excluding age (supplementary table 4.8). We also repeated all analyses excluding current office workers (who previously worked as a spray painter/panel beater, supplementary table 4.9) and excluding the seven panel beaters recoded as spray painters based on their work history (supplementary table 4.10), neither of which affected the results.

Table 4.3. Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms between reference workers and collision repair workers

	Reference (n=211)	All CR workers (n=370)		Panel Beaters (n=103)		Spray Painters (n=267)	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.9)	184 (49.7)	**1.6 (1.1 - 2.3)**	51 (49.5)	1.6 (0.9-2.8)	133 (49.8)	**1.5 (1.0-2.3)**
≥ 5 symptoms	48 (22.7)	140 (37.8)	**2.0 (1.3 – 3.3)**	41 (39.8)	**2.1 (1.2-3.8)**	99 (37.1)	**1.9 (1.2-3.1)**
≥ 10 symptoms	14 (6.6)	54 (14.6)	**2.4 (1.2 - 4.8)**	19 (18.5)	**3.3 (1.4-7.8)**	35 (13.1)	**2.1 (1.0-4.6)**
≥ 15 symptoms	4 (1.9)	28 (7.6)	**6.4 (1.8 - 23.0)**	11 (10.6)	**8.2 (2.2-31.0)**	17 (6.4)	**6.3 (1.5-27.4)**
Symptom domains							
≥ 3 Neurological	3 (1.4)	19 (5.1)	**4.2 (1.2 - 15.3)**	8 (7.8)	**5.4 (1.3-22.6)**	11 (4.1)	3.2 (0.8-13.2)
≥ 3 Psychosomatic	6 (2.8)	27 (7.3)	**3.2 (1.2 - 9.1)**	10 (9.7)	**4.1 (1.3-13.2)**	17 (6.4)	2.5 (0.8-7.6)
≥ 3 Mood	12 (5.7)	45 (12.2)	**2.1 (1.0 - 4.3)**	14 (13.6)	**2.7 (1.1-6.7)**	31 (11.6)	1.9 (0.9-4.2)
≥ 3 Memory	7 (3.3)	37 (10.0)	**2.9 (1.2 - 7.0)**	16 (15.5)	**5.9 (2.1-16.8)**	21 (7.9)	1.9 (0.9-4.0)
≥ 3 Concentration	1 (0.5)	5 (1.4)	3.3 (0.2 - 48.7)	1 (1.0)	1.7 (0.1-50.3)	4 (1.5)	3.9 (0.3-59.2)
≥ 3 Fatigue	20 (9.5)	48 (12.9)	1.4 (0.7 - 2.5)	13 (12.6)	1.2 (0.5-2.8)	35 (13.1)	1.4 (0.7-2.8)
≥ 3 Sleep Disturbance	12 (5.7)	35 (9.5)	1.8 (0.9 - 3.7)	9 (8.7)	1.7 (0.7-4.3)	26 (9.7)	2.0 (0.9-4.4)
≥ 3 Memory and Conc.	13 (6.2)	54 (14.6)	**2.4 (1.2 - 4.8)**	20 (19.4)	**4.3 (1.8-10.3)**	34 (12.7)	2.1 (0.8-5.9)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age, ethnicity, smoking, alcohol consumption, education and personality traits

Table 4.4. Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms in reference workers and collision repair workers stratified by employment duration (tertiles)

				Employment duration (Mean)			
	Reference group n=211	**<10 years (5.4) n=125**		**10 – 19 years (14.8) n=123**		**≥20 years (31.3) n=122**	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.7)	54 (43.2)	1.0 (0.6-1.7)	70 (56.9)	**2.2 (1.3-3.7)**	60 (49.1)	**1.7(1.0-3.0)**
≥ 5 symptoms	48 (22.7)	38 (30.4)	1.3 (0.7-2.3)	58 (47.2)	**3.2 (1.9-5.6)**	44 (36.0)	**1.9 (1.0-3.4)**
≥ 10 symptoms	14 (6.6)	15 (12.0)	1.7 (0.7-4.2)	22 (18.0)	**3.3 (1.5-7.5)**	17 (13.9)	2.5 (0.9-6.3)
≥ 15 symptoms	4 (1.9)	5 (4.0)	1.9 (0.3-10.1)	14 (11.4)	**11.5 (3.0-44.6)**	9 (7.3)	**7.7 (1.5-38.1)**
Symptom Domains							
≥ 3 Neurological	3 (1.4)	3 (2.4)	1.8 (0.3-11.4)	9 (7.3)	**6.2 (1.5-25.4)**	7 (5.7)	4.5 (0.9-22.5)
≥ 3 Psychosomatic	6 (2.8)	4 (3.2)	1.0 (0.2-4.4)	12 (9.8)	**5.0 (1.6-15.8)**	11 (9.0)	**4.7 (1.2-18.0)**
≥ 3 Mood	12 (5.7)	11 (8.8)	1.1 (0.4-2.9)	23 (18.7)	**3.7 (1.6-8.3)**	11 (9.0)	2.2 (0.7-6.5)
≥ 3 Memory	7 (3.3)	11 (8.8)	1.7 (0.6-5.2)	13 (10.6)	**3.3 (1.2-9.3)**	13 (10.7)	**4.9 (1.4-17.5)**
≥ 3 Concentration	1 (0.5)	2 (1.6)	0.6 (0.0-16)	2 (1.6)	-	1 (0.82)	-
≥ 3 Fatigue	20 (9.5)	8 (6.4)	0.5 (0.2-1.4)	20 (16.3)	1.9 (0.9-4.0)	20 (16.4)	2.0 (0.8-4.6)
≥ 3 Sleep Disturbance	12 (5.7)	6 (4.8)	1.1 (0.3-3.2)	12 (9.8)	2.0 (0.8-4.9)	17 (13.9)	2.2 (0.9-5.5)
≥ 3 Memory and Conc.	13 (6.2)	17 (13.6)	1.5 (0.6-3.6)	23 (18.7)	**3.5 (1.5-7.8)**	14 (11.5)	**3.0 (1.0-8.9)**

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

"-"= No ORs available due to non-convergence

Collision repair workers were less likely to report sensitivity to environmental stimuli including strong smells, heat, and cold ($p<0.05$) with most pronounced differences observed in spray painters (table 4.5). In contrast, we did not find a statistically significant difference between collision repair workers and the reference group in acute symptoms including eye, mouth and throat dryness/irritation, feeling drunk without drinking and having an unpleasant taste in the mouth, although odds ratios were elevated for some symptoms (table 4.5).

Table 4.5. Prevalence odds ratios of dichotomised (yes/no) acute symptom and sensitivity to environmental conditions EUROQUEST questions between reference workers and collision repair workers

	Reference (n=211)	**All collision repair workers (n=370)**		**Panel beaters (n=103)**		**Spray painters (n=267)**	
	n (%)	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
Acute EQ symptoms							
Irritation of eyes	18 (8.5)	39 (10.6)	1.2 (0.7 - 2.2)	10 (9.7)	1.1 (0.5-2.6)	29 (10.8)	1.2 (0.7-2.4)
Feeling drunk w/o. drinking	0 (0.0)	3 (0.8)	-	2 (1.9)	-	1 (0.4)	-
Dryness mouth/throat	17 (8.1)	41 (11.1)	1.4 (0.7 - 2.6)	9 (8.7)	1.0 (0.4-2.6)	32 (11.9)	1.5 (0.8-2.9)
Throat irritation	8 (3.8)	26 (7.0)	1.7 (0.7 - 4.0)	9 (8.7)	2.2 (0.8-6.1)	17 (6.4)	1.5 (0.6-3.8)
A runny nose	21 (10.0)	24 (6.5)	0.6 (0.3 - 1.1)	10 (9.7)	0.9 (0.4-2.2)	14 (5.2)	**0.4 (0.2-0.9)**
Unpleasant taste in mouth	4 (1.9)	13 (3.5)	1.9 (0.6 - 6.7)	5 (4.9)	2.7 (0.6-11.5)	8 (3.0)	1.6 (0.4-6.2)
Sensitivity to environmental conditions							
Bright lights	68 (32.2)	123 (33.2)	1.1 (0.8 - 1.6)	43 (41.7)	1.5 (0.9-2.4)	80 (30.0)	1.0 (0.6-1.5)
Traffic noise, loud music, etc.	53 (25.1)	77 (20.8)	0.7 (0.5 - 1.1)	25 (24.3)	0.8 (0.4-1.4)	52 (19.5)	0.7 (0.4-1.1)
Strong smells	82 (38.9)	108 (29.2)	**0.6 (0.4 - 0.9)**	35 (34.0)	0.7 (0.4-1.2)	73 (27.3)	**0.6 (0.4-0.9)**
Rough fabrics next to skin	64 (30.3)	85 (23.1)	0.7 (0.5 – 1.0)	30 (29.1)	0.9 (0.5-1.5)	55 (20.6)	**0.6 (0.4-0.9)**
Heat	82 (38.9)	78 (21.1)	**0.4 (0.3 - 0.6)**	27 (26.2)	**0.5 (0.3-0.9)**	51 (19.1)	**0.3 (0.2-0.5)**
Cold	81 (38.4)	91 (24.6)	**0.5 (0.3 - 0.7)**	33 (32.0)	0.6 (0.4-1.1)	58 (21.7)	**0.4 (0.3-0.6)**

Odds Ratios in bold are statistically significant ($p<0.05$)

All analyses were adjusted for age, ethnicity, smoking, alcohol consumption, education, and personality traits

"-" No ORs available due to non-convergence

4.4 Discussion

Collision repair workers consistently reported more symptoms of neurotoxicity than reference workers, primarily in the domains of neurological, psychosomatic, mood and memory symptoms. Differences were most pronounced in panel beaters. The strongest risks were observed in workers with medium employment duration in the collision repair industry (15 years) compared to those with shorter (5 years) or longer (31 years) work duration.

The current study has shown an elevated risk of neurotoxicity in collision repair workers consistent with previous studies in car spray painters**,** particularly those that also focused on smaller enterprises (17, 45), industrial and dockyard painters (19, 299, 302) and other occupational groups with mixed solvent exposures (67, 288). The increased reports of neurological symptoms suggest peripheral neuropathy which has been shown to be associated with long-term exposure to solvents in case studies (347) and a cross-sectional study of industrial painters which showed an increased risk of leg and arm paraesthesia (abnormal sensation, pins and needles) (19).

The increased risk of neurotoxicity observed in this study appears to occur at airborne solvent levels below international exposure standards. Due to the potential long latency of solvent-related neurotoxic effects a role for high historic exposures cannot be excluded. However, increased risks are also observed in those with a short employment duration (table 4.4), suggesting that symptoms are not solely attributable to historic exposures. Also, as observed internationally, significant reductions in solvent exposure levels in this industry are likely to have occurred as early as two

decades ago (13). This suggests that contemporary low-level solvent exposure may indeed have contributed to the observed elevated risks, particularly given that the strongest associations were found in those who worked on average 15 years in the collision repair industry (i.e. after the reported reduction in exposure levels seen in this industry). If true, effects may be due to short duration high peak exposures which contribute little to full-shift average exposures as measured in the current study, but may act as a "tipping point" in the development of neurotoxic symptoms (28). Alternatively, airborne exposures do not accurately reflect the total solvent burden, and dermal exposures (which we have not measured) may be more important. In fact, previous studies have suggested that if workers wear effective respiratory protection, dermal exposures may contribute >50% of the total body burden of solvents (26, 30, 74). It is also possible that the frequent use of vibrating air-powered and oscillating tools may have contributed to at least some of the observed increased risks, particularly by panel beaters (302, 348). However, this would account only for neurological symptoms and not other neurobehavioural symptoms which were also more frequently reported by collision repair workers.

The strongest risks of neurotoxicity were observed in panel beaters despite no direct involvement in the painting process, and detected airborne levels being only a quarter of those in spray painters. It is unclear why this is the case, but may be due to exposure to solvents not tested for. In particular, the panel repair process involves regular use of heavy duty cleaning and degreasing aerosol sprays which often contain chlorinated solvents such as perchloroethylene, tetrachloroethylene and methylene chloride, which have been associated with neurobehavioural and neurological effects

(176). Air samples were not tested for these chemicals. Panel beating was also often performed in close proximity (and without respiratory protection) to spray painting activities and in confined spaces, such as the interior of vehicles increasing the likelihood of secondary exposures. The differences may also be due to differences in historic exposures between spray painters and panel beaters (45), but this could not be assessed in this cross-sectional study. Finally, as noted above, dermal exposures may be more important than airborne exposures and this may be particularly the case for panel beaters.

Collision repair workers, and particularly spray painters, reported less sensitivity to environmental conditions than the reference group (table 4.5), including sensitivity to strong smells. Deficits in olfactory function have previously been shown in solvent exposed workers, and effects on olfactory neuroepithelial function are suspected (180). Reduced sensation to rough fabrics next to the skin, and heat and cold were also reported less by spray painters, which may be indicative of altered peripheral nervous system function (39). This might be due to 2,5-hexanedione which has been associated with peripheral neuropathy in both animal models and occupationally exposed populations [38 39] and is a metabolite of N-hexane and methyl ethyl ketone, both of which were detected in many of the exposure samples collected in this study.

Although based on relatively small numbers in each work duration category results suggested (as noted above), that those working in the collision and repair industry for a medium duration had a greater risk of reporting symptoms overall, as well as for each of the symptom domains separately, compared to those with short and long employment duration. Despite signs of multicolinearity with confidence limits

widening, this trend was unaffected when the analyses were adjusted for age, suggesting employment duration is, at least to some degree, independently associated with symptoms. However, a clear work duration-response association was not observed which is consistent with previous findings on hydrocarbon exposures and neurobehavioural effects (297) and may be due to 'healthy worker survivor bias'—a selection phenomenon where those least susceptible to the effects of solvents continue work in high exposure jobs, whereas those who develop symptoms leave the industry or move to jobs with lower exposure (16). Evidence of this effect has been reported in several other studies of solvent exposed workers (22, 23) including a 2008 meta-analysis (16).

The response rate in collision repair and reference workers was 69% and 64% respectively, which is relatively high for these types of surveys and suggests that non-response bias, if present, would be small. No differences between responders and non-responders were found for several key symptoms of neurotoxicity, further suggesting that non-response bias is negligible and unlikely to explain the increased risks observed in collision repair workers. However, this study had other limitations including the potential that some reference workers may have had occupational exposure to solvents. However, analyses excluding reference workers who reported occupational solvent exposure did not alter the results suggesting that this is not a major issue (supplementary table 4.11). However, even if it had played a role, it would have led to an underestimate of the true risks. There were differences in age, ethnicity, attained education, smoking habits, and alcohol consumption between collision repair workers and reference workers, but these were controlled for in the

analyses and study results were consistent with previous international studies suggesting that they are robust. Duration of employment in the industry is generally not considered the most reliable proxy for cumulative exposure (297), but historical data of solvent levels in this industry was not available and exposure misclassification would likely lead to an underestimation of risk. Finally, neurotoxicity was assessed using self-reported symptoms, which were not confirmed by a clinical assessment, and therefore some misclassification may have occurred. However, EUROQUEST was designed specifically to assess symptoms associated with occupational exposure to neurotoxic agents (233), and is widely used and well validated against clinical criteria (175, 224, 232, 234, 349). In addition, as suggested recently (7), standardised symptom assessment represents an important starting point for identifying populations "at risk" of effects associated with solvent exposure. Also, the same questionnaires were used in collision repair workers and the reference population and administered according to the same standardised protocol, and comparisons are therefore valid. Nonetheless, additional research including objective neuropsychological tests would be useful to clarify further the nature and extent of any effects on psychological or neurological function.

In conclusion, despite solvent exposures in the collision repair industry having declined steadily over the past two decades internationally and current airborne exposures in New Zealand being well under international standards, collision repair workers in small to medium-sized enterprises continue to have a significantly elevated risk of neurotoxicity. Thus, further preventive measures may need to be implemented to reduce hazardous exposures and associated neurotoxicity in the collision repair

industry and potentially in other industries where workers are similarly exposed to solvents, including a revision of the relevant workplace exposure standards.

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4.5 Supplementary material

Table 4.6. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms in reference workers and collision repair workers stratified by employment duration quartiles

		Employment duration (Mean)							
	Reference group	**<7.5 years (4.0)**		**7.5-15 years (11.0)**		**15 - 25 years (19.0)**		**≥25 years (34.1)**	
	n=211	**n=125**		**n=123**		**n=122**		**n=122**	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.7)	42 (45.7)	1.1 (0.6-2.0)	45 (49.5)	1.5 (0.8-2.6)	52 (54.7)	**2.1 (1.2-3.6)**	45 (48.9)	1.7 (0.9-3.2)
≥ 5 symptoms	48 (22.7)	30 (32.6)	1.4 (0.7-2.7)	35 (38.5)	**2.0 (1.1-3.7)**	41 (43.2)	**2.7 (1.5-4.8)**	34 (37.0)	**1.9 (1.0-3.8)**
≥ 10 symptoms	14 (6.6)	11 (12.0)	1.6 (0.6-4.5)	14 (15.4)	**2.6 (1.0-6.5)**	16 (16.8)	**3.3 (1.4-7.7)**	13 (14.1)	2.2 (0.8-6.4)
≥ 15 symptoms	4 (1.9)	4 (4.4)	2.2 (0.3-14.5)	8 (8.8)	**8.4 (1.8-39.5)**	10 (10.5)	**12.0 (2.9-49.0)**	6 (6.5)	4.4 (0.8-24.8)
Symptom Domains									
≥ 3 Neurological	3 (1.4)	3 (3.3)	3.4 (0.5-23.9)	4 (4.4)	4.3 (0.8-23.7)	8 (8.4)	**7.6 (1.8-31.4)**	4 (4.4)	2.3 (0.4-12.9)
≥ 3 Psychosomatic	6 (2.8)	2 (2.2)	0.6 (0.1-4.1)	8 (8.8)	**4.6 (1.2-17.4)**	10 (10.5)	**6.1 (1.8-19.9)**	7 (7.6)	2.7 (0.6-11.8)
≥ 3 Mood	12 (5.7)	8 (8.7)	1.1 (0.4-3.3)	15 (16.5)	**2.7 (1.1-6.5)**	14 (14.7)	**3.3 (1.3-8.1)**	8 (8.7)	1.8 (0.5-6.1)
≥ 3 Memory	7 (3.3)	9 (9.9)	2.0 (0.6-6.6)	9 (9.5)	2.6 (0.8-8.1)	9 (9.5)	**3.7 (1.2-11.3)**	10 (10.9)	**3.8 (1.0-14.6)**
≥ 3 Concentration	1 (0.5)	2 (2.2)	1.4 (0.1-35.0)	2 (2.2)	6.4 (0.3-142.7)	1 (1.1)	8.0 (0.2-391.1)	0 (0.0)	-
≥ 3 Fatigue	20 (9.5)	7 (7.6)	0.7 (0.2-2.0)	13 (14.3)	1.7 (0.7-4.0)	12 (12.6)	1.4 (0.6-3.2)	16 (17.4)	1.8 (0.7-4.4)
≥ 3 Sleep Disturbance	12 (5.7)	5 (5.4)	1.3 (0.4-4.4)	7 (7.7)	1.7 (0.6-4.8)	9 (9.5)	1.8 (0.7-4.6)	14 (15.2)	2.2 (0.8-5.9)
≥ 3 Memory and Conc.	13 (6.2)	14 (15.2)	1.7 (0.7-4.4)	16 (16.8)	2.2 (0.9-5.3)	16 (16.8)	**4.0 (1.6-9.7)**	10 (10.9)	2.4 (0.7-7.9)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

"-" No ORs available due to non-convergence

Table 4.7. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms between reference workers and collision repair workers – Alternative EUROQUEST symptom domain cut points (≥ 2 and ≥4 symptoms per domain)

	Reference (n=211)	All CR workers (n=370)		Panel Beaters (n=103)		Spray Painters (n=267)	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
Symptom domains							
≥ 2 Neurological	11 (5.2)	35 (9.4)	1.9 (0.9-4.0)	15 (14.6)	**2.7 (1.2-6.4)**	20 (7.5)	1.5 (0.6-3.3)
≥ 2 Psychosomatic	13 (6.2)	57 (15.4)	**3.0 (1.5-6.1)**	20 (19.4)	**4.0 (1.7-9.2)**	37 (13.9)	**2.6 (1.2-5.7)**
≥ 2 Mood	27 (12.8)	72 (19.5)	1.4 (0.8-2.4)	19 (18.5)	1.3 (0.6-2.7)	53 (19.9)	1.4 (0.8-2.5)
≥ 2 Memory	20 (9.5)	71 (19.2)	**2.1 (1.2-3.6)**	27 (26.2)	**3.5 (1.7-7.2)**	44 (16.5)	1.6 (0.9-3.0)
≥ 2 Concentration	5 (2.4)	16 (4.3)	1.4 (0.4-4.2)	6 (5.8)	2.4 (0.6-9.8)	10 (3.6)	0.8 (0.2-2.8)
≥ 2 Fatigue	37 (17.5)	90 (24.3)	1.4 (0.9-2.3)	24 (23.3)	1.2 (0.6-2.3)	66 (24.7)	1.5 (0.9-2.5)
≥ 2 Sleep Disturbance	32 (15.2)	83 (22.4)	**1.6 (1.0-2.6)**	21 (20.4)	1.3 (0.7-2.5)	62 (23.2)	**1.9 (1.1-3.1)**
≥ 2 Memory and Conc.	28 (13.3)	85 (23.0)	**1.7 (1.0-2.9)**	29 (28.2)	**2.4 (1.2-4.5)**	56 (21.0)	1.5 (0.9-2.6)
≥ 4 Neurological	1 (0.5)	10 (2.7)	8.3 (0.9-74.0)	5 (4.9)	**17.5 (1.2-248.8)**	5 (1.9)	4.4 (0.4-48.7)
≥ 4 Psychosomatic	2 (1.0)	10 (2.7)	3.8 (0.6-24.0)	2 (1.9)	-	8 (3.0)	5.2 (0.7-38.8)
≥ 4 Mood	7 (3.3)	28 (7.6	1.9 (0.7-4.6)	11 (10.7)	**3.5 (1.1-10.6)**	17 (6.4)	1.3 (0.5-3.5)
≥ 4 Memory	5 (2.4)	23 (6.2)	2.3 (0.8-6.5)	12 (11.7)	**6.0 (1.8-19.8)**	11 (4.1)	1.3 (0.4-4.6)
≥ 4 Concentration	0 (0.0)	0 (0.0)	-	0 (0.0)	-	0 (0.0)	-
≥ 4 Fatigue	11 (5.2)	25 (6.8)	1.4 (0.6-3.2)	7 (6.8)	1.2 (0.4-3.8)	18 (6.7)	1.6 (0.7-3.9)
≥ 4 Sleep Disturbance	3 (1.4)	7 (1.9)	1.4 (0.3-6.3)	0 (0.0)	-	7 (2.6)	2.4 (0.5-11.4)
≥ 4 Memory and Conc.	6 (2.8)	37 (10.0)	**3.3 (1.3-8.4)**	16 (15.5)	**6.4 (2.2-18.6)**	21 (7.9)	2.3 (0.8-6.6)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

"-"= No ORs available due to non-convergence

Table 4.8. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms in reference workers and collision repair workers stratified by employment duration (tertiles) – Age excluded from regression model

		Employment duration (Mean)					
	Reference group	**<10 years (5.4)**		**10 – 19 years (14.8)**		**≥20 years (31.3)**	
	n=211	**n=125**		**n=123**		**n=122**	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.7)	54 (43.2)	1.1 (0.7-1.9)	70 (56.9)	**2.3 (1.4-3.8)**	60 (49.1)	1.5 (0.9-2.5)
≥ 5 symptoms	48 (22.7)	38 (30.4)	1.3 (0.8-2.3)	58 (47.2)	**3.2 (1.9-5.5)**	44 (36.0)	**1.7 (1.0-3.0)**
≥ 10 symptoms	14 (6.6)	15 (12.0)	1.9 (0.8-4.3)	22 (18.0)	**3.4 (1.5-7.6)**	17 (13.9)	**2.3 (1.0-5.4)**
≥ 15 symptoms	4 (1.9)	5 (4.0)	2.4 (0.5-11.5)	14 (11.4)	**12.2 (3.1-47.4)**	9 (7.3)	**6.2 (1.4-26.5)**
Symptom Domains							
≥ 3 Neurological	3 (1.4)	3 (2.4)	1.7 (0.3-8.9)	9 (7.3)	**6.1 (1.5-24.4)**	7 (5.7)	**5.0 (1.1-21.5)**
≥ 3 Psychosomatic	6 (2.8)	4 (3.2)	1.2 (0.3-4.8)	12 (9.8)	**5.2 (1.7-16.4)**	11 (9.0)	**4.0 (1.2-13.2)**
≥ 3 Mood	12 (5.7)	11 (8.8)	1.6 (0.6-3.9)	23 (18.7)	**3.9 (1.7-8.7)**	11 (9.0)	1.4 (0.5-3.6)
≥ 3 Memory	7 (3.3)	11 (8.8)	2.6 (0.9-7.6)	13 (10.6)	**3.6 (1.3-10.1)**	13 (10.7)	**2.8 (1.0-8.2)**
≥ 3 Concentration	1 (0.5)	2 (1.6)	5.4 (0.3-104.7)	2 (1.6)	3.8 (0.2-66.7)	1 (0.82)	2.3 (0.1-63.9)
≥ 3 Fatigue	20 (9.5)	8 (6.4)	0.6 (0.2-1.4)	20 (16.3)	1.9 (0.9-4.1)	20 (16.4)	1.8 (0.8-4.0)
≥ 3 Sleep Disturbance	12 (5.7)	6 (4.8)	0.8 (0.3-2.3)	12 (9.8)	1.8 (0.8-4.4)	17 (13.9)	2.8 (1.2-6.6)
≥ 3 Memory and Conc.	13 (6.2)	17 (13.6)	**2.4 (1.1-5.5)**	23 (18.7)	**3.6 (1.6-8.0)**	14 (11.5)	1.6 (0.7-3.9)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for ethnicity, smoking, alcohol consumption, education, and personality traits

Table 4.9. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms between reference workers and collision repair workers – Excluding current office workers

	Reference (n=211)	**All CR workers (n=324)**		**Panel Beaters (n=86)**		**Spray Painters (n=238)**	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.9)	158 (48.8)	**1.5 (1.0-2.2)**	43 (50.0)	1.6 (0.9-2.7)	115 (48.3)	1.4 (0.9-2.2)
≥ 5 symptoms	48 (22.7)	120 (37.0)	**1.9 (1.2-2.9)**	34 (39.5)	**2.0 (1.1-3.7)**	86 (36.1)	**1.8 (1.1-2.9)**
≥ 10 symptoms	14 (6.6)	47 (14.5)	**2.3 (1.2-4.6)**	16 (18.6)	**3.1 (1.3-7.6)**	31 (13.0)	**2.1 (1.0-4.4)**
≥ 15 symptoms	4 (1.9)	23 (7.1)	**5.4 (1.5-19.3)**	9 (10.5)	**7.8 (1.9-31.1)**	14 (5.9)	**4.7 (1.1-19.9)**
Symptom domains							
≥ 3 Neurological	3 (1.4)	17 (5.3)	**4.5 (1.2-16.4)**	7 (8.1)	**6.7 (1.5-30.0)**	10 (4.2)	3.2 (0.8-13.0)
≥ 3 Psychosomatic	6 (2.8)	22 (6.8)	**2.9 (1.0-8.3)**	8 (9.3)	**3.9 (1.1-13.2)**	14 (5.9)	2.1 (0.7-6.8)
≥ 3 Mood	12 (5.7)	39 (12.0)	**2.0 (1.0-4.1)**	12 (14.0)	**2.5 (1.0-6.6)**	27 (11.3)	1.8 (0.8-3.9)
≥ 3 Memory	7 (3.3)	34 (10.5)	**3.1 (1.2-7.6)**	16 (18.6)	**6.9 (2.4-19.7)**	18 (7.6)	2.0 (0.7-5.6)
≥ 3 Concentration	1 (0.5)	5 (1.5)	3.7 (0.2-57.6)	4 (1.68)	2.4 (0.1-8.2)	1 (0.47)	4.1 (0.3-63.8)
≥ 3 Fatigue	20 (9.5)	39 (12.0)	**2.4 (1.2-4.9)**	9 (10.5)	0.9 (0.4-2.4)	30 (12.6)	1.3 (0.7-2.6)
≥ 3 Sleep Disturbance	12 (5.7)	30 (9.3)	1.2 (0.6-2.3)	6 (7.0)	1.4 (0.5-4.0)	24 (10.1)	**2.2 (1.0-4.8)**
≥ 3 Memory and Conc.	13 (6.2)	49 (15.1)	1.9 (0.9-4.0)	20 (23.3)	**5.3 (2.2-13.0)**	29 (12.8)	1.7 (0.8-3.6)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

Table 4.10. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms between reference workers and collision repair workers – Excluding 7 panel beaters recoded as spray painters

	Reference (n=211)	All CR workers (n=360)		Panel Beaters (n=103)		Spray Painters (n=260)	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	78 (36.9)	181 (49.9)	**1.6 (1.1-2.3)**	43 (50.0)	1.6 (0.9-2.7)	130 (50.0)	**1.5 (1.0-2.3)**
≥ 5 symptoms	48 (22.7)	138 (38.0)	**2.0 (1.3-3.1)**	34 (39.5)	**2.0 (1.1-3.7)**	97 (37.3)	**1.9 (1.2-3.0)**
≥ 10 symptoms	14 (6.6)	53 (14.6)	**2.4 (1.2-4.8)**	16 (18.6)	**3.1 (1.3-7.6)**	34 (13.1)	**2.2 (1.0-4.8)**
≥ 15 symptoms	4 (1.9)	27 (7.4)	**6.0 (1.7-21.3)**	9 (10.5)	**7.8 (1.9-31.1)**	16 (6.2)	**6.2 (1.4-27.9)**
Symptom domains							
≥ 3 Neurological	3 (1.4)	18 (5.0)	**4.1 (1.1-15.1)**	7 (8.1)	**6.7 (1.5-30.0)**	10 (3.9)	2.9 (0.7-12.7)
≥ 3 Psychosomatic	6 (2.8)	26 (7.2)	**3.2 (1.1-9.1)**	8 (9.3)	**3.9 (1.1-13.2)**	16 (6.2)	2.5 (0.8-8.1)
≥ 3 Mood	12 (5.7)	45 (12.4)	**2.2 (1.1-4.5)**	12 (14.0)	**2.5 (1.0-6.6)**	31 (11.9)	**2.1 (1.0-4.6)**
≥ 3 Memory	7 (3.3)	36 (9.9)	**2.8 (1.1-6.8)**	16 (18.6)	**6.9 (2.4-19.7)**	20 (7.7)	2.1 (0.8-6.0)
≥ 3 Concentration	1 (0.5)	5 (1.4)	3.6 (0.2-55.6)	4 (1.68)	2.4 (0.1-8.02)	4 (1.5)	3.9 (0.3-58.3)
≥ 3 Fatigue	20 (9.5)	47 (13.0)	1.4 (0.7-2.5)	9 (10.5)	0.9 (0.4-2.4)	34 (13.1)	1.4 (0.7-2.6)
≥ 3 Sleep Disturbance	12 (5.7)	35 (9.6)	1.9 (0.9-3.8)	6 (7.0)	1.4 (0.5-4.0)	26 (10.1)	2.0 (0.9-4.6)
≥ 3 Memory and Conc.	13 (6.2)	53 (14.6)	**2.4 (1.2-4.7)**	20 (23.3)	**5.3 (2.2-13.0)**	33 (12.7)	1.9 (0.9-4.1)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

Table 4.11. Supplementary table - Prevalence odds ratios of dichotomised (yes/no) EUROQUEST symptoms between reference workers and collision repair workers – Excluding reference workers 'exposed' to solvents (n=19)

	Reference (n=192)	All CR workers (n=370)		Panel Beaters (n=103)		Spray Painters (n=267)	
Cut-points	**n (%)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
≥ 3 symptoms	68 (35.4)	184 (49.7)	**1.6 (1.1-2.4)**	51 (49.5)	1.5 (0.9-2.6)	133 (49.8)	**1.5 (1.0-2.4)**
≥ 5 symptoms	39 (20.3)	140 (37.8)	**2.2 (1.4-3.4)**	41 (39.8)	**2.2 (1.2-4.0)**	99 (37.1)	**2.1 (1.3-3.4)**
≥ 10 symptoms	11 (5.3)	54 (14.6)	**2.8 (1.3-6.0)**	19 (18.5)	**4.3 (1.7-11.0)**	35 (13.1)	**2.7 (1.2-6.2)**
≥ 15 symptoms	4 (2.1)	28 (7.6)	**5.1 (1.5-17.9)**	11 (10.6)	**7.7 (2.0-29.4)**	17 (6.4)	**5.4 (1.3-23.5)**
Symptom domains							
≥ 3 Neurological	3 (1.6)	19 (5.1)	**3.5 (1.0-12.9)**	8 (7.8)	**4.9 (1.1-21.3)**	11 (4.1)	2.7 (0.6-11.4)
≥ 3 Psychosomatic	5 (2.6)	27 (7.3)	**3.6 (1.2-10.9)**	10 (9.7)	**4.6 (1.3-16.9)**	17 (6.4)	2.9 (0.8-10.0)
≥ 3 Mood	9 (4.7)	45 (12.2)	**2.6 (1.2-5.7)**	14 (13.6)	**2.9 (1.1-8.0)**	31 (11.6)	**2.4 (1.0-5.7)**
≥ 3 Memory	6 (3.1)	37 (10.0)	**3.0 (1.2-7.9)**	16 (15.5)	**7.0 (2.2-22.2)**	21 (7.9)	2.4 (0.8-7.0)
≥ 3 Concentration	1 (0.5)	5 (1.4)	1.7 (0.1-22.2)	1 (1.0)	-	4 (1.5)	2.9 (0.2-44.7)
≥ 3 Fatigue	17 (8.9)	48 (12.9)	1.4 (0.7-2.8)	13 (12.6)	1.3 (0.5-3.2)	35 (13.1)	1.5 (0.7-3.0)
≥ 3 Sleep Disturbance	11 (5.7)	35 (9.5)	1.7 (0.8-3.6)	9 (8.7)	1.6 (0.6-4.3)	26 (9.7)	1.9 (0.8-4.2)
≥ 3 Memory and Conc.	11 (5.7)	54 (14.6)	2.6 (1.2-5.4)	20 (19.4)	**4.8 (1.9-12.5)**	34 (12.7)	2.0 (0.9-4.6)

Odds ratios and confidence intervals in bold signify a p value ≤0.05

All analyses were adjusted for age**,** ethnicity, smoking, alcohol consumption, education, and personality traits

"-"= No OR available due to non-convergence

5 Neuropsychological performance in solvent-exposed vehicle collision repair workers in New Zealand

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Objectives: To assess whether contemporary solvent exposures in the vehicle collision repair industry are associated with objectively measured neuropsychological performance in collision repair workers.

Methods: The RBANS battery and additional tests were administered to 47 vehicle collision repair and 51 comparison workers randomly selected from a previous questionnaire study.

Results: Collision repair workers performed lower on tests of attention (digit span backwards: -1.5, 95% CI -2.4, -0.5; digit span total: -1.7, CI -3.3, -0.0; coding: -6.1, CI -9.9, -2.8; total attention scale: -9.3, CI -15.9, -2.8) and the RBANS total scale (-5.1, CI -9.1, -1.2). Additional tests also showed deficits in visual attention and reaction time (Trails B: -11.5, CI -22.4, -0.5) and motor speed/dexterity (coin rotation dominant hand & non-dominant: -2.9, CI -5.3, -0.4 and -3.1, CI -5.6, -0.7 respectively). The strongest associations were observed in panel beaters. Applying dichotomised RBANS outcomes based on the lowest percentile scores of a normative comparison group showed strongly increased risks for attention (5th percentile: OR 20.1, 95% CI 1.5, 263.3; 10th percentile: 8.8, CI 1.7, 46.2; and 20th percentile: 5.1, CI 1.5, 17.6, respectively). Those employed in the industry for ≤ 17 years (the median work duration) generally had lower scores in the attention domain scale and RBANS total scale compared to those employed >17 years suggesting a healthy worker survivor bias, but trends were inconsistent for other domains.

Conclusions: This study has found significant deficits in cognitive performance in collision repair workers despite low current airborne exposures in New Zealand.

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5.1 Introduction

Millions of tons of organic solvents are produced globally each year and used in many industrial processes, (42) including the automotive repair industry where they are used extensively in raw form, and in bodywork fillers and various spray coatings. Workers exposed to solvents, through inhalation and dermal absorption, are at risk of developing symptoms of neurotoxicity including memory impairment, changes in personality and deficits in cognitive function. (156, 183) Prolonged exposure has also been associated with chronic solvent-induced encephalopathy (CSE, a condition caused by long-term solvent exposure and characterised by symptoms associated with central nervous system depression and deficits in neurobehavioural performance, which may persist even upon cessation of exposure (191)), as reported in automotive repair workers (17, 45) and other occupations. (22, 67, 69)

In a recent questionnaire survey of 370 collision repair workers and 211 comparison workers, we reported that collision repair workers in New Zealand continue to have a significantly increased risk of symptoms of neurotoxicity, including neurological (e.g. numbness, tingling or decreased sensation in extremities, dropping things unintentionally, balance problems, etc.), mood, memory, and concentration symptoms. (331) This is despite considerable changes in technology and health and safety practices in this industry and an associated decline in solvent exposures over the past 2 decades. (13) However, it is unclear whether these effects extend to cognitive deficits as measured by objective neuropsychological tests. Previous studies using these tests have reported reductions in attention span and sustained attention, immediate and delayed memory and motor speed. (16, 17, 67, 69) However, the

findings have been inconsistent with some studies showing no association, suggesting that workers may be at risk of only 'mild' symptoms. (20, 21, 162, 309) Alternatively, the inconsistent results may be due to small sample sizes for most studies, inadequate control for confounding, insufficiently sensitive neuropsychological tests, (29) or underestimation of the importance of relatively small average changes measured across workers. (35)

In the current study a neuropsychological test battery was administered to a randomly selected subset of collision repair (n=47) and comparison workers (n=51) who participated in our previous questionnaire study (331) in order to assess associations between contemporary mixed-solvent exposures and objectively measured neuropsychological performance.

5.2 Methods

Study Population

The study participants comprised a random sample of 47 collision repair and 51 comparison workers from our previous questionnaire survey, the methods and results of which have been described elsewhere. (331) In brief, 370 collision repair workers (spray painters, panel beaters or auto-body repair workers, and office staff) were recruited from workshops throughout the north island of New Zealand. Office staff (n=46) were all ex-tradesmen and were recoded as a spray painter or panel beater according to their previous job title, as this more accurately reflected their working life exposures; also the majority still performed some repair work, especially during busy periods, suggesting that, at least occasionally, they are at risk of being exposed. (331) A comparison group of 211 construction workers with negligible/no exposure to solvents was recruited in the same regions using a similar strategy. Informed written consent was obtained from all participants for involvement in each stage of the study and the study protocol was approved by the New Zealand Multiregional Ethics Committee (Application MEC/10/08/081). A sample of participants from the previous study (69 collision repair and 80 comparison workers) was re-contacted with the aim of recruiting at least 50 collision repair and 50 comparison workers for neuropsychological testing. The group size was based on power calculations conducted by Hooisma, Hänninen (312) which indicated that approximately 50 participants per group was sufficient to detect meaningful differences for individual tests comparable to those used in the current study (see below).

Seven collision repair workers and 20 comparison workers declined to participate, leaving a total of 59 (90%) collision repair and 60 (75%) comparison workers. Of those, ten collision repair and eight comparison workers met the exclusion criteria i.e., current recreational/sedative/anti-anxiety prescription drug use, history of major head trauma, and/or history of neurological or neurodegenerative disease including meningitis. Women (2 collision repair workers and 1 comparison worker) were also excluded due to low numbers. This resulted in complete test results being available for 47 collision repair workers (34 spray painters and 13 panel beaters) and 51 comparison workers.

Neuropsychological test battery

Prior to testing, participants completed a brief questionnaire on issues likely to affect test performance (e.g., sleep, alcohol consumption and drug use in the past 48 hours). To ensure a uniform testing environment, all tests were conducted in a mobile station at the participant's workplace by a single examiner. Tests were conducted throughout the day.

The test battery consisted of a modified (see below) version of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS, NCS Pearson Ltd, MN, USA). (260) The battery includes tests of immediate memory, visuospatial and construction skills, language, attention and delayed memory. The immediate memory tasks include a verbal serial list learning task (list of words) and recall of a short story. The shortened version of the Digit Span test for attention and working memory was

substituted for the full version of the test (244) to improve test sensitivity and comparability with other studies. A coding task similar to the Digit Symbol Modalities test (246) was included to cover attention, visual scanning, tracking and motor speed. Tasks assessing language included both a picture naming and semantic fluency exercise. Assessment of delayed memory involved the recall of words or figures from earlier sections of the test after an intermission involving other, unrelated tasks. Also, a list recognition test was included to assess prompted delayed memory.

In addition to the RBANS, the following tests were administered: Trails A and B (242) and the Stroop Colour-Word test (Stoelting Co., Illinois, USA), (248) to measure aspects of cognitive function associated with attention, reaction time and processing speed; the Coin Rotation Test for motor speed and dexterity; (269) the Rey 15 item test for assessment of malingering/symptom validity; (275) the National Adult Reading Test (NART) for verbal intelligence; (273) and the Depression, Anxiety and Stress Scale (DASS). (350) The last three tests were included to assess participant effort and to allow for test analyses to be adjusted for premorbid intelligence and/or psychological factors that may influence test performance (16) Completed tests were scored twice, once by the test examiner and once by a clinical psychologist who was blinded to the occupation of the test subjects. Any inter-rater discrepancies were discussed and resolved before test results were entered into the database.

Information on demographics and other potential confounders used in the analyses was collected by questionnaire in our previous study. (331)

Exposure groups

Workers were stratified according to their current job title (i.e. spray painter, panel beater), except office workers (as described above). Also, one panel beater in the current study reported working for a defined period as a spray painter in the past and was recoded accordingly. Job title was subsequently used as a proxy of current and previous exposure combined i.e. for the majority of workers job title had not changed since they had commenced working in this industry.

We assessed current airborne solvent exposure by conducting full-shift airborne personal exposure measurements in a random sample of spray painters (n=50) and panel beaters (n=36) and a small group of office workers (n=6) with no history of exposure work (these workers were not included in the previous questionnaire survey or current study). Results (and detailed methods) are described elsewhere (10) and briefly discussed in the discussion of the current paper.

Statistical analyses

Test results were compared between collision repair and comparison workers for individual test scores, combined 'scale' scores for each neurobehavioural domain and for the RBANS 'total scale' score (reflecting overall performance on the RBANS) using linear regression. The 'scaled' scores are the combined score for each domain normalised based on the participant's age, as per RBANS guidelines. (260) For Trails A and B, coin rotation, 15 Item, NART, and DASS tests raw scores were used (with appropriate adjustment for age in the analyses, see below). For the Stroop test the

'interference' score was used, consistent with international guidelines. (248) In addition to analysing RBANS scores on a continuous scale we also used dichotomised scores based on cut-points representing the lowest 5th, 10th and 20th percentile scores of an RBANS normative comparison group(282) for each of the domain 'scaled' scores. These approximate RBANS definitions of 'Low', 'Borderline' and 'Low average' test performance. (282) For analyses comparing dichotomised outcomes we used logistic regression.

Regression analyses for individual test results were adjusted for age, ethnicity, smoking status, alcohol consumption in the past 48 hours, depression, anxiety and stress (DASS), premorbid verbal intelligence (NART), malingering/participant effort (15 Item), test time during the day, and day of week. (175) We did not adjust for age for the scaled domain and total scores as these are already normalised for age. Other potential confounders including different measures of alcohol consumption (lifetime frequency and lifetime drinks per week), sleep quality, chronic diseases (e.g., diabetes), minor head injuries/concussion, chronic fatigue and pre-existing health issues were also considered, but these did not appreciably affect the observed associations. As a higher score on the Trail Making Tests (A and B) indicates lower performance, the algebraic signs of the coefficients and confidence intervals for these variables were inverted for ease of interpretation. For the analyses by percentile groups we adjusted for a more restricted set of potential confounders (ethnicity, test time during the day and day of week, alcohol consumption in the past 48 hours, smoking status, depression, anxiety and stress (DASS) and verbal intelligence (NART))

as small numbers in some strata did not permit for adjustment for all potential confounders.

The effect of employment duration was assessed by dichotomising collision repair workers based on median work duration i.e., those who had worked in the industry for ≤17 years (average of 10.5 years; range 5.4 – 16.2; n=23) and those who had worked in the industry for >17 years (average 28.3 years; range 16.8 – 50; n=24). Due to the high correlation of age with employment duration (Spearman's correlation coefficient = 0.92) and the resulting potential for multicollinearity, a second regression for the individual test scores (domain scores are already scaled for age) was conducted controlling for all confounders except age, and results were compared with those of the full regression model including age. Due to the low number of panel beaters (n=13) stratified analyses for spray painters and panel beaters were not conducted for comparisons between the two employment duration groups; instead, the analyses were adjusted for job title (spray painter/panel beater).

5.3 Results

Māori and Pacific people were underrepresented in the collision repair workers compared to the comparison group (Māori, 6% vs 25%, $p<0.05$; Pacific, 4% vs.16%, $p<0.05$) (table 5.1). Collision repair workers were also less likely to smoke (28% vs 33%, $p=0.55$) or to have had a tertiary education (4% vs. 12%, $p=0.17$) and generally scored lower on the depression, anxiety and stress scale (Depression, 4.4 vs. 5.1, $p=0.14$, anxiety, 3.4 vs. 5.1, $p<0.1$, stress, 8.6 vs. 10.6, $p=0.13$), but this did not reach statistical significance. Panel beaters were on average older (not statistically significant) than both spray painters (45.1 vs 38.8 years, $p<0.1$) and the comparison group (45 vs 39.0 years, $p=0.13$). Collision repair workers scored lower on the National Adult Reading Test (not statistically significant) for premorbid intelligence (19.2 vs 18.1 errors, $p=0.62$). All analyses were controlled for these potential confounders.

Table 5.1. Characteristics of study population

	Comparison group (n=51)		All Collision repair (n=47)		Panel beaters (n=13)		Spray painters (n=34)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ethnicity								
Māori	13	25	3	6	0	0	3	8
Pacific	8	16	2	4	1	8	1	3
European New Zealanders and others	30	59	42**	89	12	92	30	88
Smoking Status								
Non-smoker	18	35	19	40	3	23	16	47
Ex-smoker	16	31	15	32	6	46	9	26
Current smoker	17	33	13	28	4	31	9	26
Lifetime alcohol (frequency)								
Never	1	2	1	2	0	0	1	3
Less than once month	8	16	4	9	2	15	2	6
1-2 times week	25	49	25	53	6	46	19	56
3-5 times week	14	27	16	34	5	38	11	32
Daily	3	6	1	2	0	0	1	3
Education level								
primary school	0	0	2	4	0	0	2	6
secondary school	36	71	38	81	11	85	27	79
trade certification	9	18	5	11	2	15	3	9
Tertiary/University	6	12	2	4	0	0	2	6
	Mean	**Range**	**Mean**	**Range**	**Mean**	**Range**	**Mean**	**Range**
Age	39.0	19 - 65	37.8	21 - 62	45.1	32 - 64	38.8	24 - 60
Lifetime Alcohol (Mean drinks per week)	15.8	0 - 100	14.3	0 - 50	12.4	1 - 36	15.1	0 - 50
Alcohol in past 48 hours (mean drinks)	2.5	0 - 42	3.3	0 - 40	2.5	0 - 8	3.6	0 - 40
Duration of employment (Yrs)	-	-	19.6	5.4 - 50.0	22.5	12.6 - 46.6	18.5	5.4 - 50.0
Validation Test Scores	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
15 item	14.1	1.7	13.2	2.2	13.6	1.6	13.1	2.4
NART	18.1	10.8	19.2	10.4	22.8	11.3	17.8	9.8
DASS Depression	5.1	4.6	3.8	4.4	2.9	2.8	4.1	4.9
DASS Anxiety	5.1	4.7	3.6^	3.4	2.8	3.1	3.9	3.4
DASS Stress	10.6	6.7	8.6	6.1	8.8	5.2	8.5	6.5

^ = p<0.1,* = p<0.05, **= p<0.01 (Students t-test)

Collision repair workers performed significantly lower on tests reflecting attentional performance (table 5.2). In particular, significant deficits were observed for the digit span backwards (-1.5; 95% CI -2.4, -0.5), digit span total (-1.7; CI -3.3, - 0.0), coding (-6.1; CI 9.9, -2.2) and the aggregate total attention scale (-9.3; CI -15.9, -2.8). The overall RBANS total scale was also lower for collision repair workers (-5.1; CI -9.1, -1.2) with the most pronounced deficit observed for panel beaters. Collision repair workers also performed lower for the additional tests including dominant and non-dominant hand coin rotation (-2.9; CI -5.3, -0.4 and -3.1; CI -5.6, -0.7, respectively) and Trail Making Test B (-11.5; CI -22.4, -0.5) with the strongest effects observed in panel beaters (table 5.2).

Table 5.2. Neuropsychological test scores for comparison and collision repair workers

RBANS battery	Comparison group (n=51)	All Collision repair (n=47)		Panel Beaters (n= 13)		Spray painters (n=34)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	28.4 (4.5)	-0.8 (-2.4, 0.8)	27.4 (4.6)	**-2.0 (-4.2, 0.2)^**	28.8 (4.4)	-0.2 (-2.0, 1.5)
RBANS 2 (story memory)	16.9 (3.6)	15.7 (3.9)	-1.3 (-2.8, 0.3)	16.7 (3.1)	-0.9 (-3.1, 1.3)	15.3 (4.2)	**-1.4 (-3.2, 0.3)^**
Total scale Immediate Memory	95.6 (12.6)	91.9 (13.9)	-2.5 (-7.8, 2.9)	93.5 (9.3)	-5.0 (-12.7, 2.7)	91.3 (15.3)	-1.3 (-7.2, 4.5)
Visuospatial/Construction							
RBANS 3 (figure copy)	17.1 (2.5)	17.8 (1.8)	0.6 (-0.4, 1.5)	17.5 (1.7)	0.3 (-1.0, 1.7)	17.9 (1.9)	0.7 (-0.3, 1.8)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.1)	-0.1 (-1.0, 0.8)	19.3 (1.44)	0.5 (-0.8, 1.8)	18.4 (2.3)	-0.4 (-1.4, 0.6)
Total scale vis./const.	99.6 (15.8)	99.7 (15.2)	-2.2 (-8.9, 4.5)	100.2 (16.0)	-3.6 (-13.2, 6.0)	99.5 (15.1)	-1.6 (-8.9, 5.7)
Language							
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.5, 0.8)	10.0 (0.0)	0.3 (-0.6, 1.1)	10.0 (0.0)	0.1 (-0.6, 0.8)
RBANS 6 (semantic fluency)	21.5 (5.2)	21 (3.9)	-1.0 (-3.0, 1.0)	20.5 (3.7)	-1.7 (-4.6, 1.2)	21.2 (4.0)	-0.7 (-2.9, 1.5)
Total scale Language	98.1 (15.0)	97.2 (12.0)	-2.4 (-8.3, 3.4)	97.1 (8.1)	-3.6 (-12.0, 4.8)	97.2 (13.3)	-2.0 (-8.4, 4.5)
Attention							
RBANS 7a (digit span forward)	10.5 (2.3)	10.3 (2.4)	-0.2 (-1.2, 0.8)	9.9 (2.3)	-1.1 (-2.6, 0.3)	10.5 (2.5)	0.2 (-0.9, 1.3)
RBANS 7b (digit span backward)	7.8 (2.3)	6.1 (2.0)	**-1.5 (-2.4, -0.5)****	6.1 (1.6)	**-1.8 (-3.2, -0.4)***	6.1 (2.2)	**-1.3 (-2.4, -0.2)***
RBANS 7c (digit span total)	18.2 (4.1)	16.5 (3.7)	**-1.7 (-3.3, -0.0)***	16.0 (2.7)	**-2.9 (-5.3, -0.6)***	16.7 (4.1)	-1.1 (-2.9, 0.8)
RBANS 8 (coding)	50.6 (9.4)	46.1 (8.4)	**-6.1 (-9.9, -2.2)****	45.0 (6.9)	**-7.7 (-13.2, -2.2)***	46.5 (8.9)	**-5.3 (-9.6, -1.0)***
Total scale Attention	94.6 (14.2)	88.6 (16.2)	**-9.3 (-15.9, -2.8)****	87.7 (11.4)	**-13.1 (-22.5, -3.7)****	88.9 (17.8)	**-7.7 (-14.8, -0.5)***
Delayed Memory							
RBANS 9 (list recall)	7.0 (1.7)	5.7 (2.2)	**-1.0 (-1.7, -0.3)****	5.4 (2.3)	**-1.0 (-2.0, 0.1)^**	5.8 (2.2)	**-1.0 (-1.8, -0.2)***
RBANS 10 (list recognition)	19.6 (1.7)	19.6 (0.6)	0.0 (-0.6, 0.6)	19.6 (0.7)	0.0 (-0.9, 0.9)	19.6 (0.6)	0.0 (-0.7, 0.7)
RBANS 11 (story recall)	9.2 (2.2)	8.4 (2.5)	-0.6 (-1.5, 0.3)	8.8 (2.4)	-0.3 (-1.6, 1.0)	8.2 (2.5)	-0.8 (-1.8, 0.2)
RBANS 12 (figure recall)	14.2 (3.4)	13.9 (3.1)	0.0 (-1.4, 1.5)	13.4 (3.3)	-0.3 (-2.4, 1.8)	14.0 (3.1)	0.2 (-1.4, 1.8)
Total scale Delayed Memory	96.8 (8.4)	93.3 (8.5)	-1.4 (-5.4, 2.5)	94.3 (8.1)	-1.6 (-7.3, 4.1)	92.9 (8.7)	-1.4 (-5.7, 3.0)
RBANS total scale	96.4 (10.1)	92.0 (10.5)	**-5.1 (-9.1, -1.2)***	91.9 (7.1)	**-7.8 (-13.4, -2.2)****	92.0 (11.7)	**-4.0 (-8.3, - 0.3)^**
Additional Tests							
Visual Attention/Reaction Time							
Trails A[¥]	23.8 (9.9)	24.4 (6.9)	-2.0 (-5.6, 1.6)	28.15 (8.1)	**-5.6 (- 10.6, -0.6)***	22.9 (5.8)	-0.3 (- 4.2, 3.6)
Trails B[¥]	68.1 (29.1)	73.4 (27.7)	**-11.5 (- 22.4, -0.5)***	67.4 (22.1)	-6.4 (- 22.0, 9.2)	75.8 (29.5)	**-13.9 (-26.1, -1.8)***
Stroop (I)	2.0 (10.7)	0.5 (7.3)	-3.1 (-7.4, 1.2)	-1.5 (6.7)	-4.4 (-10.6, 1.7)	1.2 (7.5)	-2.5 (-7.3, 2.3)
Motor speed/Dexterity							
Coin rot. Dominant hand	33.7 (5.3)	31.9 (6.2)	**-2.9 (-5.3, -0.4)***	30.00 (6.3)	**-4.0 (-7.5, -0.5)***	32.6 (6.1)	**-2.3 (-5.0, -0.4)^**
Coin rot. Non-dominant	31.3 (5.2)	28.2 (5.7)	**-3.1 (-5.6, -0.7)***	26.69 (5.0)	**-4.3 (-7.8, -0.8)***	28.8 (5.8)	**-2.6 (-5.3, -0.2)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering (Rey 15 item) and premorbid intelligence (NART).

[¥]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Analyses based on the RBANS definitions of 'low' (5th percentile), 'borderline' (10th percentile) and 'low average' (20th percentile) test performance showed a similar pattern, and highlight that observed deficits are relatively large especially for the domain of attention (table 5.3). In particular, for collision repair workers we found a twenty-fold ($p<0.05$) increased risk for "low" test results after adjusting for potential confounders, although due to small numbers in some strata confidence limits were wide. Also, although crude unadjusted analyses (table 5.3) did show increased risks, the magnitude of the effects was considerably lower. This difference was largely due to adjustment for ethnicity; subsequent sensitivity analyses excluding Māori and Pacific people resulted in similarly high odds ratios (Supplementary table 5.5) suggesting that adjusted risk estimates are robust.

Table 5.3. Neuropsychological test scores based on the bottom 5th, 10th and 20th percentiles for Comparison and collision repair workers

	Comparison group (n=51)	All Collision repair (n=47)		
RBANS battery	**N (%)**	**N (%)**	**Unadjusted OR (95%CI)**	**Adjusted OR (95%CI)**
Immediate memory				
5th percentile	2 (3.9)	4 (8.5)	2.3 (0.4, 13.1)	-
10th percentile	4 (7.8)	10 (21.3)	**3.2 (0.9, 10.9)^**	**11.6 (1.4, 99.7)***
20th percentile	17 (33.3)	21 (44.7)	1.6 (0.7, 3.7)	2.0 (0.6, 6.8)
Visuospatial/Construction				
5th percentile	4 (7.8)	1 (2.1)	0.3 (0.0, 2.4)	-
10th percentile	5 (9.8)	4 (8.5)	0.9 (0.2, 3.4)	6.3 (0.2, 166.2)
20th percentile	13 (25.5)	13 (27.7)	1.1 (0.5, 2.7)	1.9 (0.6, 6.3)
Language				
5th percentile	3 (5.9)	1 (2.1)	0.3 (0.0, 3.5)	-
10th percentile	5 (9.8)	3 (6.4)	0.6 (0.1, 2.8)	5.7 (0.1, 259.7)
20th percentile	7 (13.7)	9 (19.2)	1.5 (0.5, 4.4)	**4.5 (0.9, 22.3)^**
Attention				
5th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	**20.1 (1.5, 263.3)***
10th percentile	8 (15.7)	15 (31.9)	**2.5 (1.0, 6.7)^**	**8.8 (1.7, 46.2)***
20th percentile	12 (23.5)	22 (46.8)	**2.9 (1.2, 6.8)***	**5.1 (1.5, 17.6)****
Delayed Memory				
5th percentile	1 (2.0)	2 (4.3)	2.2 (0.2, 25.3)	-
10th percentile	2 (3.9)	2 (4.3)	1.1 (0.1, 8.1)	-
20th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	3.0 (0.7, 12.2)
RBANS total scale				
5th percentile	2 (3.9)	1 (2.1)	0.5 (0.0, 6.1)	-
10th percentile	5 (9.8)	5 (10.6)	1.1 (0.3, 4.1)	6.3(0.4, 90.7)
20th percentile	9 (17.7)	17 (36.2)	**2.6 (1.0, 6.7)***	**14.1 (2.4, 83.6)****

^ = p<0.1,* = p<0.05, ** = p<0.01
Adjusted for ethnicity, alcohol in the past 48 hours, smoking status, DASS A, S and D, NART, test time (of day) and test day (of week).
"-"= No ORs available due to non-convergence

Those with shorter employment duration (i.e. <17 years) performed lower on the domain scale score for attention (-20.6; 95% CI -30.6, -10.6, versus -6.8; CI -16.5, 2.8) as well as the non-dominant hand coin rotation task (-6.5; CI -10.4, -2.6 versus -2.3; CI -6.2, 1.5, table 5.4). However, the trend of lower performance in those with shorter employment duration was not observed consistently across different domains with tests of immediate and delayed memory showing somewhat more pronounced effects in workers with longer employment duration. Adjusting for age altered the effect measures for some outcomes, but the effect on trends was negligible when compared to the model excluding age (Supplementary table 5.6).

Table 5.4. Neuropsychological test scores for collision repair workers stratified by employment duration

		Employment Duration (mean years)			
	Comparison group (n=51)	**< 17 years (10.5) (N = 23)**		**>17 years (28.4) (n = 24)**	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	30.8 (4.2)	-0.9 (-3.4, 1.7)	26.2 (3.5)	**-3.0 (-5.5, -0.6)***
RBANS 2 (story memory)	16.9 (3.6)	15.7 (4.4)	-1.1 (-3.6, 1.5)	15.6 (3.5)	-0.8 (-3.3, 1.7)
Total scale Immediate Memory	95.6 (12.6)	93.2 (16.8)	-3.4 (-12.1, 5.2)	90.7 (10.6)	-6.3 (-14.7, 2.0)
Visuospatial/Construction					
RBANS 3 (figure copy)	17.1 (2.5)	18.0 (1.5)	0.1 (-1.5, 1.6)	17.6 (2.1)	0.5 (-1.0, 2.1)
RBANS 4 (line orientation)	18.8 (1.9)	18.9 (2.2)	0.7 (-0.7, 2.2)	18.5 (2.1)	0.2 (-1.2, 1.7)
Total scale vis./const.	99.6 (15.8)	97.4 (14.2)	-5.0 (-15.8, 5.9)	101.9 (16.1)	-2.5 (-13.0, 8.1)
Language					
RBANS 5 (picture naming)	9.5 (2.0)	10 (0.0)	0.2 (-0.8, 1.2)	10.0 (0.0)	0.3 (-0.7, 1.3)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.6 (4.4)	-1.8 (-5.1, 1.5)	20.4 (3.4)	-1.6 (-4.8, 1.6)
Total scale Language	98.1 (15.0)	99.1 (11.3)	-1.7 (-11.2, 7.8)	93.4 (12.6)	-5.1 (-14.3, 4.0)
Attention					
RBANS 7a (digit span forward)	10.5 (2.3)	10.2 (2.3)	**-1.6 (-3.2, 0.1)^**	10.5 (2.5)	-0.8 (-2.3, 0.8)
RBANS 7b (digit span backward)	7.8 (2.3)	6.4 (2.0)	**-1.8 (-3.4, -0.2)***	5.8 (2.0)	**-1.9 (-3.5, -0.3)***
RBANS 7c (digit span total)	18.2 (4.1)	16.7 (3.6)	**-3.3 (-6.0, -0.5)***	16.3 (3.9)	**-2.6 (-5.3, 0.1)^**
RBANS 8 (coding)	50.6 (9.4)	46.4 (8.0)	**-10.0 (-16.3, -3.8)****	45.8 (8.9)	**-5.6 (-11.7, 0.5)^**
Total scale Attention	94.6 (14.2)	82.3 (14.2)	**-20.6 (-30.6, -10.6)****	94.6 (16.0)	-6.8 (-16.5, 2.8)
Delayed Memory					
RBANS 9 (list recall)	7.0 (1.7)	7.2 (1.3)	0.0 (-1.1, 1.2)	4.3 (1.9)	-1.9 (-3.0, -0.8)
RBANS 10 (list recognition)	19.6 (1.7)	19.8 (0.4)	0.1 (-0.9, 1.1)	19.5 (0.7)	-0.1 (-1.1, 0.8)
RBANS 11 (story recall)	9.2 (2.2)	9.3 (2.2)	0.3 (-1.1, 1.8)	7.5 (2.5)	-0.8 (-2.3, 0.6)
RBANS 12 (figure recall)	14.2 (3.4)	15.4 (2.5)	0.6 (-1.7, 3.0)	12.3 (3.0)	-1.1 (-3.4, 1.1)
Total scale Delayed Memory	96.8 (8.4)	95.5 (6.3)	0.9 (-5.4, 7.3)	91.1 (9.8)	-3.7 (-9.9, 2.4)
RBANS total scale^	96.4 (10.1)	91.0 (11.5)	**-8.7 (-15.1, -2.4)****	92.9 (9.7)	**-7.0 (-13.2, -0.9)***
Additional Tests					
Visual Attention/Reaction Time					
Trails A[ɣ]	23.8 (9.9)	22.8 (6.6)	-7.0 (- 12.7, 1.2)	25.8 (6.9)	-4.4 (- 10.0, 1.2)
Trails B[ɣ]	68.1 (29.1)	71.2 (27.9)	-11.0 (- 28.9, 6.9)	75.6 (27.9)	-2.3 (- 19.8, 15.2)
Stroop (I)	2.0 (10.7)	3.0 (7.4)	-2.4 (-9.4, 4.7)	-1.9 (6.6)	**-6.3 (-13.2, 0.6)^**
Motor speed/Dexterity					
Coin rot. Dominant hand	33.7 (5.3)	32.0 (6.7)	-	31.9 (5.8)	**3.3 (-0.4, 7.0)^**
Coin rot. Non-dominant hand	31.3 (5.2)	27.6 (6.7)	**-6.5 (-10.4, -2.6)****	28.8 (4.5)	-2.3 (-6.2, 1.5)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, alcohol consumption in the past 48 hours, Job title (spray painter/panel beater), smoking status, DASS A, S and D, test time (of day) and test day (of week), malingering/symptom validity (Rey 15 item) and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

"-"= No values available due to non-convergence

5.4 Discussion

Collision repair workers performed significantly lower in the domains of attention, visual attention/reaction time, motor speed/dexterity and, to a lesser extent, memory, with lowest performance reported in panel beaters. No consistent difference with employment duration was found.

The findings of poorer test performance, particularly for attentional performance and memory are consistent with those of our previous questionnaire study (331), where workers reported significantly more symptoms indicative of memory/attention deficits (e.g. general forgetfulness, difficulty remembering names/dates/schedules, difficulty concentrating, absent-mindedness, confusion when concentrating etc.). The findings of lower attentional, memory and motor performance are also consistent with previous international studies in car painters and other solvent exposed workers. (16, 17, 67, 69, 166) including a large 2008 meta-analysis(16), which assessed the impact of solvent mixtures on neurobehavioural performance using the findings of 46 epidemiological studies conducted between 1976 and 2004, involving 53 groups of solvent-exposed workers (i.e. house, car or other industrial painters. (17, 45, 72, 312)) Findings consistent with adverse effects of solvent exposures on neurobehavioural function were found for 43 of the 48 tests used; of those, 12 were statistically significant ($p \leq 0.05$). The strongest effects were shown for attention, with 40% of these tests demonstrating significant effects. Tests of memory, construction and motor speed also showed significant negative effects. Although the test results are not directly comparable, the domains most strongly affected in the meta-analysis were consistent with those affected in the current study. This was particularly the case for the

attentional performance tests of Digit span and Trail making A and B. Furthermore, the meta-analysis showed that longer duration of solvent exposure was associated with reduced effect sizes in 7 of 12 tests, suggesting a healthy worker effect, similar to what we observed in the current study and our previous study. (331)

The deficit in motor speed and dexterity (Coin Rotation Task) observed in the current study may be suggestive of peripheral nervous system effects (351) which may also explain the significantly increased risk of 'neurological' symptoms (i.e., weakness, numbness or tingling in the extremities, dropping things unintentionally, sensorial changes, balance problems, etc.) observed in our previous questionnaire study. (331) Collision repair workers also performed lower on the RBANS total scale score, which is considered one of the measures least susceptible to natural variations in baseline performance, (352) suggesting that the differences in performance observed are likely due to differences in exposure rather than baseline performance.

The effects on neuropsychological performance appear to occur at airborne solvent levels below international exposure standards i.e., our previous survey, in which the current study was nested, found geometric mean concentrations for all solvents combined over a full-work shift of only 2.3 ppm in spray painters and 0.6 ppm in panel beaters. (331) Alternatively, effects observed in this study may be attributable to high historical exposures resulting in persistent deficits in performance. (39) However, this is unlikely to fully explain the lower performance observed in workers with shorter durations of employment (5-17 years), especially as significant reductions in solvent exposure levels in this industry are likely to have occurred as early as two decades ago. (13) It is also highly plausible, as we have suggested previously, (331) that airborne

exposures do not accurately reflect the total body burden of solvent exposure and that dermal exposures (which we did not measure) may be more important. In fact, other studies have suggested that dermal solvent exposures may contribute >50% of the total body burden, particularly when respiratory protection is adequate. (26, 74) It is also possible that other exposures including heavy metals (e.g. lead), alcohol consumption and frequent use of vibrating tools may have contributed to at least some of the observed increased risks. (302, 348, 353) Although lead was used historically, it was largely phased out with the introduction of polyester resin-based fillers in the 1970's. It is currently used occasionally in New Zealand for classic vehicle restorations, however, none of the shops involved in the current or previous study (331)) reported using lead. Alcohol consumption in the past 48 hours was adjusted for in the analyses as acute intoxication is associated with deficits in cognitive and motor performance. (354) However, recent consumption may not take into account the effects of long-term alcohol use. (355) Nonetheless, adjusting for lifetime rather than recent alcohol use had little effect on the results (Supplementary tables 5.7-5.11) and neither did adjusting for both simultaneously (Supplementary table 5.18). Finally use of vibrating tools would account only for the lower performance in motor speed/manual dexterity and not for other test results for which scores were also lower.

Of the collision repair subgroups, panel beaters generally performed the lowest, which is similar to the findings of our previous questionnaire study. A study by Daniell, Stebbins (45) also reported an increased risk of cognitive deficits in panel beaters, but only in those who had previously worked as a spray painter. In our study, only seven panel beaters from the larger survey (331)—and one who completed the

neuropsychological tests—reported having worked as a spray painter. These were recoded as spray painters for all analyses. The effects observed are therefore unlikely to be due to the misclassification of panel beaters and the reasons for more pronounced effects in this group therefore remain unclear, particularly since airborne exposures were lower than those in spray painters (331). However, exposure assessment in our previous study did not include chlorinated solvents (perchloroethylene, tetrachloroethylene and methylene chloride) which have been associated with symptoms of neurotoxicity (176) and are a likely exposure source for panel beaters through the regular use of heavy duty cleaning and degreasing aerosol sprays. Alternatively, as noted above, dermal exposures may be of particular importance for panel beaters and could explain the stronger associations in this group.

Several studies have reported increased risks of subjective symptoms in collision repair and other solvent exposed workers, but did not find associations with objectively measured cognitive performance. This has led to the suggestion that contemporary low-level exposures may be associated with “only” low-grade nervous system dysfunction. (20, 21, 162, 309) However, the results of our analyses focussing on more severe outcomes (i.e. dichotomised by lowest percentile cut-points based on the RBANS normative comparison group) suggest that such a conclusion may not be warranted. In particular, although the numbers were small in some strata, with correspondingly wide confidence intervals, collision repair workers were significantly more likely to score in the ‘low’, ‘borderline’ and ‘low average’ range for attention, in the ‘borderline’ range for immediate memory and in the ‘low average’ range for the RBANS total scale (table 5.3). This is consistent with the findings of our previous

questionnaire study which showed the most pronounced effects when using symptom cut-points reflecting a greater number of symptoms. (331)

For some tests and scaled scores the lowest performance was reported in those workers who had the shortest work duration (table 5.4). This lack of a clear work duration-response trend is consistent with the findings of our previous study, where those with the longest employment duration (20+ years) reported fewer symptoms than those with medium duration (10-19 years). (331) Other studies also failed to find a clear work duration-response trend (22, 23) as demonstrated in a large meta-analysis. (16) This is likely due to healthy worker survivor bias(16) which results from workers who develop symptoms leaving the industry or moving to roles with lower exposures, with those remaining potentially being less susceptible to the effects of solvents or having a higher cognitive 'reserve'. (71, 313) Further evidence for this was found when we repeated the analyses using outcomes defined as lowest percentile scores which showed particularly strong associations (albeit with wide confidence intervals) for attention in those who had been in the industry for ≤17 years (5^{th} percentile: OR=53.3, 95% CI 3.3, 862.5; 10^{th} percentile: 12.5, CI 2.3, 68.6 and 20^{th} percentile: 21.1, CI 4.2, 105.9) compared to those who worked in this industry for >17 years (4.6, CI 0.3, 73.9; 4.3, CI 0.6, 28.8; and 1.2, CI 0.3, 5.5 respectively, (Supplementary table 5.13).

Although workers were invited at random to take part in neuropsychological testing, thus representing a random sample of the workers involved in our previous study (n=370) (331), this may not necessarily be representative of all collision repair workers in New Zealand. However, as noted in our previous study, workers were recruited to

be representative of all workers in this industry, although this was not formally tested. Of those who were invited to take part in the neuropsychological testing, 90% of the collision repair workers and 75% of the comparison group agreed to participate. This is relatively high for these types of studies suggesting that selection bias, if present, is likely to be small. Analyses of demographic characteristics and subjective symptoms between responders and non-responders for both the current study and our previous study showed no differences between groups, confirming that selection bias is unlikely to be an issue. Some differences in alcohol consumption, ethnicity, duration of employment in the industry and the number of workers who had completed a trade certification were observed between those who were re-recruited for testing and those who were not; however differences were for the most part minor and the participant groups were otherwise representative of the previous study groups (Supplementary table 5.19).

It is possible that some of the effects observed may be due to cross shift and/or cross-workweek exposures and are at least partially reversible. However, analyses controlling for when neuropsychological tests were conducted (time during the day and week) did not show appreciable differences in neuropsychological performance (tables 5.2-5.4). Subsequent analyses stratified by time of the week (i.e. Monday-Wednesday versus Thursday/Friday) showed that performance was similarly low in those tested at the start of the week compared to those tested at the end of the week (Supplementary table 5.14) suggesting that the influence of cross-week exposures (as opposed to long-term chronic exposure) on performance is small.

Some participants in the comparison group may have had occupational exposure to solvents and this is a potential limitation of the study. However, excluding workers who reported working regularly with solvents (n=7) made little difference to the results (Supplementary table 5.15). Also, we included office workers (n=4) for whom we reclassified their job titles (see above) which may have resulted in misclassification. However, at the time of the study all four workers performed some repair work on the shop floor, especially during busy periods and therefore were likely to be at risk of at least some 'current' exposure. Analyses excluding them did not affect the results (Supplementary table 5.16).

Differences in age, ethnicity, smoking, alcohol consumption, education, verbal intelligence and depression, anxiety and stress were present between exposure groups, but these were adjusted for in the analysis. Nonetheless, some residual confounding may still have occurred, but the neuropsychological domains affected and the pattern of the effects observed was consistent with our previous study and other international studies of comparable workers, suggesting results are robust. Also, additional sensitivity analyses excluding Māori or Pacific people, who performed lower on some tests, had little effect on the results (Supplementary table 5.17). Another limitation was the high correlation between age and duration of employment (Spearmans coefficient, 0.91). However, trends observed in analyses adjusted for age were very similar to analyses not adjusting for age (Supplementary table 5.6) suggesting employment duration is, at least to some degree, independently associated with performance. The limited time available for testing (30-40 minutes) only allowed for a brief test battery, but the tests applied covered functionality previously reported

to be affected in solvent exposed workers, (16) and the trends observed were consistent with international studies which employed more comprehensive test batteries. (69, 308) Finally, the sample size was relatively small which prevented more detailed subgroup analyses.

In conclusion, consistent with our previous questionnaire survey in a larger sample of workers, this study has reported significant deficits in objectively measured cognitive performance in solvent- exposed collision repair workers. Analyses focussing on those with the poorest performance suggest that effects in some workers may be relatively severe, despite current airborne exposures in New Zealand being well below international exposure standards.

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5.5 Supplementary material

Table 5.5. Supplementary table - Neuropsychological test scores based on the lowest 5th, 10th and 20th percentiles for comparison and collision repair workers – Excluding Māori and Pacific persons

	Reference Group	**All Collision repair**		
	(n=30)	**(n=42)**		
RBANS battery	**N (%)**	**N (%)**	**Unadjusted OR (95%CI)**	**Adjusted OR (95%CI)**
Immediate memory				
5th percentile	0 (0.0)	3 (7.1)	-	-
10th percentile	0 (0.0)	8 (19.1)	-	-
20th percentile	8 (26.7)	18 (42.9)	2.1 (0.7-5.7)	2.6 (0.6-10.7)
Visuospatial/Construction				
5th percentile	1 (3.3)	0 (0.0)	-	-
10th percentile	2 (6.7)	2 (4.7)	0.7 (0.1-5.3)	1.8 (0.0-70.4)
20th percentile	6 (20.0)	10.0 (23.8)	1.3 (0.4-3.9)	1.7 (0.4-6.9)
Language				
h5th percentile	0 (0.0)	1 (2.4)	-	-
10th percentile	0 (0.0)	2 (4.8)	-	-
20th percentile	1 (3.3)	7 (16.7)	5.8 (0.7-49.9)	**8.2 (0.7-95.2)^**
Attention				
5th percentile	1 (3.3)	7 (16.7)	5.8 (0.7-49.9)	-
10th percentile	2 (6.7)	11 (26.2)	**5.0 (1.0-24.4)***	**10.9 (1.1-104.0)***
20th percentile	5 (16.7)	17 (40.5)	**3.4 (1.1-10.6)***	2.9 (0.8-10.9)
Delayed Memory				
5th percentile	1 (3.3)	2 (4.8)	1.5 (0.1-16.8)	-
10th percentile	2 (6.7)	2 (4.8)	0.7 (0.1-5.3)	-
20th percentile	4 (13.3)	9 (21.4)	1.8 (0.5-6.4)	1.6 (0.4-7.1)
RBANS total scale				
5th percentile	0 (0.0)	1 (2.4)	-	-
10th percentile	0 (0.0)	3 (7.1)	-	-
20th percentile	3 (10.0)	12 (28.6)	**3.6 (0.9-14.1)^**	**6.1 (0.9-40.4)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week) and premorbid intelligence (NART).

"-"= No ORs available due to non-convergence

Table 5.6. Supplementary table – Neuropsychological test scores for collision repair workers stratified by employment duration – Excluding age from the regression model

	Reference Group (n=51)	Employment Duration (mean years) < 17 years (10.5) (N = 23)		>17 years (28.4) (n = 24)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95% CI)**	**Mean (SD)**	**Difference (95% CI)**
RBANS 1 (list learning)	29.6 (4.0)	30.0 (4.6)	-0.1 (-2.7, 2.5)	26.5 (3.6)	**-4.0 (-6.5, -1.4)****
RBANS 2 (story memory)	16.9 (3.6)	15.6 (4.4)	-0.6 (-3.1, 2.0)	15.6 (3.1)	-1.4 (-3.9, 1.1)
Visuospatial/Construction					
RBANS 3 (figure copy)	17.1 (2.5)	18.1 (1.5)	0.5 (-1.1, 2.1)	17.5 (2.0)	0.1 (-1.5, 1.6)
RBANS 4 (line orientation)	18.8 (1.9)	19.0 (2.0)	0.9 (-0.6, 2.3)	18.3 (2.1)	0.1 (-1.3, 1.5)
Language					
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.4 (-0.6, 1.4)	10.0 (0.0)	0.1 (-0.9, 1.0)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.2 (4.4)	-1.4 (-4.6, 1.9)	20.9 (3.3)	-2.2 (-5.3, 1.0)
Attention					
RBANS 7a (digit span forward)	10.5 (2.3)	10.1 (2.2)	**-1.4 (-3.0, 0.2)^**	10.9 (2.7)	-1.0 (-2.5, 0.6)
RBANS 7b (digit span backward)	7.8 (2.3)	6.3 (2.0)	**-1.6 (-3.2, 0.0)***	6.2 (2.1)	**-2.1 (-3.6, -0.5)****
RBANS 7c (digit span total)	18.2 (4.1)	16.4 (3.5)	**-2.9 (-5.6, -0.3)***	17.1 (4.2)	**-3.0 (-5.6, -0.4)***
RBANS 8 (coding)	50.6 (9.4)	46.6 (7.9)	**-8.3 (-14.7, -1.9)***	45.1 (9.8)	**-7.7 (-13.9, -1.5)***
Delayed Memory					
RBANS 9 (list recall)	7.0 (1.7)	6.8 (1.6)	0.4 (-0.8, 1.5)	4.1 (2.0)	**-2.3 (-3.4, -1.2)****
RBANS 10 (list recognition)	19.6 (1.7)	19.8 (0.4)	0.2 (-0.7, 1.2)	19.4 (0.7)	-0.3 (-1.2, 0.7)
RBANS 11 (story recall)	9.2 (2.2)	9 (2.3)	0.8 (-0.7, 2.4)	7.2 (2.5)	**-1.5 (-3.0, 0.0)^**
RBANS 12 (figure recall)	14.2 (3.4)	15.1 (3.0)	1.0 (-1.3, 3.3)	12.4 (2.8)	-1.5 (-3.8, 0.7)
Additional Tests					
Visual Attention/Reaction Time					
Trails A[ɣ]	23.8 (9.9)	23.3 (6.7)	-4.8 (- 10.9, 1.3)	25.1 (6.9)	**-7.0 (- 12.9, -1.1)***
Trails B[ɣ]	68.1 (29.1)	71.2 (27.4)	-4.7 (- 23.5, 14.2)	77.4 (30.2)	-9.8 (- 28.1, 8.4)
Stroop (I)	2.0 (10.7)	2.4 (7.3)	-1.6 (-8.5, 5.4)	-2.4 (7.2)	**-7.3 (-14.0, -0.6)***
Motor speed/Dexterity					
Coin rot. Dominant hand	33.7 (5.3)	31.9 (6.4)	-	32.7 (6.1)	1.0 (-2.4, 4.4)
Coin rot. Non-dominant hand	31.3 (5.2)	27.7 (6.5)	**-5.6 (-9.6, -1.7)****	28.9 (4.8)	**-3.4 (-7.2, 0.4)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for ethnicity, job title, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test – Algebraic sign of coefficient changed accordingly

"-"= No values available due to non-convergence

Table 5.7. Supplementary table - Neuropsychological test scores for Comparison and collision repair workers – Adjusted for lifetime alcohol (mean drinks per week) in place of alcohol consumption in the past 48 hours

RBANS battery	Comparison group (n=51)	All Collision repair (n=47)		Panel Beaters (n= 13)		Spray painters (n=34)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	28.4 (4.5)	-0.9 (-2.5, 0.6)	27.4 (4.6)	**-2.1 (-4.3, 0.2)^**	28.8 (4.4)	-0.4 (-2.1, 1.3)
RBANS 2 (story memory)	16.9 (3.6)	15.7 (3.9)	-1.2 (-2.7, 0.3)	16.7 (3.1)	-0.9 (-3.1, 1.3)	15.3 (4.2)	**-1.3 (-3.0, 0.4)^**
Total scale Immediate Memory	95.6 (12.6)	91.9 (13.9)	-2.6 (-7.9, 2.7)	93.5 (9.3)	-5.2 (-12.8, 2.5)	91.3 (15.3)	-1.6 (-7.3, 4.2)
Visuospatial/Construction							
RBANS 3 (figure copy)	17.1 (2.5)	17.8 (1.8)	0.6 (-0.3, 1.6)	17.5 (1.7)	0.3 (-1.0, 1.7)	17.9 (1.9)	0.8 (-0.3, 1.8)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.1)	-0.1 (-1.0, 0.8)	19.3 (1.44)	0.4 (-0.8, 1.7)	18.4 (2.3)	-0.4 (-1.4, 0.6)
Total scale vis./const.	99.6 (15.8)	99.7 (15.2)	-1.9 (-8.5, 4.8)	100.2 (16.0)	-3.5 (-13.1, 6.2)	99.5 (15.1)	-1.2 (-8.5, 6.1)
Language							
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.4, 0.8)	10.0 (0.0)	0.3 (-0.6, 1.1)	10.0 (0.0)	0.1 (-0.6, 0.8)
RBANS 6 (semantic fluency)	21.5 (5.2)	21 (3.9)	-1.0 (-3.1, 1.0)	20.5 (3.7)	-1.7 (-4.5, 1.2)	21.2 (4.0)	-0.8 (-3.0, 1.4)
Total scale Language	98.1 (15.0)	97.2 (12.0)	-3.1 (-9.2, 2.9)	97.1 (8.1)	-3.4 (-12.2, 5.4)	97.2 (13.3)	-3.0 (-9.7, 3.6)
Attention							
RBANS 7a (digit span forward)	10.5 (2.3)	10.3 (2.4)	-0.2 (-1.2, 0.8)	9.9 (2.3)	-1.1 (-2.5, 0.3)	10.5 (2.5)	0.2 (-0.9, 1.3)
RBANS 7b (digit span backward)	7.8 (2.3)	6.1 (2.0)	**-1.5 (-2.5, -0.5)****	6.1 (1.6)	**-1.8 (-3.2, -0.4)***	6.1 (2.2)	**-1.3 (-2.4, -0.2)***
RBANS 7c (digit span total)	18.2 (4.1)	16.5 (3.7)	**-1.7 (-3.3, 0.0)***	16.0 (2.7)	**-2.9 (-5.3, -0.5)***	16.7 (4.1)	-1.1 (-2.9, 0.7)
RBANS 8 (coding)	50.6 (9.4)	46.1 (8.4)	**-6.2 (-10, -2.3)****	45.0 (6.9)	**-7.6 (-13.1, -2)***	46.5 (8.9)	**-5.6 (-9.8, -1.3)***
Total scale Attention	94.6 (14.2)	88.6 (16.2)	**-9.5 (-16, -2.9)****	87.7 (11.4)	**-13.0 (-22.4, -3.6)****	88.9 (17.8)	**-8.0 (-15.1, -0.8)***
Delayed Memory							
RBANS 9 (list recall)	7.0 (1.7)	5.7 (2.2)	**-1.0 (-1.7, -0.2)****	5.4 (2.3)	**-1.0 (-2.1, 0.1)^**	5.8 (2.2)	**-1.0 (-1.8, -0.1)***
RBANS 10 (list recognition)	19.6 (1.7)	19.6 (0.6)	0.0 (-0.6, 0.6)	19.6 (0.7)	0.0 (-0.9, 0.8)	19.6 (0.6)	0.0 (-0.7, 0.7)
RBANS 11 (story recall)	9.2 (2.2)	8.4 (2.5)	-0.6 (-1.5, 0.3)	8.8 (2.4)	-0.2 (-1.5, 1.0)	8.2 (2.5)	-0.7 (-1.7, 0.3)
RBANS 12 (figure recall)	14.2 (3.4)	13.9 (3.1)	0.1 (-1.3, 1.6)	13.4 (3.3)	-0.2 (-2.3, 1.8)	14.0 (3.1)	0.3 (-1.3, 1.9)
Total scale Delayed Memory	96.8 (8.4)	93.3 (8.5)	-1.4 (-5.4, 2.5)	94.3 (8.1)	-1.6 (-7.3, 4.1)	92.9 (8.7)	-1.3 (-5.7, 3.0)
RBANS total scale	96.4 (10.1)	92.0 (10.5)	**-5.2 (-9.2, -1.3)***	91.9 (7.1)	**-7.8 (-13.5, -2.2)****	92.0 (11.7)	**-4.1 (-8.4, 0.1)^**
Additional Tests							
Visual Attention/Reaction Time							
Trails A[¥]	23.8 (9.9)	24.4 (6.9)	-1.8 (-1.8, 5.3)	28.15 (8.1)	**-5.5 (-10.5, -0.5)**	22.9 (5.8)	-0.1 (-3.9, 3.8)
Trails B[¥]	68.1 (29.1)	73.4 (27.7)	**-11.0 (-22.0, -0.1)***	67.4 (22.1)	-6.4 (-9.3, 22.1)	75.8 (29.5)	**-13.1 (-25.3, -1.0)***
Stroop (I)	2.0 (10.7)	0.5 (7.3)	-3.3 (-7.6, 1.0)	-1.5 (6.7)	-4.6 (-10.7, 1.6)	1.2 (7.5)	-2.8 (-7.5, 2.0)
Motor speed/Dexterity							
Coin rot. Dominant hand	33.7 (5.3)	31.9 (6.2)	**-2.8 (-5.3, -0.4)***	30.00 (6.3)	-4.0 (-7.5, -0.5)	32.6 (6.1)	**-2.3 (-5.0, 0.4)^**
Coin rot. Non-dominant	31.3 (5.2)	28.2 (5.7)	**-3.2 (-5.6, -0.7)***	26.69 (5.0)	-4.3 (-7.8, -0.8)	28.8 (5.8)	**-2.6 (-5.3, 0.1)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, Lifetime Alcohol (Mean drinks p/week**)**, smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering (Rey 15 item) and premorbid intelligence (NART).

[¥]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Table 5.8. Supplementary table - Neuropsychological test scores based on the bottom 5th, 10th and 20th percentiles for Comparison and collision repair workers – Adjusted for lifetime alcohol (mean drinks per week) in place of alcohol consumption in the past 48 hours

	Comparison group (n=51)	**All Collision repair (n=47)**		
RBANS battery	**N (%)**	**N (%)**	**Unadjusted OR (95%CI)**	**Adjusted OR (95%CI)**
Immediate memory				
5th percentile	2 (3.9)	4 (8.5)	2.3 (0.4, 13.1)	-
10th percentile	4 (7.8)	10 (21.3)	**3.2 (0.9, 10.9)^**	**10.6 (1.3, 89.6)***
20th percentile	17 (33.3)	21 (44.7)	1.6 (0.7, 3.7)	2.1 (0.6, 6.9)
Visuospatial/Construction				
5th percentile	4 (7.8)	1 (2.1)	0.3 (0.0, 2.4)	
10th percentile	5 (9.8)	4 (8.5)	0.9 (0.2, 3.4)	4.0 (0.3, 61.8)
20th percentile	13 (25.5)	13 (27.7)	1.1 (0.5, 2.7)	1.9 (0.6, 6.2)
Language				
5th percentile	3 (5.9)	1 (2.1)	0.3 (0.0, 3.5)	-
10th percentile	5 (9.8)	3 (6.4)	0.6 (0.1, 2.8)	1.5 (0.1, 15.1)
20th percentile	7 (13.7)	9 (19.2)	1.5 (0.5, 4.4)	**4.3 (0.9, 20.5)^**
Attention				
5th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	**19.0 (1.4, 252.6)***
10th percentile	8 (15.7)	15 (31.9)	**2.5 (1.0, 6.7)^**	**8.6 (1.7, 44.9)***
20th percentile	12 (23.5)	22 (46.8)	**2.9 (1.2, 6.8)***	**5.2 (1.5, 17.8)****
Delayed Memory				
5th percentile	1 (2.0)	2 (4.3)	2.2 (0.2, 25.3)	-
10th percentile	2 (3.9)	2 (4.3)	1.1 (0.1, 8.1)	0.0 (0.0, 7.6)
20th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	3.1 (0.8, 12.3)
RBANS total scale				
5th percentile	2 (3.9)	1 (2.1)	0.5 (0.0, 6.1)	-
10th percentile	5 (9.8)	5 (10.6)	1.1 (0.3, 4.1)	4.1 (0.4, 40.8)
20th percentile	9 (17.7)	17 (36.2)	**2.6 (1.0, 6.7)***	**14.2 (2.4, 84.5)****

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for ethnicity, Lifetime Alcohol (Mean drinks per week**)**, smoking status, DASS A, S and D, NART, test time (of day) and test day (of week).

"-"= No ORs available due to non-convergence

Table 5.9. Supplementary table - Neuropsychological test scores for collision repair workers stratified by employment duration. – Adjusted for lifetime alcohol (mean drinks per week) in place of alcohol consumption in the past 48 hours

		Employment Duration (mean years)			
	Comparison group (n=51)	**< 17 years (10.5) (N = 23)**		**>17 years (28.4) (n = 24)**	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	30.8 (4.2)	-0.9 (-3.4, 1.6)	26.2 (3.5)	**-3.1 (-5.6, -0.6)***
RBANS 2 (story memory)	16.9 (3.6)	15.7 (4.4)	-0.9 (-3.5, 1.6)	15.6 (3.5)	-0.8 (-3.3, 1.7)
Total scale Immediate Memory	95.6 (12.6)	93.2 (16.8)	-3.5 (-12.2,5.1)	90.7 (10.6)	-6.5 (-14.9, 1.8)
Visuospatial/Construction					
RBANS 3 (figure copy)	17.1 (2.5)	18.0 (1.5)	0.1 (-1.5, 1.6)	17.6 (2.1)	0.6 (-1.0, 2.1)
RBANS 4 (line orientation)	18.8 (1.9)	18.9 (2.2)	0.6 (-0.9, 2.0)	18.5 (2.1)	0.3 (-1.1, 1.7)
Total scale vis./const.	99.6 (15.8)	97.4 (14.2)	-5.0 (-15.9,5.9)	101.9 (16.1)	-2.2(-12.7-8.4)
Language					
RBANS 5 (picture naming)	9.5 (2.0)	10 (0.0)	0.2 (-0.8, 1.2)	10.0 (0.0)	0.3 (-0.7, 1.3)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.6 (4.4)	-1.7 (-5.0, 1.7)	20.4 (3.4)	-1.7 (-4.9, 1.6)
Total scale Language	98.1 (15.0)	99.1 (11.3)	-0.7(-10.6, 9.1)	93.4 (12.6)	-5.6 (-15.2, 3.9)
Attention					
RBANS 7a (digit span forward)	10.5 (2.3)	10.2 (2.3)	**-1.5 (-3.1, 0.1)^**	10.5 (2.5)	-0.8 (-2.4, 0.8)
RBANS 7b (digit span backward)	7.8 (2.3)	6.4 (2.0)	**-1.8 (-3.4, -0.2)***	5.8 (2.0)	**-1.9 (-3.5, -0.3)***
RBANS 7c (digit span total)	18.2 (4.1)	16.7 (3.6)	**-3.2 (-5.9, -0.5)***	16.3 (3.9)	**-2.6 (-5.3, 0.0)^**
RBANS 8 (coding)	50.6 (9.4)	46.4 (8.0)	**-9.6 (-15.9, -3.2)****	45.8 (8.9)	**-5.8 (-12.0, 0.4)^**
Total scale Attention	94.6 (14.2)	82.3 (14.2)	**-20.1(-30.2, -10.0)****	94.6 (16.0)	-7.1 (-16.9, 2.7)
Delayed Memory					
RBANS 9 (list recall)	7.0 (1.7)	7.2 (1.3)	0.0 (-1.2, 1.1)	4.3 (1.9)	-1.9 (-3.0, -0.8)
RBANS 10 (list recognition)	19.6 (1.7)	19.8 (0.4)	0.0 (-1.0, 1.0)	19.5 (0.7)	-0.1 (-1.1, 0.9)
RBANS 11 (story recall)	9.2 (2.2)	9.3 (2.2)	0.4 (-1.1, 1.9)	7.5 (2.5)	-0.8 (-2.2, 0.6)
RBANS 12 (figure recall)	14.2 (3.4)	15.4 (2.5)	0.8 (-1.6, 3.1)	12.3 (3.0)	-1.1 (-3.4, 1.2)
Total scale Delayed Memory	96.8 (8.4)	95.5 (6.3)	1.0 (-5.4, 7.3)	91.1 (9.8)	-3.7 (-9.8, 2.5)
RBANS total scale^	96.4 (10.1)	91.0 (11.5)	**-8.6 (-15, -2.2)****	92.9 (9.7)	**-7.2 (-13.3, -1.0)***
Additional Tests					
Visual Attention/Reaction Time					
Trails A[¥]	23.8 (9.9)	22.8 (6.6)	-6.7 (-12.5, 1.0)	25.8 (6.9)	4.4 (-10.0, 1.2)
Trails B[¥]	68.1 (29.1)	71.2 (27.9)	-11.4 (-29.4, 6.7)	75.6 (27.9)	2.0 (-19.5, 15.5)
Stroop (I)	2.0 (10.7)	3.0 (7.4)	-2.5 (-9.6, 4.5)	-1.9 (6.6)	**-6.3 (-13.2, 0.5)^**
Motor speed/Dexterity					
Coin rot. Dominant hand	33.7 (5.3)	32.0 (6.7)	-	31.9 (5.8)	**3.2 (-0.5, 6.9)^**
Coin rot. Non-dominant hand	31.3 (5.2)	27.6 (6.7)	**-6.6 (-10.5, -2.6)****	28.8 (4.5)	-2.4 (-6.2, 1.5)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, Job title (spray painter/panel beater), Lifetime Alcohol (Mean drinks p/week), smoking status, DASS A, S and D, test time (of day) and test day (of week), malingering/symptom validity (Rey 15 item) and premorbid intelligence (NART).

[¥]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

"-"= No ORs available due to non-convergence

Table 5.10. Supplementary table - Neuropsychological test scores for Comparison and collision repair workers – Adjusted for lifetime alcohol consumption (frequency) in place of alcohol consumption in the past 48 hours

RBANS battery	Comparison group (n=51)	All Collision repair (n=47)		Panel Beaters (n= 13)		Spray painters (n=34)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	28.4 (4.5)	-0.9 (-2.4, 0.7)	27.4 (4.6)	-2.0 (-4.2, 0.3)	28.8 (4.4)	-0.3 (-2.1, 1.4)
RBANS 2 (story memory)	16.9 (3.6)	15.7 (3.9)	-1.2 (-2.0, 0.3)	16.7 (3.1)	-0.9 (-3.1, 1.3)	15.3 (4.2)	-1.4 (-3.1, 0.3)
Total scale Immediate Memory	95.6 (12.6)	91.9 (13.9)	-2.6 (-7.9, 2.7)	93.5 (9.3)	-5.1 (-12.8, 2.6)	91.3 (15.3)	-1.6 (-7.4, 4.2)
Visuospatial/Construction							
RBANS 3 (figure copy)	17.1 (2.5)	17.8 (1.8)	0.6 (-0.3, 1.6)	17.5 (1.7)	0.3 (-1.0, 1.7)	17.9 (1.9)	0.8 (-0.3, 1.8)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.1)	-0.1 (-1.0, 0.8)	19.3 (1.44)	0.5 (-0.8, 1.7)	18.4 (2.3)	-0.3 (-1.3, 0.7)
Total scale vis./const.	99.6 (15.8)	99.7 (15.2)	-2.0 (-8.7, 4.6)	100.2 (16.0)	-3.7 (-13.4, 5.9)	99.5 (15.1)	-1.3 (-8.6, 6.0)
Language							
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.4, 0.8)	10.0 (0.0)	0.3 (-0.6, 1.1)	10.0 (0.0)	0.2 (-0.5, 0.8)
RBANS 6 (semantic fluency)	21.5 (5.2)	21 (3.9)	-1.0 (-3.0, 1.0)	20.5 (3.7)	-1.7 (-4.5, 1.2)	21.2 (4.0)	-0.8 (-3.0, 1.5)
Total scale Language	98.1 (15.0)	97.2 (12.0)	-3.0 (-9.0, 3.0)	97.1 (8.1)	-3.3 (-12, 5.4)	97.2 (13.3)	-2.9 (-9.5, 3.7)
Attention							
RBANS 7a (digit span forward)	10.5 (2.3)	10.3 (2.4)	-0.2 (-1.2, 0.8)	9.9 (2.3)	-1.1 (-2.6, 0.3)	10.5 (2.5)	0.2 (-0.9, 1.3)
RBANS 7b (digit span backward)	7.8 (2.3)	6.1 (2.0)	**-1.5 (-2.5, -0.5)****	6.1 (1.6)	**-1.8 (-3.2, -0.4)***	6.1 (2.2)	**-1.3 (-2.4, -0.2)***
RBANS 7c (digit span total)	18.2 (4.1)	16.5 (3.7)	**-1.7 (-3.3, -0.0)***	16.0 (2.7)	**-2.9 (-5.3, -0.5)***	16.7 (4.1)	-1.1 (-2.9, 0.7)
RBANS 8 (coding)	50.6 (9.4)	46.1 (8.4)	**-6.2 (-10.0, -2.3)****	45.0 (6.9)	**-7.6 (-13.1, -2.0)***	46.5 (8.9)	**-5.5 (-9.8, -1.3)***
Total scale Attention	94.6 (14.2)	88.6 (16.2)	**-9.4 (-16.0, -2.9)****	87.7 (11.4)	**-13.0 (-22.4, -3.6)****	88.9 (17.8)	**-7.9 (-15.1, -0.8)***
Delayed Memory							
RBANS 9 (list recall)	7.0 (1.7)	5.7 (2.2)	**-0.9 (-1.7, 0.2)****	5.4 (2.3)	**-1.0 (-2.0, 0.1)^**	5.8 (2.2)	**-0.9 (-1.7, -0.1)***
RBANS 10 (list recognition)	19.6 (1.7)	19.6 (0.6)	0.0 (-0.6, 0.6)	19.6 (0.7)	0.0 (-0.9, 0.8)	19.6 (0.6)	0.0 (-0.7, 0.7)
RBANS 11 (story recall)	9.2 (2.2)	8.4 (2.5)	-0.6 (-1.5, 0.3)	8.8 (2.4)	-0.2 (-1.5, 1.0)	8.2 (2.5)	-0.7 (-1.7, 0.3)
RBANS 12 (figure recall)	14.2 (3.4)	13.9 (3.1)	0.1 (-1.3, 1.6)	13.4 (3.3)	-0.3 (-2.3, 1.8)	14.0 (3.1)	0.3 (-1.3, 1.9)
Total scale Delayed Memory	96.8 (8.4)	93.3 (8.5)	-1.3 (-5.2, 2.6)	94.3 (8.1)	-1.4 (-7.1, 4.2)	92.9 (8.7)	-1.2 (-5.5, 3.0)
RBANS total scale	96.4 (10.1)	92.0 (10.5)	**-5.2 (-9.2, -1.3)****	91.9 (7.1)	**-7.8 (-13.4, -2.2)***	92.0 (11.7)	**-4.1 (-8.4, 0.1)^**
Additional Tests							
Visual Attention/Reaction Time							
Trails A[¥]	23.8 (9.9)	24.4 (6.9)	-1.8 (-5.3, 1.8)	28.15 (8.1)	**-5.5 (-10.5, -0.5)***	22.9 (5.8)	0.1 (-3.9, 3.8)
Trails B[¥]	68.1 (29.1)	73.4 (27.7)	**-11.1 (-22.1, -0.2)***	67.4 (22.1)	-6.5 (-22.1, 9.2)	75.8 (29.5)	**13.2 (-25.3, -1.1)***
Stroop (I)	2.0 (10.7)	0.5 (7.3)	-3.3 (-7.6, 1.0)	-1.5 (6.7)	-4.5 (-10.7, 1.6)	1.2 (7.5)	-2.8 (-7.5, 2.0)
Motor speed/Dexterity							
Coin rot. Dominant hand	33.7 (5.3)	31.9 (6.2)	**-2.9 (-5.3, -0.4)***	30.00 (6.3)	**-4.0 (-7.5, -0.5)***	32.6 (6.1)	**-2.3 (-5.0, 0.4)^**
Coin rot. Non-dominant	31.3 (5.2)	28.2 (5.7)	**-3.1 (-5.6, -0.7)***	26.69 (5.0)	**-4.3 (-7.8, -0.8)***	28.8 (5.8)	**-2.6 (-5.3, 0.1)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, Lifetime alcohol consumption (frequency), smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering (Rey 15 item) and premorbid intelligence (NART).

[¥]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Table 5.11. Supplementary table - Neuropsychological test scores based on the bottom 5th, 10th and 20th percentiles for Comparison and collision repair workers - Adjusted for lifetime alcohol consumption (frequency) in place of alcohol consumption in the past 48 hours

	Comparison group (n=51)	**All Collision repair (n=47)**		
RBANS battery	**N (%)**	**N (%)**	**Unadjusted OR (95%CI)**	**Adjusted OR (95%CI)**
Immediate memory				
5th percentile	2 (3.9)	4 (8.5)	2.3 (0.4, 13.1)	-
10th percentile	4 (7.8)	10 (21.3)	**3.2 (0.9, 10.9)^**	**11.0 (1.3, 95.6)***
20th percentile	17 (33.3)	21 (44.7)	1.6 (0.7, 3.7)	2.1 (0.6, 7.0)
Visuospatial/Construction				
5th percentile	4 (7.8)	1 (2.1)	0.3 (0.0, 2.4)	-
10th percentile	5 (9.8)	4 (8.5)	0.9 (0.2, 3.4)	4.7 (0.3, 77.7)
20th percentile	13 (25.5)	13 (27.7)	1.1 (0.5, 2.7)	1.8 (0.6, 5.9)
Language				
5th percentile	3 (5.9)	1 (2.1)	0.3 (0.0, 3.5)	
10th percentile	5 (9.8)	3 (6.4)	0.6 (0.1, 2.8)	1.6 (0.1, 18.0)
20th percentile	7 (13.7)	9 (19.2)	1.5 (0.5, 4.4)	**4.3 (0.9, 20.6)^**
Attention				
5th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	**20.4 (1.5, 280.6)***
10th percentile	8 (15.7)	15 (31.9)	**2.5 (1.0, 6.7)^**	**9.5 (1.7, 52.4)***
20th percentile	12 (23.5)	22 (46.8)	**2.9 (1.2, 6.8)***	**5.1 (1.5, 17.4)****
Delayed Memory				
5th percentile	1 (2.0)	2 (4.3)	2.2 (0.2, 25.3)	-
10th percentile	2 (3.9)	2 (4.3)	1.1 (0.1, 8.1)	-
20th percentile	4 (7.8)	11 (23.4)	**3.6 (1.1, 12.2)***	2.8 (0.7, 11.4)
RBANS total scale				
5th percentile	2 (3.9)	1 (2.1)	0.5 (0.0, 6.1)	-
10th percentile	5 (9.8)	5 (10.6)	1.1 (0.3, 4.1)	4.5 (0.4, 47.3)
20th percentile	9 (17.7)	17 (36.2)	**2.6 (1.0, 6.7)***	**14.3 (2.4, 85.2)****

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for ethnicity, Lifetime alcohol consumption (frequency**)**, smoking status, DASS A, S and D, NART, test time (of day) and test day (of week).

"-"= No ORs available due to non-convergence

Table 5.12. Supplementary table - Neuropsychological test scores for collision repair workers stratified by employment duration

	Comparison group (n=51)	Employment Duration (mean years) < 17 years (10.5) (N = 23)		>17 years (28.4) (n = 24)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95%CI)**	**Mean (SD)**	**Difference (95%CI)**
RBANS 1 (list learning)	29.6 (4.0)	30.8 (4.2)	-0.8 (-3.3, 1.7)	26.2 (3.5)	**-3.1 (-5.6, -0.6)***
RBANS 2 (story memory)	16.9 (3.6)	15.7 (4.4)	-1.1 (-3.6, 1.5)	15.6 (3.5)	-0.8 (-3.2, 1.7)
Total scale Immediate Memory	95.6 (12.6)	93.2 (16.8)	-3.4 (-12, 5.2)	90.7 (10.6)	-6.5 (-14.9, 1.8)
Visuospatial/Construction					
RBANS 3 (figure copy)	17.1 (2.5)	18.0 (1.5)	0.1 (-1.5, 1.6)	17.6 (2.1)	0.6 (-0.9, 2.1)
RBANS 4 (line orientation)	18.8 (1.9)	18.9 (2.2)	0.7 (-0.8, 2.1)	18.5 (2.1)	0.3 (-1.2, 1.7)
Total scale vis./const.	99.6 (15.8)	97.4 (14.2)	-5.2 (-16.1, 5.6)	101.9 (16.1)	-2.4 (-13.0, 8.1)
Language					
RBANS 5 (picture naming)	9.5 (2.0)	10 (0.0)	0.2 (-0.8, 1.2)	10.0 (0.0)	0.3 (-0.6, 1.3)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.6 (4.4)	-1.7 (-5.0, 1.6)	20.4 (3.4)	-1.6 (-4.9, 1.6)
Total scale Language	98.1 (15.0)	99.1 (11.3)	-0.8 (-10.6, 9.0)	93.4 (12.6)	-5.4 (-14.9, 4.1)
Attention					
RBANS 7a (digit span forward)	10.5 (2.3)	10.2 (2.3)	**-1.5 (-3.2, 0.1)^**	10.5 (2.5)	-0.8 (-2.3, 0.8)
RBANS 7b (digit span backward)	7.8 (2.3)	6.4 (2.0)	**-1.8 (-3.4, -0.1)***	5.8 (2.0)	**-1.9 (-3.5, -0.3)***
RBANS 7c (digit span total)	18.2 (4.1)	16.7 (3.6)	**-3.2 (-6.0, -0.5)***	16.3 (3.9)	**-2.6 (-5.3, 0.0)^**
RBANS 8 (coding)	50.6 (9.4)	46.4 (8.0)	**-9.7 (-16, -3.4)****	45.8 (8.9)	**-5.7 (-11.8, 0.5)^**
Total scale Attention	94.6 (14.2)	82.3 (14.2)	**-20.2 (-30.2, -10.1)****	94.6 (16.0)	-6.9 (-16.7, 2.8)
Delayed Memory					
RBANS 9 (list recall)	7.0 (1.7)	7.2 (1.3)	0.0 (-1.1, 1.1)	4.3 (1.9)	**-1.9 (-3.0, -0.8)****
RBANS 10 (list recognition)	19.6 (1.7)	19.8 (0.4)	0.1 (-0.9, 1.1)	19.5 (0.7)	-0.1 (-1.1, 0.8)
RBANS 11 (story recall)	9.2 (2.2)	9.3 (2.2)	0.3 (-1.1, 1.8)	7.5 (2.5)	-0.8 (-2.2, 0.6)
RBANS 12 (figure recall)	14.2 (3.4)	15.4 (2.5)	0.6 (-1.7, 3.0)	12.3 (3.0)	-1.1 (-3.4, 1.2)
Total scale Delayed Memory	96.8 (8.4)	95.5 (6.3)	1.0 (-5.3, 7.3)	91.1 (9.8)	-3.5 (-9.5-2.6)
RBANS total scale^	96.4 (10.1)	91.0 (11.5)	**-8.6 (-14.9, -2.2)****	92.9 (9.7)	**-7.1 (-13.3, -1.0)***
Additional Tests					
Visual Attention/Reaction Time					
Trails A[ɣ]	23.8 (9.9)	22.8 (6.6)	**6.9 (-12.6, -1.2)***	25.8 (6.9)	4.3 (-9.9, 1.3)
Trails B[ɣ]	68.1 (29.1)	71.2 (27.9)	11.4 (-29.3, 6.5)	75.6 (27.9)	2.0 (-19.5, 15.5)
Stroop (I)	2.0 (10.7)	3.0 (7.4)	-2.4 (-9.4, 4.6)	-1.9 (6.6)	**-6.4 (-13.3, 0.4)^**
Motor speed/Dexterity					
Coin rot. Dominant hand	33.7 (5.3)	32.0 (6.7)	**-5.7 (-9.6, -1.7)****	31.9 (5.8)	-2.5 (-6.4, 1.4)
Coin rot. Non-dominant hand	31.3 (5.2)	27.6 (6.7)	**-6.4 (-10.3, -2.5)****	28.8 (4.5)	-2.3 (-6.2, 1.5)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, lifetime alcohol consumption (frequency), Job title (spray painter/panel beater), smoking status, DASS A, S and D, test time (of day) and test day (of week), malingering/symptom validity (Rey 15 item) and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Table 5.13. Supplementary table - Neuropsychological test scores based on the lowest 5th, 10th and 20th percentiles for collision repair workers stratified by employment duration

	Reference Group (n=51)	**< 17 years (10.5) (N = 23)**		**>17 years (28.4) (n = 24)**	
RBANS battery	**N (%)**	**N (%)**	**OR (95%CI)**	**N (%)**	**OR (95%CI)**
Immediate memory					
5th percentile	2 (3.9)	2 (8.7)	-	2 (8.3)	-
10th percentile	4 (7.8)	6 (26.9)	**13.0 (1.5-117.2)***	4 (16.7)	**8.8 (0.7-107.7)^**
20th percentile	17 (33.3)	11 (57.8)	2.0 (0.5-9.0)	10 (41.7)	2.0 (0.5-8.6)
Visuospatial/Construction					
5th percentile	4 (7.8)	1 (4.3)	-	0 (0.0)	-
10th percentile	5 (9.8)	3 (13.0)	13.3 (0.3-569.0)	1 (4.2)	2.1 (0-142.6)
20th percentile	13 (25.5)	6 (26.1)	1.6 (0.4-6.3)	7 (29.2)	2.4 (0.6-9.6)
Language					
5th percentile	3 (5.9)	0 (0.0)	-	1 (4.2)	-
10th percentile	5 (9.8)	2 (8.7)	7.5 (0.2-364.1)	1 (4.2)	3.5 (0.1-238.5)
20th percentile	7 (13.7)	5 (21.7)	**4.7 (0.8-27.8)^**	4 (16.7)	4.2 (0.6-27.5)
Attention					
5th percentile	4 (7.8)	8 (34.8)	**53.3 (3.3-862.5)****	3 (12.5)	4.6 (0.3-73.9)
10th percentile	8 (15.7)	10 (43.5)	**12.5 (2.3-68.6)****	5 (20.8)	4.3 (0.6-28.8)
20th percentile	12 (23.5)	16 (69.6)	**21.1 (4.2-105.9)****	**6 (25.0)**	1.2 (0.3-5.5)
Delayed Memory					
5th percentile	1 (2.0)	0 (0.0)	-	2 (8.3)	-
10th percentile	2 (3.9)	0 (0.0)	-	2 (8.3)	-
20th percentile	4 (7.8)	3 (13.0)	1.3 (0.2-8.4)	8 (33.3)	**4.8 (1-21.9)***
RBANS total scale					
5th percentile	2 (3.9)	1 (4.4)	-	0 (0.0)	-
10th percentile	5 (9.8)	4 (17.4)	**16.4 (0.7-387.6)^**	1 (4.2)	1.8 (0.1-53.5)
20th percentile	9 (17.7)	8 (34.8)	**10.6 (1.5-73.4)***	9 (37.5)	**19.7 (2.5-152.7)****

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for ethnicity, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week) and premorbid intelligence (NART).

"-"= No ORs available due to non-convergence

Table 5.14. Supplementary table - Neuropsychological test scores for collision repair workers tested at the start of the week (Monday-Wednesday) and the end of the week (Thursday-Friday)

	Reference group	All Collision repair workers			
	n=51	Early week (n=38)	Adjusted*	Late week (n=13)	Adjusted*
RBANS battery	**N (%)**	**N (%)**	**OR (95%CI)**	**N (%)**	**OR (95%CI)**
Immediate memory					
RBANS 1 (list learning)	29.6 (4.0)	28.1 (4.7)	**-2.7 (-5.2, -0.1)***	29.3 (3.8)	-0.8 (-4.1, 2.4)
RBANS 2 (story memory)	16.9 (3.6)	16.4 (3.7)	-0.5 (-2.8, 1.8)	13.8 (3.9)	**-2.6 (-5.5, 0.3)^**
Total scale Immediate Memory	95.6 (12.6)	**92.4 (13.3)**	-5.5 (-13.4, 2.3)	**90.8 (15.9)**	-3.4 (-13.6, 6.6)
Visuospatial/Construction					
RBANS 3 (figure copy)	17.1 (2.5)	17.9 (1.8)	0.5 (-1.0, 1.9)	17.5 (2.0)	-0.2 (-2.0, 1.7)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.2)	0.6 (-0.8, 1.9)	18.7 (2.2)	0.3 (-1.4, 2.0)
Total scale vis./const.	99.6 (15.8)	100.5 (16.4)	-2.7 (-12.6, 7.2)	97.5 (11.7)	-5.7 (-18.3, 6.9)
Language					
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.7, 1.2)	10.0 (0.0)	0.2 (-1.0, 1.4)
RBANS 6 (semantic fluency)	21.5 (5.2)	22.2 (3.9)	-2.3 (-5.2, 0.7)	22.2 (3.9)	-0.4 (-4.1, 3.4)
Total scale Language	98.1 (15.0)	95.9 (12.7)	-4.8 (-13.3, 3.8)	100.7 (9.4)	0.1 (-10.9, 11)
Attention					
RBANS 7a (digit span forward)	10.5 (2.3)	10.8 (2.2)	-0.8 (-2.2, 0.6)	9.2 (2.7)	**-2.3 (-4.2, -0.5)***
RBANS 7b (digit span backward)	7.8 (2.3)	6.1 (1.7)	**-1.9 (-3.3, -0.5)****	6.2 (2.7)	**-1.8 (-3.7, -0.0)***
RBANS 7c (digit span total)	18.2 (4.1)	16.9 (3.3)	**-2.6 (-5.0, -0.2)***	15.4 (4.6)	**-4.1 (-7.2, -1.1)****
RBANS 8 (coding)	50.6 (9.4)	46.2 (7.9)	**-8.3 (-14.2, -2.5)****	45.6 (9.9)	**-7.0 (-14.4, -0.4)^**
Total scale Attention	94.6 (14.2)	90.7 (14.2)	**-12.1 (-21.6, -2.5)****	83.0 (20.1)	**-16.8 (-29.1, -4.6)****
Delayed Memory					
RBANS 9 (list recall)	7.0 (1.70)	5.5 (2.3)	**-1.2 (-2.5, -0.0)***	6.2 (2.0)	-0.6 (-2.2, 0.9)
RBANS 10 (list recognition)	19.6 (1.7)	19.6 (0.7)	-0.1 (-1.0, 0.8)	19.8 (0.4)	0.1 (-1.1, 1.2)
RBANS 11 (story recall)	9.2 (2.2)	8.8 (2.4)	-0.1 (-1.6, 1.3)	7.4 (2.6)	-1.4 (-3.3, 0.5)
RBANS 12 (figure recall)	14.2 (3.4)	13.6 (3.1)	-0.7 (-2.9, 1.5)	14.5 (3.3)	0.3 (-2.5, 3.1)
Total scale Delayed Memory	96.8 (8.4)	92.9 (8.0)	-2.1 (-8.0, 3.8)	94.2 (10.0)	-0.3 (-7.7, 7.2)
RBANS total scale	96.4 (10.1)	92.5 (10.2)	**-7.9 (-13.7, -2.1)***	90.5 (11.6)	**-8.1 (-15.5, -0.7)***
Additional Tests					
Visual Attention/Reaction Time					
Trails A[ɣ]	23.8 (7.0)	24.7 (7.0)	-6.0 (-11.6, 0.5)	23.5 (9.7)	-5.6 (-12.6, 1.5)
Trails B[ɣ]	68.1 (29.1)	74.7 (27.8)	-10.6 (-27.5, 6.4)	70.2 (28.2)	2.2 (-19.4, 23.8)
Stroop (I)	2.0 (10.7)	-0.5 (6.9)	-5.3 (-11.7, 1.1)	3.1 (8.0)	-1.9 (-10.0, 6.2)
Motor speed/Dexterity					
Coin rot. Dominant hand	33.7 (5.3)	31.5 (6.8)	-1.0 (-4.9, 3.0)	33.0 (4.3)	-
Coin rot. Non-dominant	31.3 (5.2)	27.4 (5.7)	**-4.9 (-8.6, -1.2)****	30.2 (5.1)	-3.3 (-8.0, 1.3)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week) and premorbid intelligence (NART).

[ɣ]Trails A and B - time (in seconds) to complete each test, therefore higher score represents poorer performance on test – Algebraic sign of coefficient changed accordingly

"-"= No ORs available due to non-convergence

Table 5.15. Supplementary table – Neuropsychological test scores for Comparison and collision repair workers - Excluding reference workers who reported exposure to solvents (n=7)

RBANS battery	Reference Group (n=44)	All Collision repair n=47	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95% CI)**
RBANS 1 (list learning)	29.7 (4.1)	28.4 (4.5)	-1.2 (-2.9, 0.5)
RBANS 2 (story memory)	16.8 (3.7)	15.7 (3.9)	-1.1 (-2.7, 0.6)
Total scale Immediate Memory	95.5 (12.6)	91.9 (13.9)	-2.8 (-8.5, 2.8)
Visuospatial/Construction			
RBANS 3 (figure copy)	17.0 (2.6)	17.8 (1.8)	0.6 (-0.4, 1.6)
RBANS 4 (line orientation)	18.7 (1.9)	18.7 (2.1)	-0.2 (-1.1 , 0.8)
Total scale vis./const.	99.7 (16.0)	99.7 (15.2)	-3.5 (-10.4, 3.4)
Language			
RBANS 5 (picture naming)	9.5 (2.1)	10.0 (0.0)	0.2 (-0.5, 0.9)
RBANS 6 (semantic fluency)	21.2 (5.1)	21.2 (3.9)	-0.8 (-3.0, 1.3)
Total scale Language	97.2 (15.4)	97.2 (12.0)	-1.7 (-8.1, 4.6)
Attention			
RBANS 7a (digit span forward)	10.3 (2.2)	10.3 (2.4)	0.0 (-1.1, 1.0)
RBANS 7b (digit span backward)	7.7 (2.3)	6.1 (2.0)	**-1.3 (-2.4, -0.3)***
RBANS 7c (digit span total)	17.9 (3.9)	16.5 (3.7)	-1.3 (-3.1, 0.5)
RBANS 8 (coding)	49.7 (8.9)	46.1 (8.4)	**-5.0 (-9.1, -1.0)***
Total scale Attention	93.8 (13.8)	88.6 (16.2)	**-9.1 (-15.9, -2.3)****
Delayed Memory			
RBANS 9 (list recall)	6.9 (1.7)	5.7 (2.2)	**-0.9 (-1.7, -0.1)***
RBANS 10 (list recognition)	19.6 (1.8)	19.6 (0.6)	0.0 (-0.7, 0.7)
RBANS 11 (story recall)	9.2 (2.3)	8.4 (2.5)	-0.7 (-1.7, 0.3)
RBANS 12 (figure recall)	14.1 (3.5)	13.9 (3.1)	0.1 (-1.5, 1.6)
Total scale Delayed Memory	96.5 (8.8)	93.3 (8.5)	-0.9 (-5.3, 3.5)
RBANS total scale	96.1 (10.1)	92.0 (10.5)	**-5.5 (-9.7, -1.4)****
Additional Tests			
Visual Attention/Reaction Time			
Trails A[ɣ]	24.4 (10.5)	24.4 (6.9)	-1.6 (- 5.6, 2.4)
Trails B[ɣ]	69.6 (30.3)	73.4 (27.7)	**10.4 (- 22.2, -1.4)^**
Stroop (I)	1.8 (10.9)	0.5 (7.3)	-3.3 (-7.9, 1.3)
Motor speed/Dexterity			
Coin rot. Dominant hand	33.1 (5.5)	31.9 (6.2)	**-2.5 (-5.3, 0.2)^**
Coin rot. Non-dominant	31.2 (5.5)	28.2 (5.7)	**-3.2 (-6.0, -0.5)***

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Table 5.16. Supplementary table - Neuropsychological test scores for Comparison and collision repair workers – Excluding current office workers (n=4)

RBANS battery	Reference Group (n=51)	All Collision repair (n=43)		Panel Beaters (n= 11)		Spray painters (n=32)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95% CI)**	**Mean (SD)**	**Difference (95% CI)**	**Mean (SD)**	**Difference (95% CI)**
RBANS 1 (list learning)	29.6 (4.0)	28.6 (4.5)	-0.5 (-2.0, 1.0)	28.2 (4.6)	-1.0 (-3.3, 1.2)	28.8 (4.6)	-0.3 (-2.0, 1.3)
RBANS 2 (story memory)	16.9 (3.6)	15.6 (3.9)	-1.4 (-3.0, 0.2)	16.2 (3.2)	-1.2 (-3.6, 1.2)	15.4 (4.2)	**-1.5 (-3.3, 0.3)^**
Total scale Immediate Memory	95.6 (12.6)	92.2 (14.4)	-1.9 (-7.4, 3.6)	93.8 (10.1)	-3.3 (-11.5, 4.9)	91.7 (15.8)	-1.4 (-7.3, 4.6)
Visuospatial/Construction							
RBANS 3 (figure copy)	17.1 (2.5)	17.8 (1.7)	0.5 (-0.4, 1.4)	17.0 (1.4)	-0.3 (-1.6, 1.1)	18.1 (1.7)	0.8 (-0.2, 1.8)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.1)	-0.2 (-1.1, 0.7)	19.2 (1.5)	0.4 (-0.9, 1.8)	18.5 (2.2)	-0.4 (-1.4, 0.6)
Total scale vis./const.	99.6 (15.8)	99.3 (14.2)	-3.1 (-9.6, 3.5)	95.5 (12.2)	-8.0 (-17.8, 1.8)	100.6 (14.8)	-1.2 (-8.3, 5.8)
Language							
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.5, 0.8)	10.0 (0.0)	0.3 (-0.6, 1.3)	10.0 (0.0)	0.1 (-0.6, 0.8)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.0 (4.0)	-1.1 (-3.2, 1.0)	20.5 (3.6)	-1.8 (-4.8 ,1.3)	21.3 (4.1)	-0.8 (-3.1, 1.5)
Total scale Language	98.1 (15.0)	97.2 (12.4)	-2.7 (-8.7, 3.3)	97.0 (8.3)	-3.7 (-12.8, 5.3)	97.3 (13.7)	-2.3 (-8.8, 4.3)
Attention							
RBANS 7a (digit span forward)	10.5 (2.3)	10.4 (2.5)	-0.2 (-1.2, 0.9)	10.(2.4)	-1.0 (-2.6, 0.5)	10.6 (2.5)	0.2 (-1.0, 1.3)
RBANS 7b (digit span backward)	7.8 (2.3)	6.3 (2.0)	**-1.3 (-2.3, -0.3)***	6.4 (1.5)	**-1.5 (-3.0, 0.0)***	6.3 (2.2)	**-1.2 (-2.4, -0.1)***
RBANS 7c (digit span total)	18.2 (4.1)	16.7 (3.8)	-1.5 (-3.2 ,0.2)	16.4 (2.7)	**-2.5 (-50.0, 0.1)^**	16.8 (4.1)	-1.1 (-3.0, 0.8)
RBANS 8 (coding)	50.6 (9.4)	46.0 (8.6)	**-6.3 (-10.2, -2.4)****	44.3 (7.4)	**-8.8 (-14.7, -3.0)****	46.6 (9.0)	**-5.3 (-9.6, -1.0)***
Total scale Attention	94.6 (14.2)	88.2 (16.8)	**-9.4 (-16.2, -2.7)****	86.3 (11.8)	**-14.1 (-24.3, -3.9)****	88.8 (18.3)	**-7.7 (-15.0, -0.4)***
Delayed Memory							
RBANS 9 (list recall)	7.0 (1.7)	5.7 (2.2)	**-1.0 (-1.7, -0.3)***	5.4 (2.3)	**-1.0 (-2.1, 0.1)^**	5.9 (2.2)	**-1.0 (-1.8, -0.2)***
RBANS 10 (list recognition)	19.6 (1.7)	19.7 (0.6)	0.0 (-0.6, 0.6)	19.7 (0.5)	0.1 (-0.9, 1.0)	19.6 (0.6)	0.0 (-0.7, 0.7)
RBANS 11 (story recall)	9.2 (2.2)	8.3 (2.5)	-0.8 (-1.7, 0.1)	8.5 (2.5)	-0.5 (-1.9, 0.9)	8.3 (2.6)	**-0.9 (-1.9, 0.1)^**
RBANS 12 (figure recall)	14.2 (3.4)	14.0 (3.2)	0.2 (-1.3, 1.6)	13.7 (3.5)	-0.1 (-2.2, 2.1)	14.1 (3.1)	0.3 (-1.3, 1.9)
Total scale Delayed Memory	96.8 (8.4)	93.5 (8.3)	-1.2 (-5.1, 2.7)	94.5 (7.0)	-0.9 (-6.8, 5.0)	93.1 (8.8)	-1.3 (-5.6, 3.0)
RBANS total scale	96.4 (10.1)	92.0 (10.7)	**-5.3 (-9.3, -1.3)***	90.4 (6.1)	**-8.9 (-14.9, -2.9)****	92.5 (11.9)	**-3.9 (-8.3, - 0.4)^**
Additional Tests							
Visual Attention/Reaction Time							
Trails A[ɣ]	23.8 (9.9)	24.0 (6.8)	1.4 (-2.2, 5.0)	27.2 (8.1)	-4.2 (-9.5, 1.1)	22.9 (6.0)	-0.2 (-3.7, 4.1)
Trails B[ɣ]	68.1 (29.1)	73.7 (28.4)	12.2 (0.9, 23.6)	68.1 (22.1)	-7.3 (-24.2, 9.7)	75.6 (20.3)	**-14.3 (- 26.7, -1.8)***
Stroop (I)	2.0 (10.7)	0.5 (7.6)	-2.9 (-7.4, 1.5)	-1.1 (7.2)	-4.3 (-11.0, 2.3)	1.4 (7.6)	-2.4 (-7.3 ,2.5)
Motor speed/Dexterity							
Coin rot. Dominant hand	33.7 (5.3)	32.2 (6.2)	**-2.9 (-5.4, -0.3)***	29.6 (6.8)	**-4.4 (-8.2, -0.7)***	33.1 (5.9)	-2.2 (-5.0, 0.6)
Coin rot. Non-dominant	31.3 (5.2)	28.2 (5.8)	**-3.3 (-5.8, -0.7)***	26.0 (5.2)	**-4.8 (-8.6, -1.0)***	28.9 (5.9)	**-2.6 (-5.4, -0.2)***

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week), symptom validity/malingering and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test - Algebraic sign of coefficient changed accordingly

Table 5.17. Supplementary table - Neuropsychological test scores for Comparison and collision repair workers - Excluding Māori and Pacific persons

RBANS battery	Reference Group (n=30)	All Collision repair (n=42)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95% CI)**
RBANS 1 (list learning)	29.9 (3.3)	28.4 (4.6)	-1.2 (-3.2, 0.7)
RBANS 2 (story memory)	17.6 (3.1)	16.0 (3.9)	-1.0 (-2.8, 0.8)
Total scale Immediate Memory	98.1 (12.0)	92.8 (14.0)	-2.6 (-9.0, 3.9)
Visuospatial/Construction			
RBANS 3 (figure copy)	17.1 (2.4)	17.9 (1.8)	0.6 (-0.5, 1.7)
RBANS 4 (line orientation)	18.8 (2.1)	19.0 (1.7)	0.6 (-0.5, 1.6)
Total scale vis./const.	101.7 (14.9)	101.2 (14.2)	-1.4 (-8.9, 6.1)
Language			
RBANS 5 (picture naming)	10.0 (0.2)	10.0 (0.0)	0.0 (0.0, 0.1)
RBANS 6 (semantic fluency)	22.3 (4.8)	21.4 (3.9)	-1.1(-3.1, 1.0)
Total scale Language	101.5 (9.9)	97.9 (12.2)	-2.2 (-7.3, 3.0)
Attention			
RBANS 7a (digit span forward)	10.7 (2.4)	10.5 (2.5)	0.0 (-1.2, 1.3)
RBANS 7b (digit span backward)	8.1 (2.5)	6.1 (2.0)	**-1.6 (-2.7, -0.4)***
RBANS 7c (digit span total)	18.7 (4.4)	16.6 (3.8)	-1.5 (-3.6, 0.6)
RBANS 8 (coding)	52.2 (10.3)	46.9 (8.2)	**-5.5 (-10.3, -0.8)***
Total scale Attention	98.8 (13.6)	90.3 (16.1)	**-8.1 (-16.5, - 0.4)^**
Delayed Memory			
RBANS 9 (list recall)	6.7 (1.7)	5.6 (2.2)	**-1.1 (-2, -0.2)***
RBANS 10 (list recognition)	19.4 (2.32	19.6 (0.6)	0.0 (-0.8, 0.8)
RBANS 11 (story recall)	9.0 (1.9)	8.6 (2.5)	-0.1 (-1.1, 1.0)
RBANS 12 (figure recall)	14.0 (2.4)	13.9 (3.2)	0.1 (-1.4, 1.6)
Total scale Delayed Memory	95.5 (8.5)	93.6 (8.8)	-0.2 (-4.9, 4.5)
RBANS total scale	98.9 (8.2)	93.3 (10.3)	**-4.7 (-9.4, -0.0)***
Additional Tests			
Visual Attention/Reaction Time			
Trails A[ɣ]	23.0 (9.1)	23.4 (5.9)	-0.4 (-4.0, 3.3)
Trails B[ɣ]	69.7 (29.5)	70.3 (27.0)	-7.6 (-19.7, 4.4)
Stroop (I)	2.6 (11.8)	0.9 (7.4)	-2.4 (-7.4, 2.6)
Motor speed/Dexterity			
Coin rot. Dominant hand	34.5 (4.5)	32.8 (5.6)	-2.0 (-4.8, 0.7)
Coin rot. Non-dominant	32.8 (4.5)	32.8 (5.6)	-2.0 (-4.5, 0.6)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, alcohol consumption in the past 48 hours, smoking status, DASS A, S and D, test time (of day) and test day (of week) and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test – Algebraic sign of coefficient changed accordingly

Table 5.18. Supplementary table - Neuropsychological test scores for Comparison and collision repair workers – Adjusted for both alcohol consumption in the past 48 hours and lifetime alcohol (mean drinks per week)

RBANS battery	Reference Group (n=51)	All Collision repair (n=43)		Panel Beaters (n= 11)		Spray painters (n=32)	
Immediate memory	**Mean (SD)**	**Mean (SD)**	**Difference (95% CI)**	**Mean (SD)**	**Difference (95% CI)**	**Mean (SD)**	**Difference (95% CI)**
RBANS 1 (list learning)	29.6 (4.0)	28.6 (4.5)	-0.9 (-2.4, 0.7)	28.2 (4.6)	**-2.1 (-4.3, 0.2)^**	28.8 (4.6)	-0.3 (-2.0, 1.5)
RBANS 2 (story memory)	16.9 (3.6)	15.6 (3.9)	-1.2 (-2.8, 0.3)	16.2 (3.2)	-0.9 (-3.1, 1.4)	15.4 (4.2)	**-1.4 (-3.1, 0.3)^**
Total scale Immediate Memory	95.6 (12.6)	92.2 (14.4)	-2.6 (-7.9, 2.8)	93.8 (10.1)	-5.2 (-12.9, 2.5)	91.7 (15.8)	-1.4 (-7.3, 4.4)
Visuospatial/Construction							
RBANS 3 (figure copy)	17.1 (2.5)	17.8 (1.7)	0.6 (-0.4, 1.6)	17.0 (1.4)	0.3 (-1.0, 1.7)	18.1 (1.7)	0.7 (-0.3, 1.8)
RBANS 4 (line orientation)	18.8 (1.9)	18.7 (2.1)	-0.2 (-1.1, 0.7)	19.2 (1.5)	0.4 (-0.8, 1.7)	18.5 (2.2)	-0.5 (-1.5, 0.5)
Total scale vis./const.	99.6 (15.8)	99.3 (14.2)	-2.1 (-8.8, 4.6)	95.5 (12.2)	-3.5 (-13.2, 6.2)	100.6 (14.8)	-1.5 (-8.9, 5.9)
Language							
RBANS 5 (picture naming)	9.5 (2.0)	10.0 (0.0)	0.2 (-0.5, 0.8)	10.0 (0.0)	0.3 (-0.6, 1.1)	10.0 (0.0)	0.1 (-0.6, 0.8)
RBANS 6 (semantic fluency)	21.5 (5.2)	21.0 (4.0)	-1.0 (-3.0, 1.1)	20.5 (3.6)	-1.7 (-4.5, 1.2)	21.3 (4.1)	-0.6 (-2.9, 1.6)
Total scale Language	98.1 (15.0)	97.2 (12.4)	-2.3 (-8.1, 3.6	97.0 (8.3)	-3.3 (-11.8, 5.1)	97.3 (13.7)	-1.8 (-8.2, 4.6)
Attention							
RBANS 7a (digit span forward)	10.5 (2.3)	10.4 (2.5)	-0.2 (-1.2, 0.8)	10.(2.4)	-1.1 (-2.5, 0.3)	10.6 (2.5)	0.2 (-0.9, 1.3)
RBANS 7b (digit span backward)	7.8 (2.3)	6.3 (2.0)	**-1.5 (-2.5, -0.5)***	6.4 (1.5)	**-1.8 (-3.3, -0.4)***	6.3 (2.2)	**-1.3 (-2.4, -0.2)***
RBANS 7c (digit span total)	18.2 (4.1)	16.7 (3.8)	**-1.7 (-3.3, 0.0)***	16.4 (2.7)	**-2.9 (-5.3, -0.5)***	16.8 (4.1)	-1.1 (-2.9, 0.8)
RBANS 8 (coding)	50.6 (9.4)	46.0 (8.6)	**-5.9 (-9.8, -2.0)****	44.3 (7.4)	**-7.5 (-13, -2.0)***	46.6 (9.0)	**-5.1 (-9.4, -0.8)***
Total scale Attention	94.6 (14.2)	88.2 (16.8)	**-9.2 (-15.8, -2.6**)**	86.3 (11.8)	**-13.0 (-22.4,-3.5)****	88.8 (18.3)	**7.6 (-14.8, -0.3)***
Delayed Memory							
RBANS 9 (list recall)	7.0 (1.7)	5.7 (2.2)	**-1.0 (-1.8, -0.3)**	5.4 (2.3)	**-1.0 (-2.1, 0.1)^**	5.9 (2.2)	**-1.0 (-1.8, -0.2)***
RBANS 10 (list recognition)	19.6 (1.7)	19.7 (0.6)	0.0 (-0.6, 0.6)	19.7 (0.5)	0.0 (-0.9, 0.8)	19.6 (0.6)	0.0 (-0.7, 0.6)
RBANS 11 (story recall)	9.2 (2.2)	8.3 (2.5)	-0.6 (-1.5, 0.3)	8.5 (2.5)	-0.2 (-1.5, 1.0)	8.3 (2.6)	-0.8 (-1.8, 0.3)
RBANS 12 (figure recall)	14.2 (3.4)	14.0 (3.2)	0.1 (-1.3, 1.6)	13.7 (3.5)	-0.2 (-2.3, 1.8)	14.1 (3.1)	0.3 (-1.3, 1.9)
Total scale Delayed Memory	96.8 (8.4)	93.5 (8.3)	-1.4 (-5.4-2.6)	94.5 (7.0)	-1.6 (-7.3-4.2)	93.1 (8.8)	-1.3 (-5.7, 3.1)
RBANS total scale	96.4 (10.1)	92.0 (10.7)	**-5.1 (-9.1, -1.2)***	90.4 (6.1)	**-7.8 (-13.5, -2.1)****	92.5 (11.9)	**-4.0 (-8.3, 0.4)^**
Additional Tests							
Visual Attention/Reaction Time							
Trails A[ɣ] REVERSE	23.8 (9.9)	24.0 (6.8)	-1.8 (-5.5, -1.8)	27.2 (8.1)	-5.5 (0.5, 10.5)	22.9 (6.0)	-0.1 (-4.0, 3.8)
Trails B[ɣ] REVERSE	68.1 (29.1)	73.7 (28.4)	**-11.5 (-22.5, -0.4)***	68.1 (22.1)	-6.4 (-9.3, 22.1)	75.6 (20.3)	**-13.9 (-26.2, -1.6)**
Stroop (I)	2.0 (10.7)	0.5 (7.6)	-3.3 (-7.6, 1.1)	-1.1 (7.2)	-4.6 (-10.7, 1.6)	1.4 (7.6)	-2.7 (-7.5, 2.2)
Motor speed/Dexterity							
Coin rot. Dominant hand	33.7 (5.3)	32.2 (6.2)	**-2.8 (-5.3, -0.3)***	29.6 (6.8)	-4.0 (-7.5, -0.5)	33.1 (5.9)	**-2.3 (-5.0, 0.5)^**
Coin rot. Non-dominant	31.3 (5.2)	28.2 (5.8)	**-3.1 (-5.6, -0.7)***	26.0 (5.2)	-4.3 (-7.9, -0.8)	28.9 (5.9)	**-2.6 (-5.3, 0.2)^**

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, alcohol consumption in the past 48 hours, mean number of alcoholic drinks consumed per week over lifetime, smoking status, DASS A, S and D, test time (of day) and test day (of week) and premorbid intelligence (NART).

[ɣ]Trails A and B - time to complete each test, therefore higher score represents poorer performance on test – Algebraic sign of coefficient changed accordingly

Table 5.19. Supplementary table - Characteristics of study populations – Comparison of demographic characteristics of current study and previous study participants

	Comparison group (n=51)		Comparison group previous study (n=160)		All Collision repair (n=47)		All Collision repair Previous study (n=323)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Ethnicity								
Māori	13	25	52	32	3	6	46	14
Pacific	8	16	15	9	2	4	28	9
European New Zealanders and others	30	59	93	58	42	89	249	77
Smoking Status								
Non-smoker	18	35	69	35	19	40	151	41
Ex-smoker	16	31	16	31	15	32	95	29
Current smoker	17	33	17	33	13	28	96	30
Lifetime alcohol (frequency)								
Never	1	2	8	5	1	2	17	5
Less than once month	8	16	29	18	4	9	33	10
1-2 times week	25	49	78	49	25	53	143	44
3-5 times week	14	27	32	20	16	34	93	29
Daily	3	6	13	8	1	2	37*	11
Education level								
primary school	0	0	4	3	2	4	8	3
secondary school	36	71	105	66	38	81	223	69
trade certification	9	18	41	26	5	11	80*	25
Tertiary/University	6	12	10	6	2	4	12	4
	Mean	**Range**	**Mean**	**Range**	**Mean**	**Range**	**Mean**	**Range**
Age	39.0	19 - 65	36.0	17 - 66	37.8	21 - 62	36.5	17-64
Lifetime Alcohol (Mean drinks per week)	15.8	0 - 100	15.8	0-120	14.3	0 - 50	13.4	0 - 140
Duration of employment (Yrs)	-	-	-	-	19.6	5.4 - 50.0	16.7	0.3 - 50

* =p<0.05 (Students t-test)

6 Effects of personal protective equipment use and good workplace hygiene on symptoms of neurotoxicity in solvent-exposed vehicle spray painters

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Objectives: To assess the association between the use of personal protective equipment (PPE) and good workplace hygiene and symptoms of neurotoxicity in solvent-exposed vehicle spray painters.

Methods: Exposure control measures including PPE-use and workplace hygiene practices and symptoms of neurotoxicity were assessed in 267 vehicle repair spray painters. Symptoms were assessed using an adapted version of the EUROQUEST Questionnaire.

Results: Frequent respirator and glove use was inversely and significantly associated with symptoms of neurotoxicity in a dose-dependent manner ($p<0.05$ for trend) with the strongest protective effect found for consistent glove use (OR 0.1-0.2, $p<0.01$, for reporting ≥10 and ≥5 symptoms). A clear dose-response trend was also observed when combining frequency of respirator and glove use ($p<0.05$ for reporting ≥5 and ≥10 symptoms), with an overall reduction in risk of 90% (OR, 0.1, $p<0.01$) for those who consistently used both types of PPE. Protective effects were most pronounced for the symptom domains of psychosomatic ($p<0.05$ for trend, for combined PPE use), mood ($p<0.05$) and memory and concentration symptoms combined ($p<0.05$), with reductions in risk of >80%. Poor hygiene workplace practices, such as solvent exposure to multiple body parts (OR 3.4, $p=0.11$ for reporting ≥10 symptoms), were associated with an increased risk of symptoms. When using a general workplace hygiene score derived from a combination of PPE-use and (good) workplace practice factors an inverse and significant dose-response trend was observed for reporting ≥5 ($p<0.01$) and ≥ 10 symptoms ($p<0.01$).

Conclusions: This study has shown that PPE-use and good workplace hygiene are associated with a strongly reduced risk of symptoms of neurotoxicity in solvent-exposed vehicle spray painters.

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6.1 Introduction

Solvent exposure in the vehicle collision repair industry has long been associated with symptoms of neurotoxicity (18, 19, 45, 72, 326, 331) and deficits in cognitive performance (17, 45, 69). Although considerable changes in health and safety practices have occurred in this industry with an associated decline in solvent exposures internationally over the past 20 years (13), an increased risk of symptoms of neurotoxicity continues to be reported. In particular, we have recently shown that spray painters and panel beaters (or auto body repair workers) in New Zealand report more symptoms of neurotoxicity than non-exposed reference workers, with the strongest associations observed for neurological, psychosomatic, mood, memory, and concentration symptoms (331). These effects were shown at *airborne* solvent levels well below current exposure standards suggesting that *dermal* exposures may be important.

Previous studies have shown that personal protective equipment (PPE) and good workplace hygiene reduce both airborne and dermal exposure to solvents and subsequent total body-burden in spray painters (29, 30, 36) and other solvent exposed workers (31-34). In particular, quasi-experimental studies involving PPE-use enforced by researchers showed that the total body burden was reduced by between 26% and 99% compared to no or minimal use of PPE (30, 31, 34, 36). The efficacy was dependent upon the type, quality and maintenance level of PPE, which along with consistency of use is known to vary greatly between workplaces and workers (29, 122, 135, 317, 318). Low airborne and dermal exposures and a reduced body burden of solvents have been associated with reduced risks of self-reported symptoms of

neurotoxicity and abnormal neuropsychological performance (29, 286), but few studies have directly assessed the impact of PPE use on symptoms, and none have assessed the effects of workplace hygiene.

In the current study, using a cross-sectional study design, we assessed the effect of PPE-use and workplace hygiene practices on symptoms of neurotoxicity in 267 vehicle collision repair spray painters.

6.2 Methods

Study population

Participants comprised 267 spray painters from our previous questionnaire survey in 370 collision repair workers (267 spray painters and 103 panel beaters or auto-body repair workers, including office staff who were ex-tradesmen), recruited from workshops throughout the north island of New Zealand. Office staff (n=46) were all ex-tradesmen and were recoded according to their previous job title (31 as spray painters), as this more accurately reflected their working life exposures. They generally also performed at least some repair work and were therefore still at risk of exposure. All spray painters conducted the same core tasks including mixing paint, spray painting and degreasing/cleaning before and after spray painting, with variations in the time spent on each task. Exclusion criteria for the previous study were no history of work involving solvent exposure or any history of major head injury or neurological/neurodegenerative disease, including meningitis, major depression or epilepsy. All data on PPE-use and/or workplace hygiene practices was missing for three spray painters, leaving 264 for inclusion in the final analyses. No data on PPE-use and workplace hygiene practices was available for panel beaters.

Questionnaire

Information on demographics, symptoms of neurotoxicity, work characteristics, use of solvents and solvent-based products, use of personal protective equipment and potential confounders was obtained by a face-to-face interview (331). Questions on personal protective equipment focused on respirator and glove use during key spray painting-related tasks including mixing paint, spray painting and cleaning equipment or bodywork.

Current (i.e. in the past 3 months) symptoms were assessed using an adapted version of the EUROQUEST questionnaire (232, 331), which included 59 core items covering the following domains: neurological (e.g. numbness and tingling in extremities, balance problems), psychosomatic (e.g. headaches, nausea, tinnitus), mood, memory, concentration, fatigue and sleep quality. Symptom frequency was reported on a 4-point scale, "seldom or never", "sometimes", "often" or "very often". The EUROQUEST also assessed anxiety (6 items, e.g., "*Are you generally a nervous person?", "Do you worry a lot about trivial things"*), rated on a different 4-point scale of "strongly disagree", "disagree", "agree" or "strongly agree", and perceived general health (4 items, e.g., *"how good is your health?", "How do you feel about your life in general?")*, where participants were asked to rate different aspects of their general health and wellness as "very good" "good", "poor" or "very poor".

For PPE use, participants were asked to indicate how often they wear a respirator or gloves during each task on a 5 point scale: "Seldom/never", "Sometimes", "Often", "very often" or "Always". They were also asked what types of respirator they used i.e. a positive pressure "Air-fed" unit, or one fitted with disposable absorbent cartridges,

or both. Questions on the types of glove used (i.e. material) were not included, but field observations showed that nitrile gloves were used by the vast majority of workers for tasks with a high risk of solvent exposure (mixing paint, spray painting, degreasing/cleaning). Additional questions on workplace behaviours and characteristics included: number of body parts exposed during spray painting, with a possible score of 0 to 3 (hands and wrists, upper arms and forearms, and/or head, face and neck); whether workers washed their hands in solvents and how often ("seldom", "sometimes", "often" or "very often"); and the frequency with which the absorbent cartridges were changed in the worker's respirator ("as and when required", "less than once a month" "1-2 times a month" or "weekly"). Questions also included the type of spray equipment washer used and whether local exhaust ventilation was present i.e. "un-enclosed and un-extracted", "enclosed and un-extracted", "un-enclosed and extracted" or "enclosed and extracted". We also asked for the type of paint used i.e. "mostly water based", "mostly solvent based" and "both solvent and water based", and how many hours (on a continuous scale) over 'a typical working day' workers spent spray painting, mixing paint and degreasing (panels or parts). As the vast majority of spray painting was conducted in spray booths (with down-draft or cross-draft exhaust ventilation) we were unable to assess the effect of spraying outside the booth. Almost all booths (>90%) were commercially produced, single vehicle capacity units with downdraft extraction systems (ceiling to floor air flow), built to similar specifications and compliant with New Zealand health and safety and emission control standards (confirmed through testing by regulatory authorities). The remainder were cross draft booths (which were also compliant with New Zealand

health and safety and emission control standards), a small number of which were owner-built.

For the purpose of subsequent analyses we dichotomised the EUROQUEST symptoms, with “seldom or never” or “sometimes”, “strongly disagree” or “disagree” and “very good” or “good” constituting a negative response and “often” or “very often”, “agree” or “strongly agree” and “poor” or “very poor” constituting a positive response (175, 331). Anxiety and perceived general health were included to control the analyses for individual personality traits which have been found to lead to under or over reporting of symptoms (175). Responses to these questions were aggregated to produce a total score for each domain as described previously (331).

Responses to the PPE and workplace practice questions were also dichotomised, with “seldom/never” or “sometimes” and “as and when required” or “less than once a month”, constituting a negative (i.e. infrequent) response and ‘often’, ‘very often’ or ‘always’ and “1-2 times a month” or “weekly” constituting a positive (i.e. frequent) response. For the sum of skin exposures, those with an overall ‘score’ of 0 (n=21) or 1 (92) were combined for all future analyses due to small numbers in the “0” category. Also, only a small number of workers reported using ‘mostly water-based’ paint (n= 13) so they were combined with those who reported using “both water and solvent based” paints (n= 60).

Statistical analyses

All analyses were conducted using Stata version 13.1 (StataCorp LP, Texas, USA). Associations between PPE-use and workplace practices and symptoms were assessed using logistic regression with results expressed as prevalence odds ratios (OR). EUROQUEST symptoms were grouped according to the total number of positive responses, i.e. ≥5 or ≥10 (331). For symptoms clustered by specific domains we used a cut-point of ≥ 3 positive responses, an approach previously shown to be sensitive and specific in the classification of patients diagnosed with chronic solvent neurotoxicity (175). Memory and concentration symptoms were included as a combined domain with a cut-point of ≥3 positive responses to reduce under-detection of potential cases (175). Concentration symptoms were not analysed as a standalone domain due to low numbers in many strata.

Initially analyses were conducted for each measure of PPE use and workplace practice separately, adjusted for age, ethnicity, smoking status, alcohol consumption, education level and general health and personality traits. Other potential confounders including sleep quality, chronic diseases (e.g., diabetes), minor head injuries, concussion, chronic fatigue, prescription drug use and pre-existing health issues were also tested, but these did not appreciably affect the observed associations (data not shown) and were therefore not used in subsequent analyses. Non-convergence did occur occasionally for some potential confounders in the regression models; however, additional restricted analyses including or excluding these variables had little effect on the relevant outcomes (data not shown).

In addition to analysing frequency of respirator or glove use by each work task (mixing paint, spraying or degreasing/cleaning) we created a combined metric for each type of PPE by summing their frequency of use (0 or 1) across tasks. This gave a possible 'score' of 0-3, with 0 representing infrequent PPE use for all tasks. We also created an *overall* measure of PPE-use by combining glove and respirator use, giving a possible score of 0-6; those who scored 0 (n=4) or 1 (n=32) were combined due to low numbers. Finally, as a measure of overall workplace hygiene we created a 'hygiene' metric by dichotomising each of the respirator and glove use metrics (score of 0 or 1 = 0, score of 2 or 3 = 1) and combining them with outcomes related to the use of an air-fed respirator (0 = no use; 1 = any use), frequency that respirator cartridges were changed (0 = infrequently 1 = frequently) and frequency that hands are washed in solvents (0 = frequently; 1 = infrequently), giving a possible score of 0-5 (0 representing generally 'poor' hygiene). For subsequent analyses those who scored 0 (n=20) or 1 (n=42) were combined into single categories due to low numbers; we also combined scores of 4 (n=60) and 5 (n=16) for the same reason.

For the analyses of PPE use by individual work tasks (e.g. respirator use during paint mixing) and workplace practices, a number of workers were excluded due to missing data. Workers were also excluded from the respirator use metric (n=19), glove use metric (n=10), combined PPE use metric (n=21) and hygiene metric (n=30) if data were missing for one or more of the variables used to construct the metric.

After analysing each PPE use measure and workplace practice separately, we repeated the analyses mutually adjusting for all PPE use measures and workplace practices. Although this showed similar ORs and trends (data not shown), there was significant

colinearity and non-convergence (344). To address this we applied a more restricted model including only variables showing significant associations when analysed separately. Due to further colinearity we were not able to include respirator use and glove use separately, so included only the combined PPE use metric. For the same reason only one of the two variables on hand washing with solvents was included i.e. frequency that hands were washed (rather than never or ever washed hands) which is more likely to be representative of exposure intensity. Sum of skin exposure was correlated with the combined PPE metric, so this was also analysed separately. The 'hygiene' metric (described above) was analysed separately as it was derived from variables already included in the mutually adjusted model. Neurological symptoms were not analysed as a standalone domain for the mutually adjusted analyses due to low numbers in many strata.

6.3 Results

The demographic characteristics of study participants are shown in table 6.1. Over three quarters of spray painters reported infrequent respirator use when mixing paint, and over half when cleaning or degreasing equipment/parts (table 6.2). Approximately 20% used respirators consistently across multiple tasks and 45% consistently used gloves. Twenty-seven percent of workers frequently washed their hands (by immersion and direct application) in solvent mixtures used for degreasing, cleaning spray equipment or thinning paint (comprised of varying proportions of naphtha, toluene, acetone, methyl ethyl ketone and methanol), primarily to remove paint overspray deposited on the hands and/or forearms as a result of not wearing gloves or other protective clothing. Eight percent of workers reported exposure to hands, forearms *and* head (top of face and/or neck) when spray painting, while approximately 70% reported exposure to one or two skin areas when painting. The majority of painters reported the use of primarily solvent-based paints, with only five percent using 'mostly water based paints'. Painters spent on average two-and-a-half hours spray painting (ranging from 0-8.5 hrs/day, with those spray painting 0 hrs/day being ex-tradesmen now in management (n=9) who occasionally perform some spray painting work during busy periods (331)), one hour mixing paint, and one hour degreasing parts and cleaning spray equipment.

Table 6.1. Demographic characteristics of workers

	Spray painters (n=267)	
	n	%
Ethnicity		
Maori	37	13.9
Pacific	17	6.4
Other (incl. NZ European)	213	80.8
Smoking Status		
Non-smoker	112	42.0
Ex-smoker	76	28.5
Current smoker	79	29.6
Education level		
primary	5	1.9
secondary	194	72.7
trade cert.	58	21.7
Tertiary	10	3.7
	Mean	Range
Age	36.0	17-64
Alcohol (Mean drinks per week)	13.4	0-140
Duration of employment (Years)	16.6	0.3 - 50

Table 6.2. Prevalence of PPE use and particular workplace practices

	frequency/n(%)	
PPE use		
Respirator use	**Infrequently**	**Frequently**
Mixing paint	192 (77.1%)	57 (22.9%)
Spray painting	8 (3.1%)	249 (96.9%)
Cleaning equipment/etc.	151 (60.9%)	97 (39.1%)
Sum of respirator use	**N (%)**	
0 (respirator not worn for all 3 tasks)	7 (2.9%)	
1	137 (55.9%)	
2	52 (21.2%)	
3 (respirator worn for all 3 tasks)	49 (20.0%)	
Glove use	**Infrequently**	**Frequently**
Mixing paint	130 (50.6%)	127 (49.4%)
Spray painting	80 (31.2%)	176 (68.8%)
Cleaning equipment/etc.	65 (25.3%)	192 (74.7%)
Sum of glove use	**N (%)**	
0 (gloves not worn for all 3 tasks)	41 (16.1%)	
1	53 (20.9%)	
2	45 (17.7%)	
3 (Gloves worn for all 3 tasks)	115 (45.3%)	
	Infrequently	**Frequently**
Combined PPE Metric	**N (%)**	
0 (No gloves or respirator worn for all 3 tasks)	4 (1.7%)	
1	32 (13.2%)	
2	37 (15.2%)	
3	42 (17.3%)	
4	56 (23.1%)	
5	32 (13.2%)	
6 (Both gloves and respirator worn for all 3 tasks)	40 (16.5%)	
	No	**Yes**
Ever use air fed mask	123 (46.6%)	141 (53.4%)
	Infrequently	**Frequently**
Frequency respirator cartridges changed	169 (67.4%)	82 (32.7%)
Workplace practices		
	No	**Yes**
Wash hands in solvents*	87 (33.0%)	177 (67.1%)
	Infrequently	**Frequently**
Frequency wash hands in solvents*	193 (73.1%)	71 (26.9%)
Skin exposure (body parts exposed)	**N (%)**	
0	61 (23.1%)	
1	90 (34.1%)	
2	92 (34.9%)	
3	21 (8.0%)	
Gun Cleaning method		
Unenclosed + un-extracted	55 (21.6%)	
Enclosed + un-extracted	50 (19.6%)	
Unenclosed + extracted	57 (22.4%)	
Enclosed + extracted	93 (36.5%)	
Paint type		
mostly water based	13 (5.0%)	
mostly solvent based	185 (71.7%)	
both water and solvent based	60 (23.3%)	
Hours on a typical day	**Mean (Range)**	
Mixing paint	0.9 (0.0 – 5.0)	
Spray painting	2.6 (0.0 – 8.5)	
Degreasing/cleaning	0.9 (0.0 – 7.5)	
Combined measures of workplace hygiene		
'Hygiene' Metric	**N (%)**	
0 (poor hygiene)	18 (7.7%)	
1	38 (16.2%)	
2	46 (19.7%)	
3	60 (25.6%)	
4	56 (23.9%)	
5 (good hygiene)	16 (6.8%)	

*'Frequently' or 'Yes' represents poorer hygiene

Analyses of the effects of PPE-use showed that frequent use of a respirator when mixing paint or cleaning equipment was associated with fewer total symptoms (significant only for the cut-point of ≥5 symptoms) with overall significant ($p<0.05$) and borderline significant ($p<0.1$) dose-response trends for ≥5 and ≥10 symptoms respectively (table 6.3).

Frequent glove use was also associated with a strongly reduced risk of symptoms (significant for the cut-points of ≥5 and ≥10 symptoms) following a clear and statistically significant dose-response trend (table 6.3). In addition, combined respirator and glove use was inversely and significantly associated with total symptoms with an observed 90% reduction of risk for those with the most consistent use of both types of PPE, and a significant dose-response trend was also observed. Associations with specific symptom domains showed reduced risks for all domains, particularly for psychosomatic, mood, sleep disturbance and memory and concentration symptoms combined, with the strongest and most significant effects observed for frequent and consistent glove use and combined glove and respirator use (table 6.3). Use of an air-fed respirator (ever) was associated with a reduction in risk for reporting both ≥10 and ≥15 symptoms; a similar effect was seen for ≥5 and ≥10 symptoms with frequent changing of absorbent respirator cartridges, washing of hands and infrequent versus frequent washing of hands in solvents. Surprisingly, those using mostly solvent-based paints reported fewer symptoms than those using both water-based and solvent-based paints. A trend of increasing number of symptoms with more body parts exposed during spray painting was also observed (table 6.3). An inverse and significant dose response trend was observed for hygiene scores with a

70-90% reduction in risk of reporting ≥5 and ≥10 symptoms for those workers with the best hygiene score (score of 4/5). No clear associations with symptoms were found for type of gun cleaning method.

Table 6.3. Prevalence odds ratios for symptoms of neurotoxicity and PPE use/workplace practices.

	≥ 5 symptoms†	≥ 10 symptoms†	≥ 15 symptoms†	≥ 3 Neurological	≥ 3 Psychosomatic	≥ 3 Mood	≥ 3 Memory	≥ 3 Fatigue	≥ 3 Sleep Disturbance	≥ 3 Memory & Concentration
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	99 (37.5)	35 (13.3)	17 (6.4)	11 (4.2)	17 (6.4)	31 (11.7)	21 (8.0)	35 (13.3)	26 (9.9)	34 (12.9)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
PPE-use										
Respirator use:										
Mixing paint	**0.4 (0.2-0.8)***	0.4 (0.1-1.4)	0.5 (0.1-4.8)	-	0.5 (0.1-3.4)	0.6 (0.2-2.0)	0.7 (0.2-3.1)	0.5 (0.2-1.7)	**0.1 (0.0-1.0)^**	0.4 (0.1-1.4)
Spray painting	0.7 (0.2-3.3)	0.3 (0.0-2.0)	-	0.1 (0.0-1.7)	-	-	-	1.2 (0.1-11.7)	0.6 (0.1-4.0)	0.5 (0.0-4.9)
Cleaning equipment/degreasing	**0.4 (0.2-0.8)****	0.5 (0.2-1.3)	0.4 (0.1-2.3)	-	0.8 (0.2-3.8)	0.7 (0.2-2.8)	0.5 (0.2-1.2)	0.6 (0.2-1.5)	**0.1 (0.0-0.7)***	0.5 (0.2-1.3)
Sum of respirator use										
0/1 (REF)										
2	0.5 (0.3-1.1)	0.9 (0.3-2.6)	1.5 (0.3-7.7)	-	1.1 (0.3-4.7)	0.7 (0.2-2.1)	0.8 (0.2-3.1)	1.2 (0.5-3.2)	0.3 (0.1-1.3)	0.8 (0.3-2.1)
3	**0.3 (0.1-0.7)****	**0.1 (0.0-1.1)^**	0.4 (0.0-5.2)	-	0.4 (0.0-3.8)	0.3 (0.1-1.6)	0.5 (0.1-2.9)	0.3 (0.1-1.4)	-	0.3 (0.1-1.3)
p-value for trend	**0.00**	**0.08**	0.63	-	0.50	0.14	0.46	0.23	**0.01**	**0.10**
Glove use:										
Mixing paint	**0.4 (0.2-0.8)****	**0.3 (0.1-0.7)****	0.6 (0.1-2.7)	-	**0.2 (0.0-1.0)***	0.5 (0.2-1.2)	**0.3 (0.1-1.1)^**	0.6 (0.2-1.3)	**0.4 (0.1-1.1)^**	**0.2 (0.1-0.6)****
Spray painting	**0.5 (0.3-0.9)***	**0.4 (0.2-0.9)***	0.4 (0.1-1.8)	-	**0.3 (0.1-1.2)^**	0.4 (0.2-1.1)^	1.3 (0.4-4.2)	**0.4 (0.2-1.0)***	0.9 (0.3-2.5)	0.7 (0.3-1.5)
Cleaning	**0.5 (0.2-0.9)***	**0.4 (0.2-1.0)***	0.3 (0.1-1.4)	-	**0.3 (0.1-0.9)***	0.4 (0.2-1.1)^	0.5 (0.2-1.5)	**0.5 (0.2-1.1)^**	**0.4 (0.2-1.1)^**	**0.4 (0.1-0.9)***
Sum of glove use										
0 (REF)										
1	**0.4 (0.2-1.0)^**	**0.3 (0.1-1.2)^**	0.2 (0.0-1.6)	-	**0.2 (0.0-1.2)^**	0.7 (0.2-2.4)	0.3 (0.0-1.7)	**0.3 (0.1-1.2)^**	1.1 (0.3-4.3)	0.6 (0.2-1.9)
2	0.7 (0.2-1.7)	0.7 (0.2-2.3)	0.2 (0.0-1.7)	-	0.3 (0.1-1.8)	0.4 (0.1-1.7)	1.2 (0.3-5.1)	0.6 (0.2-2.1)	1.1 (0.3-4.5)	1.1 (0.4-3.6)
3	**0.2 (0.1-0.6)****	**0.1 (0.0-0.5)****	0.2 (0.0-1.4)	-	**0.1 (0.0-0.6)****	**0.3 (0.1-1.0)^**	**0.3 (0.1-1.3)^**	**0.3 (0.1-0.8)***	0.4 (0.1-1.5)	**0.2 (0.0-0.6)****
p-value for trend	**0.00**	**0.00**	0.18	-	**0.02**	**0.04**	0.26	**0.04**	0.12	**0.01**
Combined PPE metric										
0/1 (REF)										
2	0.6 (0.2-1.6)	0.7 (0.2-2.7)	0.2 (0.0-2.4)	-	0.2 (0.0-1.6)	0.8 (0.2-3.3)	0.5 (0.1-3.0)	0.7 (0.2-2.6)	1.1 (0.3-4.6)	0.7 (0.2-2.7)
3	0.7 (0.2-1.8)	0.8 (0.2-2.9)	**0.1 (0.0-1.4)***	-	**0.1 (0.0-0.9)***	0.9 (0.2-3.6)	0.5 (0.1-3.1)	0.5 (0.1-2.0)	0.5 (0.1-2.6)	1.1 (0.3-3.9)
4	0.7 (0.3-1.8)	**0.3 (0.1-1.2)^**	0.3 (0.0-2.4)	-	**0.2 (0.0-1.1)^**	0.5 (0.1-2.0)	0.8 (0.2-3.8)	0.8 (0.3-2.7)	0.7 (0.2-2.9)	0.5 (0.1-1.7)
5	**0.4 (0.1-1.2)^**	0.2 (0.0-1.4)	0.3 (0.0-3.8)	-	0.3 (0.0-2.3)	0.3 (0.1-2.0)	0.2 (0.0-2.7)	0.4 (0.1-2.1)	0.2 (0.0-2.0)	**0.1 (0.0-1.2)^**
6	**0.1 (0.0-0.3)****	**0.1 (0.0-0.9)***	0.1 (0.0-2.6)	-	-	**0.1 (0.0-1.3)^**	0.2 (0.0-2.2)	**0.1 (0.0-1.0)***	-	**0.1 (0.0-1.0)^**
p-value for trend	**0.00**	**0.01**	0.23	-	**0.04**	**0.04**	0.24	**0.08**	**0.03**	**0.01**
Ever use air fed mask	0.8 (0.4-1.3)	**0.3 (0.1-0.7)****	0.3 (0.1-1.6)	-	0.8 (0.2-2.5)	**0.3 (0.1-0.8)***	0.5 (0.2-1.5)	0.6 (0.3-1.5)	1.4 (0.6-3.6)	0.8 (0.3-1.8)
Frequency respirator cartridges changed	**0.5 (0.3-1.0)^**	**0.3 (0.1-0.9)***	0.8 (0.2-3.7)	0.3 (0.1-2.2)	1.4 (0.4-5.1)	**0.3 (0.1-1.0)^**	0.9 (0.3-3.0)	0.5 (0.2-1.4)	0.7 (0.2-2.0)	0.7 (0.3-1.9)
Workplace practices										
Wash hands in solvents (yes/no)	**1.7 (0.9-3.1)^**	**3.2 (1.1-9.3)***	1.4 (0.3-6.9)	-	1.6 (0.4-6.3)	1.9 (0.7-4.9)	**4.6 (1.0-20.1)***	**2.7 (1.0-7.5)^**	1.5 (0.5-4.0)	**3.1 (1.1-8.5)***
Frequently wash hands in solvents	**2.0 (1.1-3.7)***	**3.1 (1.3-7.4)***	2.7 (0.7-10.8)	-	2.2 (0.6-7.5)	2.0 (0.8-4.9)	1.9 (0.6-5.8)	1.9 (0.8-4.4)	**3.0 (1.2-7.6)***	1.8 (0.7-4.2)
Skin exposure (body parts exposed)										
0/1 (REF)										
2	1.5 (0.8-2.7)	1.4 (0.6-3.7)	1.4 (0.3-7.3)	-	0.5 (0.1-2.9)	1.5 (0.6-3.7)	1.8 (0.6-5.6)	1.6 (0.7-3.8)	1.4 (0.5-3.8)	2.0 (0.8-5.0)
3	**3.5 (1.2-9.9)***	**5.7 (1.6-20.2)****	**7.8 (1.1-57.3)***	-	**19.3 (3.4-108.5)****	2.4 (0.6-9.0)	0.6 (0.1-7.4)	**3.5 (1.0-12.9)^**	2.2 (0.5-10.0)	**3.9 (1.1-14.1)***
p-value for trend	**0.02**	**0.02**	**0.08**	-	**0.01**	0.17	0.71	**0.06**	0.26	**0.02**
Gun cleaning method										
Unenclosed + un-extracted (REF)										
Enclosed + un-extracted	0.9 (0.4-2.2)	0.8 (0.2-3.0)	5.2 (0.4-65.8)	1.5 (0.2-10.4)	3.7 (0.5-29.3)	1.5 (0.4-5.8)	3.3 (0.4-23.5)	1.1 (0.3-3.9)	2.7 (0.6-12.2)	2.8 (0.7-11.5)
Unenclosed + extracted	0.7 (0.3-1.6)	1.6 (0.5-5.1)	**11.0 (0.9-135.0)^**	-	**6.0 (0.8-45.3)^**	2.0 (0.6-7.1)	**5.3 (0.8-37.3)^**	0.9 (0.2-3.0)	3.0 (0.7-12.8)	2.7 (0.7-10.7)
Enclosed + extracted	0.9 (0.4-2.0)	0.7 (0.2-2.3)	4.2 (0.4-45.3)	0.9 (0.1-6.3)	1.3 (0.2-9.9)	1.0 (0.3-3.5)	3.7 (0.6-22.6)	1.1 (0.4-3.3)	1.7 (0.4-6.8)	1.8 (0.5-6.6)
Paint type										
Both water and solvent based (REF)										
Mostly solvent based	**0.5 (0.3-1.1)^**	0.4 (0.1-1.4)	1.0 (0.2-5.0)	-	0.5 (0.1-2.7)	0.6 (0.2-2.0)	1.1 (0.3-3.8)	0.5 (0.2-1.6)	0.7 (0.2-2.5)	0.9 (0.3-2.3)
Hours on a typical day¥										
Mixing paint	1.1 (0.8-1.5)	0.8 (0.5-1.5)	0.6 (0.2-1.6)	-	0.6 (0.3-1.4)	1.1 (0.7-1.8)	0.7 (0.4-1.5)	1.1 (0.7-1.8)	**1.7 (1.2-2.6)****	0.8 (0.4-1.4)
Spray painting	1.0(0.8-1.1)	**1.3 (1.0-1.7)***	1.2 (0.8-1.8)	-	1.2 (0.8-1.7)	**1.3 (1.0-1.6)***	0.9 (0.6-1.2)	**1.3 (1.0-1.6)***	1.1 (0.8-1.4)	0.8 (0.6-1.1)
Degreasing/cleaning	1.1 (0.8-1.4)	1.1 (0.7-1.6)	1.3 (0.7-2.3)	-	0.9 (0.5-1.7)	1.2 (0.8-1.7)	1.4 (0.9-2.1)	**1.4 (1.0-1.9)^**	**1.6 (1.1-2.3)****	1.2 (0.8-1.7)

Table 6.3. Continued – Prevalence odds ratios for symptoms of neurotoxicity and PPE use/workplace practices.

	≥ 5 symptoms† n (%)	≥ 10 symptoms† n (%)	≥ 15 symptoms† n (%)	≥ 3 Neurological n (%)	≥ 3 Psychosomatic n (%)	≥ 3 Mood n (%)	≥ 3 Memory n (%)	≥ 3 Fatigue n (%)	≥ 3 Sleep Disturbance n (%)	≥ 3 Memory & Concentration n (%)
	99 (37.5)	35 (13.3)	17 (6.4)	11 (4.2)	17 (6.4)	31 (11.7)	21 (8.0)	35 (13.3)	26 (9.9)	34 (12.9)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Combined measures of workplace hygiene										
'Hygiene' Metric										
0/1 (poor hygiene)										
2	0.7 (0.3-1.8)	0.5 (0.2-1.6)	0.9 (0.1-5.9)	-	0.8 (0.2-4.3)	1.0 (0.3-3.2)	0.7 (0.2-3.3)	0.9 (0.3-2.7)	1.0 (0.3-3.5)	1.0 (0.3-3.2)
3	0.5 (0.2-1.2)	**0.3 (0.1-1.0)***	0.2 (0.0-1.7)	-	0.2 (0.0-1.8)	0.3 (0.1-1.2)	0.7 (0.2-2.9)	0.5 (0.2-1.7)	0.5 (0.1-2.2)	0.7 (0.2-2.1)
4/5 (good hygiene)	**0.3 (0.1-0.7)****	**0.1 (0.0-0.6)****	0.5 (0.1-3.3)	-	0.7 (0.2-3.4)	**0.3 (0.1-1.0)***	0.4 (0.1-1.7)	**0.3 (0.1-1.1)^**	**0.1 (0.0-0.8)***	0.4 (0.1-1.3)
p-value for trend	**0.00**	**0.00**	0.25	-	0.48	**0.02**	0.22	**0.06**	**0.02**	**0.10**

^ = p<0.1; * = p<0.05; ** = p<0.01

Adjusted for age, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits

† All EUROQUEST symptoms (all domains combined)

"-"= No ORs available due to non-convergence in model

¥ OR for every unit increase (1 hour) in time spent on task

Results for the combined PPE metric mutually adjusting for other workplace practices showed similar trends, but confidence intervals were generally wider and fewer individual results reached statistical significance (table 6.4). Nonetheless, an inverse dose-response trend remained (p for trend of 0.02 and 0.06 for reporting ≥5 and ≥10 symptoms, respectively), including for the domains of psychosomatic (p for trend = 0.02) and memory and concentration symptoms combined (p for trend = 0.05). The strength of the associations seen for use of an air fed respirator, frequency of mask cartridge changes, frequency of hand washing in solvents and time spent on work tasks were generally weaker compared to when analysed separately.

Table 6.4. Prevalence odds ratios for symptoms of neurotoxicity and combined PPE-use mutually adjusted for other variables in the table.

	≥ 5 symptoms† OR (95% CI)	≥ 10 symptoms† OR (95% CI)	≥ 15 symptoms† OR (95% CI)	≥ 3 Psychosomatic OR (95% CI)	≥ 3 Mood OR (95% CI)	≥ 3 Memory OR (95% CI)	≥ 3 Fatigue OR (95% CI)	≥ 3 Sleep Disturbance OR (95% CI)	≥ 3 Memory &Concentration OR (95% CI)
PPE-use									
Combined PPE metric									
0/1 (REF)									
2	0.6 (0.2-1.8)	0.9 (0.2-3.9)	0.2 (0.0-3.3)	0.3 (0.0-2.2)	0.8 (0.2-3.5)	0.4 (0.1-3.2)	1.2 (0.3-5.3)	1.0 (0.2-5.3)	1.0 (0.2-4.4)
3	0.9 (0.3-2.8)	1.3 (0.3-5.3)	0.1 (0.0-2.0)	**0.1 (0.0-0.8)***	1.3 (0.3-5.6)	0.8 (0.1-5.3)	0.8 (0.2-3.7)	0.6 (0.1-3.8)	2.0 (0.5-7.9)
4	0.9 (0.3-2.5)	0.3 (0.1-1.5)	0.3 (0.0-2.8)	**0.2 (0.0-1.1)^**	0.5 (0.1-2.2)	1.1 (0.2-6.2)	1.2 (0.3-4.5)	0.5 (0.1-3.0)	0.8 (0.2-3.4)
5	0.6 (0.2-1.9)	0.5 (0.1-3.2)	0.4 (0.0-6.2)	0.2 (0.0-1.9)	0.5 (0.1-3.2)	0.3 (0.0-3.8)	0.9 (0.2-4.9)	0.2 (0.0-3.5)	0.2 (0.0-2.1)
6	**0.1 (0.0-0.5)****	0.1 (0.0-1.7)	0.1 (0.0-3.1)	-	0.2 (0.0-1.7)	0.2 (0.0-2.7)	0.1 (0.0-1.7)	-	0.2 (0.0-1.8)
p-value for trend	**0.02**	**0.06**	0.21	**0.02**	**0.10**	0.37	0.26	**0.06**	**0.05**
Workplace practices									
Ever use air-fed mask	0.8 (0.4-1.7)	**0.3 (0.1-0.9)***	0.4 (0.1-2.6)	1.2 (0.3-5.7)	**0.3 (0.1-0.9)***	0.7 (0.2-2.5)	0.5 (0.2-1.3)	2.3 (0.6-8.8)	0.9 (0.3-2.3)
Frequency respirator cartridges changed	0.8 (0.4-1.7)	0.5 (0.1-1.7)	2.3 (0.3-15.4)	3.6 (0.7-17.6)	0.6 (0.2-2.0)	1.5 (0.4-5.9)	0.7 (0.2-2.0)	0.4 (0.1-2.2)	1.2 (0.4-3.6)
Frequency wash hands in solvents	1.8 (0.8-3.7)	1.3 (0.5-3.8)	1.3 (0.2-7.3)	1.6 (0.4-7.4)	0.7 (0.2-2.0)	1.9 (0.5-7.7)	1.2 (0.5-3.2)	2.8 (0.7-10.4)	1.8 (0.6-5.1)
Hours on a typical day¥									
Mixing paint	1.2 (0.7-1.8)	0.6 (0.3-1.5)	**0.2 (0.0-1.1)^**	**0.2 (0.1-1.0)^**	0.9 (0.5-1.9)	0.4 (0.1-1.3)	0.8 (0.4-1.5)	1.2 (0.6-2.4)	0.7 (0.3-1.4)
Spray painting	0.9 (0.7-1.1)	**1.4 (1.0-1.8)***	1.3 (0.7-2.3)	1.3 (0.8-2.0)	1.3 (0.9-1.7)	0.7 (0.5-1.2)	**1.5 (1.1-1.9)****	0.9 (0.6-1.3)	0.8 (0.6-1.1)
Degreasing/cleaning	1.2 (0.8-1.7)	1.5 (0.8-2.7)	2.0 (0.8-4.8)	1.5 (0.7-3.3)	1.4 (0.8-2.4)	**2.1 (1.1-4.0)***	**1.6 (1.0-2.7)***	**2.2 (1.2-4.1)***	1.6 (0.9-2.7)

^ = p<0.1; * = p<0.05; ** = p<0.01

Adjusted for age, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits, as well as all other variables listed in table

† All EUROQUEST symptoms (all domains combined)

"-"= No ORs available due to non-convergence in model

¥ OR for every unit increase (1 hour) in time spent on task

Analyses for skin exposure similarly adjusted also showed fewer statistically significant results, but again a dose-response trend remained (p for trend of 0.05 and 0.06 for ≥5 and ≥15 symptoms, respectively; supplementary table 6.7) with the strongest associations observed in the symptom domains of psychosomatic, fatigue and memory and concentration symptoms combined. Finally, in the mutually adjusted analyses, we found a significant inverse dose-response trend with increased hygiene scores and total symptoms (p for trend of 0.005 and 0.003 for reporting ≥5 and ≥10 symptoms), and symptoms in the domains of mood (p=0.02), sleep disturbance (p=0.02), fatigue and memory and concentration symptoms combined, although the last two did not reach statistical significance (p=0.05 and 0.12 respectively, supplementary table 6.8).

6.4 Discussion

This study showed that reported frequent PPE use and good workplace hygiene practices were associated with a reduced risk of total symptoms of neurotoxicity, and symptoms in the psychosomatic, mood and memory and concentration domains. In general, the strongest effects were seen for glove use but dose-response trends were also observed with other PPE-use and hygiene practices.

Previous studies in spray painters (30, 36) and other solvent exposed workers (32-34) have shown that the use of respirators, gloves and/or chemical protective suits is effective in reducing total body burden of solvents. Also, one study in solvent-exposed gun factory workers found that self-reported glove use was associated with some measures of cognitive performance, but not self-reported symptoms (29). To our knowledge, our study is therefore one of the first to show a direct protective effect of consistent PPE-use on symptoms of neurotoxicity in solvent-exposed workers. Similar protective effects of PPE on neuropsychological performance have been reported for other occupational settings/exposures such as farm workers exposed to organophosphate pesticides (356). PPE-use has also previously been associated with reduced incidence and prevalence of occupational asthma in workers exposed to toluene diisocyanate, including spray painters (319, 357). As expected, in our study PPE-use was protective for symptom domains (psychosomatic, mood and memory and concentration combined) previously identified to be associated with solvent exposure in spray painters (16), including in our previous study in which the current study was nested (331). Taken together, this strongly suggests that PPE-use and good workplace

hygiene practices and behaviours are important determinants of exposure (and related health risks) in these workers.

Due to some correlation between the use of several types of PPE, workplace hygiene measures and risk behaviours it was difficult to assess the relative contribution of each measure individually. Nonetheless, multivariate analyses including combined individual measures and mutually adjusting for workplace hygiene practices and risk behaviours showed similar trends to analyses for each of these individual variables separately, suggesting results are valid. Also, additional analyses including only those workers who wore one type of PPE (respirator only when spray painting (N=76), gloves only when mixing paint (N=79) and gloves only when degreasing/cleaning (N=102)) showed highly comparable results, although the models were less stable due to smaller numbers (data not shown). Overall, we found that consistent glove-use was most protective (table 6.2), which is consistent with evidence from other studies suggesting that dermal exposures may contribute >50% of the total body burden of solvents, particularly when airborne exposures are well controlled (25, 26, 30, 74). Although there was some variation in the type of gloves used (predominantly nitrile and latex), nitrile gloves were used by the vast majority of workers for tasks with a high risk of solvent exposure (mixing paint, spray painting, degreasing/cleaning). Latex gloves were used, but mostly for low exposure-risk tasks (e.g. sanding, final polishing). As a result, differences in the protection provided by different glove materials (i.e. permeability, breakthrough times, etc. (358)) are unlikely to have had an impact on the associations observed. A strong positive dose-response trend was also observed with increased skin exposure (table 6.4) further highlighting the critical role that

dermal exposure may play in developing symptoms of neurotoxicity. Frequent respirator use was also associated with fewer symptoms (table 6.2), which is unlikely to be entirely explained by correlation with glove use. In particular, when we combined glove and respirator use (table 6.3) we found a stronger protective effect than with glove use alone, thus showing, as previously suggested by others (29), that respirators provide additional protection, even when airborne exposures were low (331). Of the two respirator types used, air-fed respirators showed the greatest reduction in risk (table 6.4), which is consistent with previous studies (34).

Frequent changing of absorbent respirator cartridges was associated with a reduction in risk of 50 – 70%, which is consistent with previous research showing that poorly maintained PPE is associated with increased exposure (32). Nearly 70% of workers had no defined cartridge replacement schedule or changed them 'less than once a month' (table 6.2), which given the association with symptoms of neurotoxicity observed in our study is of concern. In particular, as cartridge masks were worn by all spray painters for at least some tasks, this may provide a false sense of protection for painters and shop owners. We found that frequent washing of hands in solvents was associated with an increased risk of symptoms. With almost 70% of workers reporting hand washing in solvents, and 27% reporting they did this frequently (table 6.2), this is also of considerable concern. Inconsistent glove use was, as expected, moderately correlated with washing of hands in solvents (r=0.32), but also with respirator-use (r=0.41); in turn, respirator-use was moderately correlated with the frequency that respirator cartridges were changed (r=0.27). This suggests that poor workplace hygiene practices are likely to cluster together within workers and/or workplaces and

contribute to an increased risk of neurotoxic effects, as demonstrated by the significant inverse dose-response trend between hygiene score and symptoms of neurotoxicity (supplementary table 6.8). Interestingly, the use of water-based paints (which in New Zealand at the time of the study were only available for coloured paints and not for primer and top coat paints) was associated with a greater risk of symptoms, although this failed to reach statistical significance. The reason for this is unclear, although the fact that both primer and top coat paints and many preparatory products were still solvent based suggests those who use water-based paints are still at risk of regular solvent exposure.

There were several limitations to this study. Neurotoxicity was assessed using self-reported symptoms, which were not confirmed by a clinical assessment, and therefore some misclassification may have occurred. However, EUROQUEST was specifically designed to assess symptoms associated with occupational exposure to neurotoxic agents (233), and is widely used and well validated against clinical criteria (175, 224, 232, 234, 349). PPE-use and workplace behaviours were also self-reported, which may result in bias, for example from over-reporting of PPE-use through fear of admitting non-compliance. However, any bias, if present, would most likely lead to an underestimation of the true effect. A further limitation is that the effects observed may be attributable to historical exposures, PPE-use, and workplace practices (39). However, including duration of employment in multivariate regression models (as a proxy for potential years of exposure) had little effect on the effect measures (supplementary table 6.5), and in any case, exposure misclassification would likely lead to an underestimation of the true effect. Also, we included 31 office workers

(reclassified as spray painters, see above) who may not have been comparable to the other participants in terms of work performed, use of PPE and workplace practices. However, at the time of the study, twenty-two reported performing repair work on the shop floor, and were therefore at risk of being exposed. From our observations and discussions with workers it was clear the remaining nine also performed some repair work, especially during busy periods, so were at least occasionally at risk of exposure. Furthermore, almost all (n=28) provided responses to at least some the questions on PPE use when mixing paint, spray painting or degreasing/cleaning, indicating they performed these tasks, even if irregularly. Analyses excluding the nine workers who reported not performing work on the shop floor had no effect (supplementary table 6.6), suggesting results are robust.

The 'hygiene' metric was constructed and analysed in a way that assumed every unit increase represented an equal increase in exposure, despite being derived from a combination of different PPE-use and workplace practice factors. Nonetheless, highly comparable trends were observed when the metric was constructed using different combinations of these variables and different response weightings within variables (data not shown), suggesting the use of this metric was valid.

As discussed by the authors of the EUROQUEST and others, symptoms may be at least partially reversible upon removal from exposure, (39, 175, 234), but memory and concentration symptoms and those associated with mood liability (i.e. those symptoms inversely associated with PPE use and good workplace hygiene in our study) have also been shown to persist after exposure cessation in more severely affected

individuals (175). Due to the cross-sectional design we were unable to assess whether symptoms were reversible in this study.

It is feasible that workers who have developed symptoms as a result of higher historical exposures are more likely to avoid current exposures by using PPE more frequently and applying better workplace hygiene, but this would again likely lead to an underestimation of the true effect. Also, it may be that in workshops where PPE is used more consistently and good hygiene practices are promoted, exposure controls are more likely to be in place and efficacious (e.g. newer, higher quality engineering controls which are more regularly maintained) and therefore contribute to at least part of the associations observed. We have extensively assessed a large number of exposure controls, hygiene measures and risk behaviours and therefore consider this unlikely, but we were unable to collect data on all potential exposure determinants, so it cannot be excluded. For example, variations in the design, quality and maintenance of spray booths between workshops may have affected exposure levels (and risk of symptoms). However, 'spot' measurements in booths across a range of the workshops showed consistently low solvent levels in the breathing zone of workers whilst spray painting (data not shown), suggesting that spray booths used in New Zealand are generally highly effective in controlling airborne exposures.

Our findings have considerable relevance for the development of improved intervention strategies in the collision repair industry involving increased use of PPE and promoting good workplace hygiene, at least until higher-level controls to minimise/eliminate exposure are developed and more widely implemented. Improvements in spray booth technology and local exhaust ventilation have already

resulted in significantly reduced emissions and most likely explain the low airborne exposures observed in our study (reported in (331)). However, the results of the current study indicate that more action may be required particularly focused on reducing dermal exposure. Although the focus of this study has been on neurotoxicity, a reduction in both dermal and airborne solvent exposures will also likely reduce the risk of solvent-related cancer and di-isocyanate-induced asthma (120, 320, 359, 360).

In conclusion, this study has shown that application of relatively basic exposure control measures such as PPE-use and good workplace hygiene is associated with a strongly reduced risk of symptoms of neurotoxicity in the collision repair industry. Programmes to encourage and support the use of these controls in this industry are feasible and would likely result in significantly reduced ill-health.

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6.5 Supplementary material

Table 6.5. Supplementary table – Prevalence odds ratios for symptoms of neurotoxicity by exposure group– exposure variables included in model – Adjusted for both age and duration of employment

	≥ 5 EQ OR (95% CI)	≥ 10 EQ OR (95% CI)	≥ 15 EQ	≥ 3 Psychosomatic OR (95% CI)	≥ 3 Mood OR (95% CI)	≥ 3 Memory OR (95% CI)	≥ 3 Fatigue OR (95% CI)	≥ 3 Sleep Dist. OR (95% CI)	≥ 3 Memory &Concentration OR (95% CI)
Combined PPE metric									
0 (REF)									
1	0.5 (0.2-1.6)	0.9 (0.2-3.6)	0.2 (0.0-3.2)	0.3 (0.0-2.1)	0.7 (0.2-3.3)	0.4 (0.1-3.0)	1.1 (0.3-4.5)	1.3 (0.2-6.4)	0.9 (0.2-4.0)
2	1.1 (0.4-3.1)	1.3 (0.3-4.9)	0.1 (0.0-2.0)	**0.1 (0.0-0.8)***	1.6 (0.4-6.3)	0.7 (0.1-4.4)	0.9 (0.2-3.5)	0.7 (0.1-3.7)	1.8 (0.5-7.1)
3	0.9 (0.3-2.4)	0.3 (0.1-1.3)	0.4 (0.0-2.7)	**0.1 (0.0-1.0)***	0.6 (0.2-2.4)	0.9 (0.2-5.0)	1.0 (0.3-3.6)	1.0 (0.2-4.8)	0.7 (0.2-2.9)
4	0.5 (0.2-1.6)	0.4 (0.1-2.4)	0.3 (0.0-5.3)	0.2 (0.0-1.6)	0.4 (0.1-2.4)	0.3 (0.0-3.3)	0.7 (0.1-3.5)	0.8 (0.1-4.8)	0.3 (0.0-1.8)
5	**0.1 (0.0-0.5)****	0.1 (0.0-1.6)	0.1 (0.0-3.1)	-	0.2 (0.0-1.9)	0.2 (0.0-2.4)	0.1 (0.0-1.6)	-	0.1 (0.0-1.7)
p-value for trend	**0.02***	**0.04***	0.21	**0.02***	**0.10^**	0.33	0.20	0.22	**0.05***
Ever use Air fed mask	0.9 (0.5-1.8)	**0.3 (0.1-0.9)***	0.4 (0.1-2.6)	1.3 (0.3-6.2)	**0.3 (0.1-0.8)***	0.7 (0.2-2.6)	0.6 (0.2-1.6)	2.4 (0.7-7.5)	0.9 (0.3-2.4)
Frequency Resp. Cartridges changed	0.7 (0.3-1.5)	0.5 (0.1-1.7)	2.0 (0.3-12.9)	3.5 (0.7-16.7)	0.5 (0.1-1.7)	1.6 (0.4-6.1)	0.7 (0.2-1.9)	0.9 (0.2-3.1)	1.3 (0.5-3.7)
Frequency wash hands in solvents	0.6 (0.3-1.2)	0.7 (0.3-2.0)	0.7 (0.1-3.8)	0.6 (0.1-2.9)	1.5 (0.5-4.2)	0.7 (0.2-2.7)	0.8 (0.3-2.2)	**0.2 (0.1-0.7)****	0.7 (0.3-2.0)
Hours on a typical day by task									
Mixing paint	1.1 (0.7-1.7)	0.7 (0.3-1.5)	**0.2 (0.0-1.2)^**	**0.2 (0.1-1.0)***	0.9 (0.5-1.7)	**0.3 (0.1-1.0)***	0.8 (0.4-1.6)	1.1 (0.7-2.0)	0.6 (0.3-1.3)
Spray painting	0.9 (0.7-1.1)	**1.4 (1.1-1.9)***	1.3 (0.7-2.3)	1.3 (0.8-2.0)	**1.3 (1.0-1.7)***	0.8 (0.5-1.3)	**1.4 (1.0-1.8)***	0.8 (0.6-1.2)	0.8 (0.6-1.1)
Degreasing	1.2 (0.8-1.8)	1.4 (0.8-2.4)	1.9 (0.8-4.3)	1.5 (0.7-3.2)	1.5 (0.9-2.5)	**2.2 (1.1-4.2)***	**1.7 (1.0-2.7)***	**1.8 (1.1-3.1)***	1.6 (0.9-2.7)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for Age, duration of employment, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits, and all other exposures listed in table.

"-"= No ORs available due to non-convergence

¥ OR for every unit increase (1 hour) in time spent on task

Table 6.6. Supplementary table. Prevalence odds ratios for symptoms of neurotoxicity and 'hygiene' metric - mutually adjusted with other variables in table – Excluding ex-tradesmen office workers who reported spray painting 0 hours on a typical working day (n=9).

	≥ 5 EQ	≥ 10 EQ	≥ 15 EQ	≥ 3 Psychosomatic	≥ 3 Mood	≥ 3 Memory	≥ 3 Fatigue	≥ 3 Sleep Disturbance	≥ 3 Memory & Concentration.
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	86 (37.2)	33 (14.3)	16 (6.9)	16 (6.9)	29 (12.6)	20 (8.7)	32 (13.9)	21 (9.1)	32 (13.9)
Combined measures of workplace hygiene									
Hygiene Metric									
0/1 (poor hygiene)									
2	0.8 (0.3-2.0)	0.5 (0.1-1.6)	1.2 (0.2-9.0)	1.0 (0.2-5.6)	1.0 (0.3-3.3)	0.9 (0.2-4.4)	0.8(0.3-2.7)	1.1 (0.3-4.2)	1.2 (0.4-3.7)
3	0.5 (0.2-1.2)	**0.3 (0.1-0.9)***	0.2 (0.0-1.9)	0.3 (0.0-2.2)	**0.3 (0.1-1.2)^**	0.7 (0.2-3.2)	0.4(0.1-1.4)	0.5 (0.1-2.3)	0.7 (0.2-2.4)
4/5 (good hygiene)	**0.3 (0.1-0.7)****	**0.2 (0.0-0.6)****	0.9 (0.1-7.1)	1.0 (0.2-5.0)	**0.3 (0.1-1.1)^**	0.5 (0.1-2.5)	**0.4(0.1-1.2)^**	**0.1 (0.0-1.0)***	0.4 (0.1-1.4)
p-value for trend	**0.00**	**0.00**	0.48	0.69	**0.02**	0.37	0.06	0.02	0.13
Workplace Practices									
Hours on a typical day[¥]									
Mixing paint	1.2 (0.8-1.8)	0.6 (0.3-1.3)	**0.2 (0.1-1.1)^**	0.5 (0.1-1.5)	0.9 (0.4-1.7)	0.4 (0.1-1.2)	0.7 (0.4-1.5)	1.5 (0.8-2.8)	0.7 (0.4-1.5)
Spray painting	0.9 (0.7-1.1)	**1.3 (1.0-1.7)^**	1.2 (0.7-1.9)	1.1 (0.8-1.7)	1.2 (0.9-1.6)	0.8 (0.5-1.2)	**1.4 (1.1-1.8)***	1.0 (0.7-1.4)	0.8 (0.6-1.1)
Degreasing/cleaning	1.1 (0.7-1.6)	1.3 (0.8-2.3)	**2.2 (0.9-5.4)^**	1.4 (0.7-3.0)	1.3 (0.7-2.2)	**2.0 (1.1-3.7)***	**1.5 (0.9-2.5)^**	**1.8 (1.0-3.3)***	1.4 (0.8-2.2)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits, as well as all other variables listed in table

[¥] OR for every unit increase (1 hour) in time spent on task

Table 6.7. Supplementary table. Prevalence odds ratios for symptoms of neurotoxicity and skin exposure (body parts exposed during painting) - Mutually adjusted for other variables in the table.

	≥ 5 symptoms† OR (95% CI)	≥ 10 symptoms† OR (95% CI)	≥ 15 symptoms† OR (95% CI)	≥ 3 Psychosomatic OR (95% CI)	≥ 3 Mood OR (95% CI)	≥ 3 Memory OR (95% CI)	≥ 3 Fatigue OR (95% CI)	≥ 3 Sleep Disturbance OR (95% CI)	≥ 3 Memory & Concentration OR (95% CI)
Workplace practices									
Skin exposure (body parts exposed.)									
0/1 (REF)									
2	1.3 (0.7-2.5)	0.9 (0.3-2.6)	1.3 (0.2-7.6)	0.5 (0.1-3.0)	1.1 (0.4-2.9)	1.6 (0.5-5.6)	1.5 (0.6-3.8)	1.1 (0.4-3.3)	2.1 (0.8-5.5)
3	**2.8 (0.9-8.5)^**	3.4 (0.7-15.2)	**9.0 (0.7-112.1)^**	-	1.5 (0.3-6.6)	0.5 (0.0-7.8)	3.2 (0.7-14.3)	1.4 (0.2-10.3)	**4.3 (1.0-17.9)***
p-value for trend	**0.08**	0.27	0.16	0.40	**0.01**	0.65	0.91	0.14	0.77
Frequency wash hands in solvents	1.7 (0.9-3.5)	1.5 (0.5-4.0)	1.7 (0.3-10.3)	2.0 (0.3-12.1)	0.9 (0.3-2.5)	2.0 (0.5-8.2)	1.1 (0.4-2.8)	**4.9 (1.5-16.7)***	1.6 (0.6-4.4)
Hours on a typical day¥									
Mixing paint	1.1 (0.7-1.7)	0.6 (0.3-1.5)	**0.2 (0.0-1.1)^**	**0.2 (0.1-1.0)***	1.0 (0.5-1.8)	0.4 (0.1-1.2)	0.8 (0.4-1.6)	1.2 (0.7-2.1)	0.7 (0.3-1.6)
Spray painting	0.9 (0.8-1.1)	**1.4 (1.0-1.8)***	1.3 (0.7-2.2)	1.1 (0.7-1.8)	**1.3 (1.0-1.7)***	0.8 (0.5-1.3)	**1.3 (1.0-1.7)***	0.9 (0.6-1.2)	0.8 (0.6-1.1)
Degreasing/cleaning	1.2 (0.8-1.7)	1.4 (0.8-2.4)	**2.3 (1.0-5.5)^**	1.8 (0.8-4.3)	1.4 (0.8-2.3)	**2.0 (1.1-3.8)***	**1.8 (1.1-2.9)***	**1.9 (1.1-3.1)***	1.4 (0.9-2.4)
PPE-use									
Ever use air fed mask	0.9 (0.5-1.7)	**0.4 (0.1-1.0)**	0.4 (0.1-2.7)	1.0 (0.2-5.4)	**0.3 (0.1-0.9)***	0.7 (0.2-2.5)	0.6 (0.2-1.6)	2.3 (0.7-7.5)	1.1 (0.4-2.9)
Frequency respirator cartridges changed	0.6 (0.3-1.2)	0.4 (0.1-1.3)	2.7 (0.4-17.1)	3.8 (0.7-18.9)	0.4 (0.1-1.2)	1.3 (0.4-4.6)	0.6 (0.2-1.7)	0.8 (0.2-2.6)	1.0 (0.4-2.7)

^ = p<0.1; * = p<0.05; ** = p<0.01

Adjusted for age, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits, as well as all other variables listed in table

† All EUROQUEST symptoms (all domains combined)

"-"= No ORs available due to non-convergence

¥ OR for every unit increase (1 hour) in time spent on task

Table 6.8. Supplementary table. Prevalence odds ratios for symptoms of neurotoxicity and 'hygiene' metric - Mutually adjusted with other variables in table

	≥ 5 symptoms† OR (95% CI)	≥ 10 symptoms† OR (95% CI)	≥ 15 symptoms† OR (95% CI)	≥ 3 Psychosomatic OR (95% CI)	≥ 3 Mood OR (95% CI)	≥ 3 Memory OR (95% CI)	≥ 3 Fatigue OR (95% CI)	≥ 3 Sleep Disturbance OR (95% CI)	≥ 3 Memory. & Concentration. OR (95% CI)
Combined measures of workplace hygiene									
'Hygiene' Metric									
0/1 (poor hygiene)									
2	0.7 (0.3-1.7)	0.5 (0.1-1.6)	1.2 (0.2-8.9)	0.9 (0.2-5.5)	1.0 (0.3-3.2)	0.9 (0.2-4.3)	0.8 (0.2-2.6)	1.0 (0.3-3.9)	1.1 (0.3-3.6)
3	0.5 (0.2-1.2)	**0.3 (0.1-0.9)***	0.2 (0.0-1.9)	0.3 (0.0-2.2)	**0.3 (0.1-1.2)^**	0.7 (0.2-3.2)	0.4 (0.1-1.4)	0.5 (0.1-2.2)	0.7 (0.2-2.3)
4/5 (good hygiene)	**0.3 (0.1-0.7)***	**0.2 (0.0-0.6)****	0.9 (0.1-6.5)	0.9 (0.2-4.7)	**0.3 (0.1-1.0)^**	0.5 (0.1-2.3)	**0.3 (0.1-1.2)^**	**0.1 (0.0-0.9)***	0.4 (0.1-1.4)
p-value for trend	**0.01**	**0.00**	0.45	0.66	**0.02**	0.33	**0.05**	**0.02**	0.11
Workplace Practices									
Hours on a typical dayɣ**									
Mixing paint	1.2 (0.8-1.8)	0.6 (0.3-1.3)	**0.2 (0.1-1.1)^**	0.5 (0.1-1.5)	0.9 (0.4-1.7)	0.4 (0.2-1.3)	0.7 (0.4-1.5)	1.5 (0.8-2.9)	0.7 (0.4-1.5)
Spray painting	0.9 (0.8-1.1)	**1.3 (1.0-1.7)***	1.2 (0.8-1.9)	1.2 (0.8-1.7)	1.2 (0.9-1.6)	0.8 (0.5-1.2)	**1.4 (1.1-1.8)****	1.0 (0.7-1.4)	0.8 (0.6-1.1)
Degreasing/cleaning	1.1 (0.7-1.6)	1.3 (0.8-2.3)	**2.2 (0.9-5.3)^**	1.4 (0.7-2.9)	1.3 (0.7-2.2)	**2.0 (1.1-3.6)***	**1.5 (0.9-2.5)^**	**1.9 (1.0-3.3)***	1.4 (0.8-2.2)

^ = p<0.1,* = p<0.05, ** = p<0.01

Adjusted for age, ethnicity, smoking status, alcohol consumption, education status, general health and personality traits, as well as all other variables listed in table

† All EUROQUEST symptoms (all domains combined)

ɣ OR for every unit increase (1 hour) in time spent on task

7 General discussion

7.1 Introduction

This thesis is based on a series of studies in the collision repair industry on airborne solvent exposures and determinants, symptoms of neurotoxicity, and the protective effects of personal protective equipment (PPE) and workplace hygiene practices. No such studies have previously been conducted in this industry in New Zealand, and relatively few have been conducted internationally, particularly in the last decade. The main findings are outlined below, followed by a discussion of the specific results, the strengths and limitations of the studies conducted, recommendations for future research, and overall conclusions.

7.1.1 Summary of main findings

The main study findings are as follows:

- Full-shift average airborne solvent levels in contemporary collision repair workshops are well below current workplace exposure standards (chapter 3).
- Job title and the location of both exhaust ventilation and exposure sources are important determinants of airborne solvent exposures in collision repair workshops (chapter 3).
- Non-spray painting tasks are associated with higher airborne exposures than spray painting itself (chapter 3).
- Collision repair workers are significantly more likely to report symptoms of neurotoxicity than unexposed reference workers (chapter 4).
- Collision repair workers are more likely to score lower on tests of neuropsychological (cognitive) performance compared to an unexposed reference group across a range of functional domains (chapter 5).
- The strongest effects are in functional domains which have consistently been shown to be affected by solvents in other studies (neurological, mood, and memory and concentration) (chapters 3, 4 & 5).
- Neurobehavioural effects occur in workers with average airborne exposure levels well below workplace exposure standards (chapters 4 & 5).
- Panel beaters may be more likely to have a higher prevalence of symptoms of neurotoxicity and perform poorer on neuropsychological tests than spray painters (chapters 4 & 5).

- Neurotoxicity in some workers may be more severe, as reflected by a higher risk of collision repair workers reporting a greater number of neurobehavioural symptoms, and of scoring in the lowest 5th and 10th percentiles of 'normal' performance on some elements of the RBANS cognitive test battery (chapters 4 & 5).
- The risk of neurotoxicity does not appear to increase in a dose-dependent manner, possibly due to a healthy worker survivor effect (chapters 4 & 5).
- Use of PPE and workplace hygiene are associated with a strongly reduced risk of symptoms (chapter 6).

7.2 Discussion of specific results

7.2.1 Exposures

Full-shift airborne solvent levels measured in this study were well below current New Zealand and international workplace exposure standards (average 1.2ppm, or around 8% of the combined ACGIH TLV (110) for the solvent mixture detected). Nonetheless, collision repair workers reported significantly more symptoms and scored lower on a range of objective cognitive and psychomotor tests than the reference group. The impact of historical exposures on the risks observed could not be ruled out. However, as those who had only been employed in the industry for an average of 5 years were also more likely to report symptoms, it is likely that current exposures have contributed, at least to some extent, to the effects observed.

As discussed throughout this thesis, it is likely that full-shift average airborne exposures alone may not accurately reflect total body burden, and that dermal exposures may be equally, or possibly more important in the development of symptoms. Studies have shown that dermal exposures may contribute 50% or more of a workers body burden of solvents, particularly when airborne exposures are well controlled (25, 26, 30, 74). This is supported by the finding reported in this thesis of consistent glove-use being the most protective against symptoms, and the strong positive dose-response trend observed with self-reported increased skin exposure (Chapter 6). However, the relative contribution of dermal exposures to total body burden is likely to vary greatly between individual workplaces and within and between workers, depending upon variations in PPE use and workplace behaviours, and other

determinants of both airborne and dermal exposure (123). For example, whilst the contribution of direct deposition of liquid/colloidal solvents on the skin to total body burden may be in excess of 60% (30), if measures are taken to avoid this, dermal absorption of solvent vapour may only account for 1-2% of body burden (74). It is also clear that in situations where airborne solvent exposures are inadequately controlled, exposure via inhalation is likely to remain the dominant exposure route (25, 30, 36).

The VEM data (chapter 3, figures 3.2-3.4) showed that peaks in airborne exposure of between 200 and 1100ppm can occur regularly. While peak exposures may contribute little to average levels, they can produce an augmented dose rate at target sites in the body, acting as a tipping point in the development of symptoms (28). This may explain why other studies have also observed an increased risk of symptoms of neurotoxicity at average airborne exposure levels below 8-hour TWA airborne exposure standards (18, 300). However, the VEM data was limited to a small number of observations, and a more in-depth assessment of peak exposures is required to assess the associations with neurotoxicity.

As discussed in Chapter 2, The ACGIH have produced a series of 'skin notations' (involving chemicals that can readily pass through the skin which may have a significant impact on overall body burden for specific chemicals including solvents) (110), short-term exposure limits (STELs i.e. maximum permissible exposure over a 15 minute period) and ceiling limits related to peak exposures (50, 110). However, due to a lack of standardised exposure assessment methods and limited data regarding the health risks posed from dermal and peak exposures, the quality and applicability of these standards is limited (25, 115). As a result of this, and the relative difficulty and

complexity of the exposure assessment techniques used, dermal and peak exposure assessment are rarely conducted as part of epidemiological studies (27, 28, 116), routine hazard surveillance, or assessment of workplace compliance.

Biological exposure indices (BEIs) for solvents have also been established (110), but only for a limited number of chemicals and metabolites (113). Also, while biological monitoring can provide an estimate of solvent levels in the body (by measuring either unchanged solvents or their metabolites in blood or urine) it cannot be used in isolation to assess the relative contribution of different exposure pathways to the total body burden (71). To achieve this, a combination of biological, airborne and dermal exposure assessment is required. Dermal and biological exposure monitoring could not be conducted as part of the studies in this thesis and only a small number of VEM observations of peak exposures could be conducted, largely due to time and funding constraints and, in the case of dermal monitoring, highly complex sampling methodology. However, the results suggest assessment of these exposures, and development of standardised methodologies for their assessment should be a focus of future studies, as discussed in section 7.4.

7.2.2 Determinants of exposure

After controlling for all other potential exposure determinants, job title was the strongest predictor of exposure levels (spray painters vs. office staff, ER 5.02, 95% CI 3.11-8.10) followed by the location of local exhaust ventilation (LEV) in the mixing room (Away from main mixing bench vs. next to main mixing bench, ER 0.45, 95% CI,

0.26-0.77, chapter 3, table 3.1), suggesting these job tasks, processes and work areas should be a target of interventions to reduce airborne solvent exposure. Although previous studies have reported lower exposures with the use of water-based rather than solvent-based paint systems (100), no significant differences in exposure levels were observed in this study. It is unclear why these findings differ from previous studies, but it may reflect the relatively small sample size and the fact that spray painting in general seemed to contribute less to exposure levels than non-spraying tasks (chapter 3, table 3.2).

A larger workshop volume also appeared to be associated with higher exposure levels (<1000m^3 vs. >2000m^3, ER 1.45, 0.64-3.32), which is the opposite of what has been found in other studies (14, 136) that showed that a larger workshop volume reduced the likelihood of solvents becoming concentrated in a workers' immediate environment. The association between confined space working environments and elevated exposure levels is also well recognised for a wide range of other workplace contaminants, including volatile compounds, carbon monoxide(361) and other gases (362), welding fumes (363, 364) and various dusts (365-367). It is unclear why the findings of this thesis differ, but again it may reflect the relatively small number of workshops involved (n=18). The performance of downdraft booths also appeared to be superior to cross-draft booths (downdraft vs. cross-draft, ER 0.65, 0.22-1.92). Previous studies have found similar, and in some cases even stronger associations (100, 134, 135), which may be due to the requirement for workers in a cross-draft booth to stand between the extraction source and the object being painted, resulting in higher exposures (as observed in the VEM observations, chapter 3, figure 3.3).

Time spent mixing paint, cleaning spray equipment with solvents, spraying primer paint and spraying clear coat paint were associated with increased exposure levels (chapter 3, table 3.2), as has also been observed in several other studies (14, 100, 127). Also, time spent on non-spray painting tasks combined showed a stronger association with solvent levels than spray painting tasks combined (table 3.2). This is consistent with the findings of a Finnish study (100) in which the authors concluded that exposures during tasks conducted outside the spray booth (where exposure controls are limited) may contribute more to exposures than actual spray painting.

Similarly, the VEM observations showed that the highest exposure peaks also occurred during non-spray painting tasks, particularly cleaning of spray equipment (chapter 3, figures 2-4). When analyses were restricted to spray painters, the associations between time spent on non-spraying tasks and full shift exposure levels were weaker and non-significant, suggesting that non-spraying tasks may be most important for the airborne exposures of panel beaters and office staff (chapter 3, table 3.2).

7.2.3 Health effects

Solvent-exposed collision repair workers were significantly more likely to report symptoms of neurotoxicity compared to an unexposed reference group of construction workers, with ORs of 2.0 (95% CI, 1.3-3.3), 2.4 (1.2-4.8) and 6.4 (1.8-23.0) for reporting ≥5, ≥10 and ≥15 symptoms, respectively (chapter 4, table 4.3). These symptoms were primarily in the functional domains of neurological (OR 4.2, 95% CI, 1.2-15.3), psychosomatic (OR 3.2, 1.2-9.1), mood (OR 2.1, 1.0-4.3) and memory and concentration symptoms combined (OR 2.4, 1.2-4.8). The finding of an excess risk of symptoms overall, and in these specific domains, is consistent with previous studies in vehicle spray painters (17, 45), industrial painters (19, 299, 302) and other workers exposed to solvent mixtures (67, 288).

Performance deficits on objective tests of cognitive function were also observed in collision repair workers compared to the reference group. These were again in the functional domains most consistently shown to be affected in previous studies of workers exposed to solvent mixtures (16), including attention and reaction time (digit span backwards: difference, -1.5 (95% CI, -2.4, -0.5); digit span total -1.7 (-3.3, -0.0); coding -6.1 (-9.9, -2.8); total attention scale: -9.3 (-15.9, -2.8); Trails B -11.5 (-22.4, -0.5) and motor speed/dexterity (coin rotation dominant hand & non-dominant: -2.9 (-5.3, -0.4) and -3.1 (-5.6, -0.7), respectively).

Increased risks of neurobehavioural and cognitive performance outcomes indicative of more pronounced dysfunction were observed in collision repair workers. For example, they were twice as likely as the reference group to report ≥5 symptoms, two and a

half times more likely to report ≥10, and nearly six and a half times more likely to report ≥15 symptoms than the reference group (chapter 4, table 4.3). Although a number of the symptoms included in the EUROQUEST may be considered 'mild', and are likely to occasionally occur in healthly individuals (e.g. dropping things unintentionally), the EUROQUEST is designed to minimise detection of these symptoms. In particular, for a person's response to have been coded as positive for a particular item on the EUROQUEST, they must have experienced the symptom 'often' or 'very often' (rather than 'seldom/never' or 'sometimes') over the past several (2-3) months. Therefore, symptoms as defined in this study are likely to represent a more severe spectrum that goes beyond simply mild symptoms. For the objective tests of cognitive function, collision repair workers were twenty times more likely to score in the 'low' range (5th percentile) (260) on the RBANS tests for attention compared to reference workers, and eight times more likely to score in the 'borderline' range (10th percentile, chapter 5, table 5.3). The authors of the RBANS test battery suggest average scores below these percentiles (which are based on scores of an RBANS normative comparison group (282)), may be indicative of CNS damage, and the individual may require further clinical evaluation (260). Taken together, the lower cognitive performance overall and the higher risk of outcomes indicative of more pronounced cognitive dysfunction suggests effects in some collision repair workers may be more severe, particularly as deficits in cognitive function are seen as a hallmark of potentially irreversible CNS damage (7).

A number of earlier studies of solvent-exposed workers found increased risks of self-reported symptoms, but failed to find associations with cognitive performance (20, 45,

297). This has led to suggestions that contemporary low-level solvent exposures may only be associated with low-grade nervous system dysfunction (20, 21, 297, 309). However, the results of the studies described in this thesis suggest that this may not be the case (see above). It has been suggested that methodological issues in previous studies, such as small sample sizes, insufficiently sensitive neuropsychological tests (29) and insufficient control for key confounders may explain why some studies fail to find clearer associations with health effects (16).

An alternative explanation for the findings of previous studies (which showed associations with symptoms, but not with cognitive performance) could be that they were often conducted in larger enterprises in Europe, where workplace hygiene and exposure control practices may have been more effectively managed than in the small-to-medium sized enterprises (SMEs) typical of this industry in New Zealand (45, 46) (and other countries outside of Europe (148)). Exposure levels measured in these studies were somewhat higher (Table 2.6) suggesting that this may not be a likely explanation. However, methods to measure exposures were different and levels are therefore not directly comparable, and exposures in New Zealand workshops were likely considerably higher in the past (at the time that these other studies were conducted). Another possibility is an overreliance on clinical definitions of solvent-induced neurotoxicity, which may have resulted in some studies failing to recognise the importance of relatively small changes in average performance at a group level (35, 70). Even if effects are sub-clinical, they may still have the potential to impact considerably on a person's quality of life and general wellbeing, particularly where effects include mood lability and memory and concentration deficits (70), which are

amongst those most consistently reported in epidemiological studies of solvent-exposed workers (16).

As discussed in chapter 2, a dose-response relationship is often considered a requirement for causal inference (310), but dose-response associations have generally been the least consistent finding in studies of solvent exposed workers (16, 70), including the studies described in this thesis (chapter 4, table 4.4, chapter 5, table 5.4). This may have contributed to the suggestion that long-term, low-level exposures are unlikely to be associated with irreversible neurobehavioural effects (20, 297). Alternatively, as discussed in chapters 3 and 4, a widely accepted theory to explain the lack of clear dose-response trends in studies of solvent-exposed workers may be the presence of a healthy worker survivor effect (16). This results from workers who develop symptoms leaving the industry, and those remaining potentially being less susceptible to the effects of solvents, or having a higher cognitive 'reserve' (71, 313). The findings of the studies in this thesis are consistent with this theory, as those who had worked in the collision repair industry for a medium duration (average 14.8 years) reported a greater number of symptoms overall compared to those who had been employed for a shorter (5 years) or longer (20 years) time (chapter 4). There was also some evidence of better cognitive performance in those who had been in the industry longer, although trends were less consistent, most likely due to the small sample size (chapter 5). If true, exposures in the collision repair industry may be sufficient to cause some workers to develop symptoms severe enough to warrant leaving the industry. If also true for previous studies (20, 297), then this may be a more plausible explanation for the lack of clear dose-response trends observed in workers with long-term, low-

level solvent exposures, rather than workers being at risk of 'only' mild neurobehavioural symptoms.

Despite not being directly involved in the spray painting process, and their current airborne solvent exposures being around 1/3rd of those in spray painters, panel beaters reported more symptoms of neurotoxicity and scored lower on most neuropsychological tests than spray painters (chapter 4, table 4.3 and chapter 5, table 5.2). As discussed in chapter 5, previous studies have reported an increased risk of cognitive deficits in panel beaters, but only in those who had previously worked as a spray painter (45). For the studies described in this thesis, only seven panel beaters from the larger survey and one who completed the cognitive testing reported having worked as a spray painter, and they were recoded as spray painters for all analyses. The effects observed are therefore unlikely to be due to the misclassification of panel beaters. The reasons why panel beaters are more likely to report symptoms and perform more poorly in neuropsychological tests are largely unclear, but may be in part due to exposures that were unaccounted for or exposures which were not measured.

Since the completion of the studies described in this thesis, a number of VEM observations have been conducted during panel beating operations. These showed peaks in solvent exposure of between 20 and 200ppm during the mixing and application of bodywork fillers, the main solvent constituent of which is styrene (20% w/w) (144). The average airborne exposure measurements also showed styrene exposure was highest for the panel beaters, although levels were still well below

workplace exposure standards (chapter 3, figure 3.1). In addition, panel beaters were regularly observed using aerosol degreasing sprays containing chlorinated solvents (perchloroethylene, tetrachloroethylene and methylene chloride), which have been associated with symptoms of neurotoxicity, and are amongst those considered most neurotoxic (176, 368, 369). However, air samples were not analysed for chlorinated solvents, and no VEM observations included workers using these sprays. Variations in the composition, and therefore the relative toxicity of the solvent mixture used for different spray painting and panel beating tasks could have also contributed to the associations observed. However, an assessment of whether the relative composition of the airborne samples varied by job title showed no clear trends (data not shown), other than higher styrene levels for panel beaters. This may reflect the relatively uniform composition of many of the most common solvent mixes and solvent-based products (thinners, degreasing and cleaning solvents, etc.) that both spray painters and panel beaters were observed using. The same may not be true of dermal exposures, and other exposures that could not be measured (e.g. chlorinated solvents), but this could not be assessed as part of this thesis.

Unfortunately, data on PPE use and workplace hygiene practices amongst the panel beaters were not collected, as when the study/sub-studies were designed, panel beaters were only intended to be used as an internal comparison group (a high prevalence of symptoms of neurotoxicity/poorer cognitive performance in panel beaters had not been reported previously (45), and so was not an *a priori* hypothesis of the study). However, on-site observations suggested PPE-use amongst panel beaters was very limited, which may also contribute to the effects observed. This was

confirmed in the latest VEM observations (see above), which showed respirators (other than nuisance dust masks) and gloves were rarely, if ever, worn during panel beating work.

Panel beaters may also have been exposed to other neurotoxins, namely lead (302, 348, 353). Although used historically in bodywork repair and replacement (the primary job-task of panel beaters), lead was largely replaced by resin-based fillers in the 1970's. It is currently used occasionally for classic vehicle restorations, however, none of the shops involved reported using it. Frequent use of vibrating tools by panel beaters may have contributed to at least some of the observed increased risks (348, 370); however, these would account only for the lower performance in motor speed/manual dexterity and not for other test results for which scores were also lower. The stronger effects in panel beaters may also be due to other exposures that were unaccounted for, such as isocyanates (limited evidence for neurotoxicity (371)) and acrylates (137, 372, 373); however, spray painters are also exposed to these compounds, and almost certainly at higher levels, so this is unlikely to explain the stronger effects in panel beaters. Although generally found in considerably lower concentrations than solvents (144), these substances are of concern, but largely for other reasons than their potential neurotoxicity (e.g. the respiratory effects of isocyanates (15)). They should be a focus of future research, along with the PPE use and workplace hygiene practices of panel beaters, but these were outside the scope of this thesis.

Regardless of the analytical approaches used in the studies described in this thesis, consistently increased risks of neurobehavioural symptoms and lower cognitive performance were observed in collision repair workers. The strength and consistency of the findings within and between the studies suggests that although residual confounding and biases may still be present, they are unlikely to fully explain the associations observed.

7.2.4 Exposure controls

Consistent use of respirators and gloves by spray painters whilst performing the three core tasks of mixing paint, degreasing/cleaning equipment and spray painting was strongly associated with a reduced risk of symptoms, with the strongest associations seen for frequent glove use (chapter 6, table 6.3). For total symptoms (≥5, ≥10 and ≥15 symptoms), a reduction in risk of up 90% was shown when both types of PPE were worn for all three core tasks, and a significant dose-response trend was also observed ($p<0.01$, table 6.4). Several studies have shown that PPE-use is associated with a reduced body burden of solvents (30, 32-34, 36) and performance on some neuropsychological tests (29), but to the author's knowledge no other studies have shown a direct association with neurobehavioural symptoms. As discussed above, the observation that glove-use was most protective suggests the importance of dermal exposures, as does the strong positive dose-response trend of increasing number of symptoms with greater self-reported skin exposure during spray painting (supplementary table 6.7). PPE was generally used less frequently during non-spraying

tasks, i.e. mixing paint and degreasing/cleaning equipment, whereas these tasks were associated with the highest average and peak airborne exposure levels.

A number of workplace hygiene practices and behaviours likely to result in elevated exposures were also associated with an increased risk of symptoms (table 6.3). These practices, particularly those likely to result in dermal exposure (e.g. spray painting with hands and arms exposed and washing hands in solvents, table 6.2) were relatively common amongst workers. This indicates a lack of hazard awareness and understanding of the potential for solvents to be absorbed dermally, and may in part explain the strong protective effect of consistent glove use.

Although causality cannot be assumed on the basis of cross-sectional data, these findings have considerable importance for the collision repair industry, as encouragement of improved PPE use and workplace hygiene practices would be a simple, low-cost intervention which can be implemented quickly, and which has the potential to strongly reduce morbidity, at least in the short-term until higher level controls can be put in place.

7.3 Strengths and limitations

The methodological approach and the specific methods used to assess solvent exposures and neurobehavioural symptoms in this study have considerable strengths, but also, as noted throughout, some weaknesses. These are discussed below.

Strengths

- An extensive assessment of airborne solvent exposures was conducted, which has not previously been undertaken in the collision repair industry in New Zealand. This allowed for a detailed investigation of exposure determinants. These data provide, for the first time in New Zealand, an initial evidence-base for the development of exposure interventions targeting workplace factors, practices and behaviours that are most strongly associated with airborne exposures.

- Compared to previous studies of spray painters and other solvent-exposed workers, the sample size for the questionnaire survey was relatively large (370 collision repair workers, 211 reference workers), resulting in the study having adequate statistical power to detect meaningful associations.

- In addition to spray painters, panel beaters and office workers were also included in the exposure monitoring and questionnaire survey. This differs from most previous studies in the collision repair industry, which have predominantly focused on spray painters (19, 69, 122, 162, 336). As a result, elevated risks were identified for job roles not traditionally associated with symptoms of neurotoxicity (e.g. the

higher risk of symptoms and poorer cognitive performance observed amongst panel beaters).

- The combined approach of subjective and objective assessments of neurotoxicity has rarely been applied, and allowed for informal comparisons to be made between the findings of the EUROQUEST questionnaire (232) and the adapted RBANS battery (260). The fact that results were highly comparable between measures suggests the findings are robust, and that a relatively brief assessment of symptoms and cognitive performance may be capable of detecting effects associated with long-term, low-level airborne solvent exposures.

- Comprehensive data on potential confounders was collected, including age, level of education, premorbid intelligence, alcohol and recreational/prescription drug use, personality traits (anxiety, depression, stress, etc.), general health (e.g. diabetes, cardiovascular disease etc.), brain and nervous system disorders, trauma and diseases (e.g. pre-existing neurodegenerative diseases, head injuries and concussion, meningitis), sleep and fatigue (e.g. hours of sleep in the past 2 days) and various testing-related parameters (e.g. time of day and day of week), all of which were adjusted for in the analyses. The studies described in this thesis were also highly comprehensive; in addition to external comparisons of symptoms and cognitive performance between solvent-exposed collision repair workers and an unexposed reference group (chapters 4 and 5), internal comparisons between different groups of collision repair workers (e.g. based on consistency of PPE use and good/poor workplace hygiene practices) were conducted (chapter 6). Findings were consistent across the different studies, independent of the analytical

approach used, suggesting the effects observed are unlikely to be due to chance or confounding.

- As the first of their kind to be conducted in New Zealand, these studies have facilitated the development of expertise in evaluating occupational solvent exposures and associated neurotoxicity in this setting, and will permit further studies on these, and other neurotoxic agents used in different occupational settings.

Limitations

- Although comprehensive, the exposure monitoring was limited to an assessment of airborne solvent levels, and did not include dermal or biological monitoring. As a result, it was not possible to estimate the relative contribution of different exposure pathways to solvent body burden. An assessment of dermal exposures would have been of particular interest, given the strong protective effect of glove use observed (chapter 6). Nonetheless, the monitoring provided estimates of average full-shift airborne exposures in contemporary collision repair workshops, data which has not previously been available. Also, the fact that evidence of neurotoxicity was observed at airborne exposure levels well below workplace exposure standards suggests that these standards may need to be revised, and that dermal and peak exposures (the potential importance of which has been discussed throughout this thesis) should ideally be accounted for when performing risk assessments.

- As the studies described in this thesis were cross-sectional, assessment of exposure levels was limited to one point in time. As a result, it was not possible to assess the effects of historical exposures on current symptoms, limiting the possibility of establishing causation. Nonetheless, an excess of symptoms was observed in those who had been employed in the industry for an average of only 5 years, suggesting that effects are unlikely to be solely attributable to historic exposures. Also, no baseline symptom and cognitive performance data from before employment in the collision repair industry was available, again making it difficult to establish causality. To partially mitigate this, collision repair workers were compared to unexposed reference workers who were, for the most part, comparable with regards to age, educational status and premorbid intelligence, alcohol consumption and personality profile (chapter 4, table 4.1, chapter 5, table 5.1), suggesting the reference group selected was appropriate, and the results are robust. There were some differences in demographic characteristics between groups (particularly ethnicity, smoking status), but these, along with other potential confounders, were adjusted for in the analyses, and this did not appreciably affect the results (chapter 4, tables 4.3-4.5, chapter 5, tables 5.2-5.4, supplementary tables, chapters 4 and 5). In addition, the fact that consistent PPE use and good workplace hygiene were strongly protective against symptoms (chapter 6, table 6.3 and 6.4), and the symptom domains affected were consistent between studies (e.g. neurological, mood, memory and concentration, chapter 4, tables 4.3-4.5, chapter 5, tables 5.2-

5.4, chapter 6, tables 6.3 and 6.4), provides further evidence that current exposures may contribute to the effects observed.

- It is possible that the collision repair workshops and workers that took part in the study were not representative of the industry as a whole. Although workshops were approached at random within the regions targeted (Primarily Auckland and Wellington, but also the central North Island, including some rural areas), some, particularly less visible workshops, may have been missed. It can be speculated that these may be smaller and less productive, which as suggested by others, (46, 143) may be associated with poorer management of workplace hazards. If so, exposures and the risk of solvent-induced neurotoxicity may be higher in these shops (45, 46). Therefore, not including these workers in the sample may have limited the interpretability across all workshops in New Zealand, including those with potentially higher exposures.

- It is also possible that the workers who agreed to take part in the study were not representative of the source population. As discussed in chapter 4, the response rate in collision repair and reference workers for the questionnaire study was 69% and 64% respectively, which is relatively high and suggests that non-response bias is unlikely to be a major concern. In addition, a non-respondent questionnaire was completed by fifty-three collision repair workers who declined to participate, and no appreciable differences were found between those who participated and those who declined (in general population characteristics and several key symptoms of neurotoxicity, chapter 5, table 5.1).

- Some reference workers reported some occupational exposure to solvents. However, analyses excluding these workers did not affect the results, suggesting that this too is not a major issue (chapter 4, supplementary material, table 4.6). In fact, if some reference workers were affected by solvents, it would result in an underestimation of the true effect. The same would be true if there was a bias, for any reason, towards selection of reference workers with neurobehavioural or cognitive problems (313).

- There is some evidence that women may be more susceptible to the neuroinflammatory/ neurotoxic effects of effects of solvents (374-377), and for this reason, and that there were only two women in the collision repair sample, they were excluded from the analyses of self-reported symptom prevalence (chapter 4). They were included in the analysis of neuropsychological performance (chapter 5), but primarily in order to maximise sample size and maintain statistical power. Sensitivity analyses including/excluding them had no effect on the results, but unfortunately there were too few to assess the impact of sex on symptom prevalence, cognitive performance, or any other outcomes of interest (e.g. workplace behaviours). The bias towards selection of male participants in epidemiological studies of workers exposed to hazardous agents, especially in industrial settings, is well recognised and needs to be addressed (374). However, based on the number of female collision repair tradesmen in the sample (2 out of 370), attaining a sufficiently large sample to allow for meaningful analyses was not possible for this thesis, and may not be possible in the New Zealand setting

(attaining a sample of 50 women would have theoretically required a total sample size of 9,250 workers).

- Data derived from questionnaires are limited by their inherent subjectivity. This includes issues with variance between workers in the interpretation of questions, or willingness to report certain symptoms or workplace practices and behaviours (224). However, this would only be a problem for the studies in this thesis if the exposed and un-exposed groups differentially under or over-reported symptoms, or behaviours associated with exposure. The EUROQUEST questionnaire includes an assessment of general wellbeing, anxiety and personality traits, designed to identify those who are more likely to under or over report symptoms (232, 233). All relevant analyses were adjusted for these measures. It is therefore unlikely that under or over-reporting had a major effect on the results. Even if present, under-reporting of poor, or over-reporting of good PPE-use and workplace hygiene practices between different groups of collision repair workers (e.g. through a desire to appear compliant with health and safety regulations (224), chapter 6) would likely result in an underestimation of the true effect. Also, although a number of questions on self-reported use of solvents (e.g. "*how often do you use solvents or solvent-based products?"* appendix 1) were included in the questionnaire, there was insufficient diversity in the responses (e.g. almost all spray painters reported 'often' or 'very often' using solvents) to allow for analyses of their association with symptoms/cognitive performance, or to use them for validation of other self-reported data on exposure-related behaviours/practices. Their limitations aside, questionnaires provide an important starting point for the identification of

populations at risk of solvent-induced neurotoxicity (7). The fact that the results of the EUROQUEST questionnaire were consistent with those of the cognitive tests (chapters 4 and 5) suggests this may be true for the EUROQUEST.

- Another important limitation of the study design was its restricted ability to differentiate between acute (i.e. transient) effects and chronic neurobehavioural effects (186, 187, 286). However, as described in chapter 5, no differences in cognitive performance were observed between workers tested at the start and at the end of the week, suggesting the effects observed were unlikely to be entirely due to acute exposures. Repeat cross-shift and cross-week assessments would have allowed for more accurate differentiation between acute and chronic effects, but this was not deemed practical as it would have added considerably to the time involved for the participants.

- The neuropsychological test battery was only administered to a relatively small number of workers (collision repair, n=47, comparison workers, n=51). As a result, the confidence intervals for some effect estimates were relatively large (chapter 5, table 5.3), and numbers were insufficient to stratify workers into subgroups for some additional analyses (e.g. by employment duration). However, the sample was randomly selected from, and representative of, the larger study population (chapter 5, supplementary table 5.19), and the findings were comparable to those of the EUROQUEST questionnaire, and other studies of collision repair workers (17, 45). Also, despite wide confidence intervals for some of the cognitive performance effect estimates, a consistent pattern was observed regardless of the percentile cut-point used (e.g. 10^{th} and 20^{th} percentile, table 5.3) suggesting the conclusion

that some workers may be at risk of more severe effects is valid. Furthermore, according to power calculations conducted by Hooisma, Hänninen (312), approximately 50 participants per group is sufficient to detect meaningful differences for individual tests which are comparable to those used in the study described in this thesis.

- The ability of the neuropsychological test battery to detect cognitive effects was also limited by the time available for testing, as only a brief test battery could be administered. Objective tests are seen as the gold standard for assessing neurobehavioural effects (6-8, 16). However, they can lack sensitivity and specificity, particularly when relatively crude batteries are used to assess subtle neurobehavioural impairments resulting from relatively low-level exposures(297) (as may be typical of spray painting (16, 17, 45)). In addition, solvents may affect a wide variety of neurobehavioural functions, and there are many means of testing these (172, 190, 205, 297). Nonetheless, the tests applied covered functional domains previously shown to be affected in solvent exposed workers (16) and findings were consistent with large international studies, which employed more comprehensive test batteries (69, 308).

- Prevalence odds ratios (PORs) were used for the analyses of symptoms of neurotoxicity and some cognitive performance outcomes, which some suggest are inferior to other methods for analysing cross-sectional (prevalence) data (e.g. prevalence ratios (PR), generalised estimating equations (GEE) (378, 379). For example (as discussed by Pearce (378)), where a disease is common, the PR and POR may be quite different; however, this does not indicate which is the better or

more ‘valid’ measure to use, which instead depends upon the sample population, type of exposure and the nature of the disease (378). The tendency of PORs to over-estimate the size of an association may also be a concern (71) (378). However, methods such as generalised estimating equations (GEEs) may underestimate the effect, especially where sample sizes are smaller (as was the case for some of the analyses in this thesis, e.g. chapter 5) (71, 378). It could be argued that adopting a conservative approach is more appropriate, but the strength and consistency of the findings within and between the studies described in this thesis suggests that even if the PORs presented are overestimates (although unlikely to be greatly so), it is unlikely that using a different analytical method would have yielded significantly different results, or affected the conclusions drawn from them.

7.4 Recommendations and future research

The findings of this thesis indicate the need for solvent exposures in the collision repair industry to be more effectively controlled, and for neurobehavioural health to be routinely monitored. They also provide important information on the nature of exposures, workplace practices and behaviours in contemporary collision repair workshops, all of which will be useful in the development of interventions to reduce exposures and associated morbidity. However, there are still several important knowledge gaps which should ideally be filled in order to maximise the effectiveness and acceptability (from industry) of any intervention programme developed. These include:

- The role of dermal and peak solvent exposures in the development of neurobehavioural effects;
- The impact of historical solvent exposures on current symptoms and neurobehavioural performance;
- The chronicity/potential reversibility of effects associated with solvent exposures in this industry;
- The specific nature of solvent exposures in bystanders to the spray painting process, and the reasons behind the elevated risks observed in panel beaters;
- The impact on solvent exposure of determinants not assessed as part of this research (e.g. economic and workload factors, knowledge of and attitudes towards health and safety and hazardous exposures).

Potential directions for future research to address these knowledge gaps, and general recommendations based on the findings described in this thesis are presented in the next sections.

Improved peak, dermal and biological exposure monitoring

As discussed in section 7.4, most exposure data from studies in the collision repair industry are limited to full-shift average airborne exposure levels. These do not cover dermal exposure routes or peak exposures, which would give a more detailed picture of specific exposure determinants. This may, at least in part, explain why the effectiveness of exposure control measures developed on the basis of full-shift average levels have been unsatisfactory and variable in previous studies (380, 381). Additional assessment of dermal and peak exposures would help to ensure any interventions developed are optimally effective for the conditions and tasks that contribute most to solvent body burden. Also, it will allow for more robust dose-response associations to be established. However, in order to do this, there is a need to develop more standardised methodologies for assessment of solvent exposures by these routes and of internal dose.

As discussed in chapter 2, dermal exposure assessment is difficult and complex (24, 26), but can be achieved with direct measurement of dermal deposition, or indirectly through a combination of traditional airborne exposure monitoring and biological monitoring (25, 30, 75, 382). The methodologies for assessing dermal exposure using sorbent patches, whole body suits and fluorescence techniques each have their limitations (75, 314, 382), but have been shown to correlate relatively well with

biological measurements (26, 30, 74, 382-384), and could be applied to the assessment of dermal solvent exposures in the collision repair industry.

Future studies of the determinants of both airborne and dermal solvent exposures in the collision repair industry (and others) could also include a more in-depth assessment of the relative composition/toxicity of solvent exposures associated with different job roles and tasks; this may help to clarify the specific solvent exposures involved, and help to develop interventions which are targeted at controlling exposures with the greatest potential neurotoxicity. However, any intervention that results in a reduction in exposure to any solvent, all of which are potentially neurotoxic to some degree, is likely to result in an overall reduction in risk for workers (123).

Chapter 3 showed that VEM is an appropriate tool for the assessment of peak airborne solvent exposures (14, 78). As with dermal techniques, VEM has its limitations (described in chapters 2 and 3), but is unique in its ability to identify specific tasks and actions associated with peak exposures, and evaluate how these relationships change on a real-time basis. Also, the recorded observations can be used as an educational tool to engage with the industry and workers themselves, and to evaluate the effectiveness of interventions to reduce airborne exposures (currently VEM cannot be used for dermal exposures in observational studies) (78, 79, 84).

Wider-reaching strategy for population sampling

Previous epidemiological studies in the collision repair industry have often used a 'worst-case' sampling strategy (385), focusing exposure and health outcome sampling on the spray painters as the perceived "maximum risk employees" (17-19, 21). The study described in this thesis showed that panel beaters (a job role not traditionally associated with a high risk of solvent exposures and neurotoxicity) had the greatest risk of neurobehavioural effects, something which would not have been detected had a subjective worst-case sampling strategy been used (385). Thus, future epidemiological studies in this industry should ideally include a random selection of workers from all job roles (385).

Longitudinal studies of exposures and health over time

Ideally, large, in-depth longitudinal studies would be undertaken to address the knowledge gaps outlined above, including baseline assessments (i.e. upon commencement of employment in the industry) of symptoms and cognitive performance, and ongoing assessments of health, exposures and workplace conditions over a period of years. This would provide information on the evolution of exposures and health outcomes over time, allowing for investigation of the causal relationships involved, and for the development and implementation of intervention strategies to reduce exposures (and ill-health).

As discussed throughout this thesis, the lack of a clear dose-response trend between solvent exposures and symptoms/cognitive performance in cross-sectional studies may be explained by the presence of a healthy worker survivor bias (16, 70, 311, 313).

This type of bias would be of less concern in a longitudinal study, as workers can be followed until they leave the industry. For this reason, a longitudinal study on newly hired workers would be ideal. Longitudinal studies would also be less prone to other potential sources of bias and confounding (e.g. arising from differences in pre-morbid intelligence and cognitive reserve, workplace behaviours, and key confounders such as age, alcohol and drug use, etc. between collision repair workers and an external reference group in cross sectional studies). However, the issue with longitudinal studies involving repeat measures over many years in the same workers is that they are usually difficult and expensive to conduct (71).

Interventions to reduce solvent exposures

As discussed above, a more in-depth and comprehensive understanding of causal exposures in the collision repair industry and how they can be controlled would maximise the effectiveness of any interventions/actions to reduce solvent exposures and associated morbidity. However, the studies described in this thesis provide sufficient evidence to warrant at least some immediate action, and delaying this until all research gaps have been filled may be unjustified. One approach, which would allow for both immediate action, and facilitate the development and evaluation of an intervention programme to reduce exposures, would be to conduct a randomised controlled trial (RCT) as described below.

Based on the findings of the study described in this thesis, a programme grant has been secured from the Health Research Council of New Zealand (HRC) to develop,

implement and evaluate a programme of interventions in the collision repair industry (and two other industries) using a RCT design. The intervention study involves an in-depth assessment of the sources and determinants of solvent exposure in the collision repair industry, including an extensive assessment of dermal and peak exposures. Based on these results and those presented in chapter 3 and 4, specific interventions will be developed, which are focused on the conditions and workplace practices that contribute most to exposure. Then, the effectiveness of the intervention package will be assessed, primarily by measuring solvent levels pre and post-intervention, but also changes in various indicators of neurobehavioural health (particularly neurobehavioural symptoms and cognitive performance). Urine samples will be collected to assess solvent body burden, and to assess the relative contribution of airborne and dermal exposures to body burden. The findings will be used to develop educational and training materials for employers and workers, and provide information of benefit to health and safety practitioners and policy makers.

Routine monitoring of health, exposures and workplace conditions

Routine exposure and health monitoring of collision repair workers should ideally be conducted, including surveys of workplace conditions, which would allow for changes in exposures and health outcomes to be monitored over time. This would be useful for the ongoing evaluation of workplace health and safety programmes and legislation, both in terms of whether they have been adopted and adhered to, and if they have resulted in reduced exposures and morbidity. This would also allow for improvements to the interventions to be made based on empirical data, in order to maximise their

ongoing impact and uptake. It is preferable that country-specific data are collected, as health and safety practices and the structure of the sector (e.g. independently owned SMEs vs. large franchises) may differ between countries.

As discussed above, exposure monitoring should not be limited to full-shift average airborne levels, but should ideally include at least some biological monitoring (e.g. urine analyses), dermal exposure assessment, and some task-specific VEM to measure peak exposures. Workforce surveys could include an assessment of workplace practices, conditions and behaviours, in order to identify emerging risk factors (e.g. new products or work processes which may result in elevated exposures, or exposures to new hazardous agents) and monitor trends in these practices/behaviours. Furthermore, structured walk-through hygiene surveys should ideally be conducted, preferably at the same time as exposure monitoring, to help identify potential exposure determinants and supplement the surveys of workplace conditions.

Hearing, lung function, and general health testing is conducted routinely by occupational health nurses in a range of industries in New Zealand, including the collision repair industry; however, assessment of neurotoxicity in solvent-exposed workers is uncommon and, if conducted, is limited to a very brief symptom questionnaire. This study has shown that the EUROQUEST questionnaire and a relatively brief objective test battery could both potentially be used for initial screening of solvent-exposed workers, both in New Zealand and globally, and possibly other workers who are exposed to neurotoxic agents (e.g. heavy metals, pesticides) (231, 386).

7.5 General conclusions

Results from the studies described in this thesis suggest that solvent-exposed collision repair workers continue to have a significantly increased risk of both symptoms of neurotoxicity and cognitive deficits, despite airborne exposure levels well below current occupational exposure limits. Effects in some workers may be relatively severe, as suggested by the increased risk of more significant dysfunction. Panel beaters may have the greatest risk of neurobehavioural effects, highlighting the need for exposure and health monitoring of workers performing all work-tasks, not just those traditionally associated with 'high' exposures.

The fact that Neurobehavioural effects were observed at average airborne solvent levels below workplace exposure standards suggests current standards need to be revised, and/or that dermal and peak exposures may be particularly important. Non-spray painting tasks should be a key target for intervention strategies to reduce exposures and associated morbidity, as exposure levels were highest, and PPE-use less frequent, during these tasks. Also, consistent PPE use and good workplace hygiene practices were strongly protective against symptoms and should be promoted, at least until higher-level controls can be developed and/or more widely implemented.

Given the large population potentially at risk, there is an urgent need for more effective exposure controls, potentially including a reduction of current exposure standards, improvements to the design and use of engineering and administrative control measures, and programmes to encourage and facilitate PPE use and good workplace hygiene practices. Some of these controls/interventions could be

implemented almost immediately; however, a more in-depth and comprehensive understanding of causal exposures and their determinants in this industry would help to maximise the effectiveness, practicality and acceptability of any intervention package developed.

In summary, contemporary collision repair workers are at risk of solvent-induced neurotoxicity, despite airborne exposures being below 'safe' levels, and implementing even relatively simple interventions to reduce airborne and dermal exposures has the potential to substantially reduce neurobehavioural morbidity in this population.

8 References

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9 Appendices

Appendix 1: Occupational exposures and health status Questionnaire

Appendix 2: Flow diagram of study participants included in the results chapters of this thesis (3, 4, 5 and 6).

Appendix 3: Statements of contributions to Doctoral thesis containing publications

Appendix 4: Letter confirming ethics approval from Multi-regional Ethics Committee

SURVEY OF OCCUPATIONAL EXPOSURE AND HEALTH STATUS

SUBJECT ID NUMBER: | S | E | | | | |

Employer: _____

Workplace: _____

Department: _____

Number of workers employed: _____

Name: _____

Today's date: ____/____/20____ Day
Month Year

Phone number: ( ) _____

E-mail: _____

Date of birth: ____ / ____ / 20____
Day Month Year

Sex:

☐ Male

☐ Female

What is your height? _____ cm / ft

What is your current weight? _____ kg / stone / lbs

What is your ethnicity? *(more than one option possible)*

- ☐ New Zealand European/Pakeha
- ☐ Maori
- ☐ Pacific *please specify:* _____
- ☐ Other *please specify:* _____

QUESTIONS ABOUT YOUR WORK AND WORK HISTORY

YOUR CURRENT WORK

What is your job title?

_____

Please describe your specific job in detail:

Interviewer: Try to go through each point e.g: what do you do, how do you do it etc. If no response: ask respondent to describe a typical working day.

What do you do?

How do you do it?

What materials do you use?

What tools or machinery do you use?

What type of process is it?

_____

_____

_____

_____

_____

_____

How many years have you worked in your current job?

☐ Years

How many hours per week do you work in this job on average?

☐ Hours/week

What is the main activity of the company you work for? For example, what is produced, what service is provided?

_____

What department do you work in?

_____

☐ Not applicable

Please tell me all the jobs you have held in order from the first job you ever held to the most recent job ever held.

Interviewer:

Please include all jobs that lasted at least 6 months in total. Please start with the first job after leaving school and end with the most recent.

The list should be without gaps, meaning that also e.g. unemployed periods or periods taking care of children should be reported here.

The last year in the work history should be the year of interview.

Job Number	Who was your **employer**?	Over what **period** did you work for this employer?	What was the **main activity** of the company or organisation you worked for? *(Example: sheep farming, selling shoes, making clothes)*	What **department** did you work in, and what was your **job title**?
1.	Name …… Location …….	From: ……../……. (mm/yy) To: ……../……. (mm/yy)		Department: …… Job title: ……
2.	Name …… Location …….	From: ……../……. (mm/yy) To: ……../……. (mm/yy)		Department: …… Job title: ……
3.	Name …… Location …….	From: ……../……. (mm/yy) To: ……../……. (mm/yy)		Department: …… Job title: ……

GENERAL HEALTH QUESTIONS

1. Have you **ever** had any of the following medical conditions?

High blood pressure?

☐ Yes → Year of diagnosis: _____

☐ No

☐ Don't know

Heart attack?

☐ Yes → Year: _____

☐ No

☐ Don't know

Stroke?

☐ Yes → Year: _____

☐ No

☐ Don't know

Diabetes?

☐ Yes → Year of diagnosis: _____

☐ No

☐ Don't know

2. Have you **ever** had any of the following injuries?

Head injury?

☐ Yes → Year of diagnosis: _____

☐ No

☐ Don't know

Concussion?

☐ Yes → Year of diagnosis: _____

☐ No

☐ Don't know

3. Have you **ever** had An itchy rash that has been coming and going for at least 6 months and at some time has affected skin creases?

(By skin creases we mean folds of elbows, behind the knees, fronts of ankles, under buttocks, around the neck, ears or eyes)

☐ Yes →

☐ No

☐ Don't know

4. Have you ever had hand eczema?

☐ Yes

☐ No

5. Have you ever eczema on your wrists or forearms?

☐ Yes

☐ No → **IF YOU ALSO ANSWERED NO TO QUESTION 11, GO TO QUESTION 14**

6. How often have you had eczema on your hands, wrists and forearms?

(one answer in each column if applicable)	**Hand eczema**	**Wrist/forearm eczema**
Only once and for less than two weeks	☐	☐
Only once but for two weeks or more	☐	☐
More than once	☐	☐
Nearly all the time	☐	☐

7. Have you **ever** had any of the following nervous system problems/diseases?

Muscular tremor (shaking of the muscles)?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Sensation of pins and needles?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Epilepsy, Parkinson's, motor neuron disease (including amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease), multiple sclerosis (MS)?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Alzheimers's?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Other dementia?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Question 14 Continued

Coma?

☐ Yes → When? _____

☐ No

☐ Don't know

Chronic fatigue?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

Other Neurological Disease (eg meningitis, encephalitis)?

☐ Yes → When was this first observed or diagnosed?
_____

☐ No

☐ Don't know

8. Do you **currently** have any of the following general symptoms?

A. ☐ Do you have short memory?

B. ☐ Do you often have to make notes about what you have to remember?

C. ☐ Do you often have to go back and check things that you have done such as turned off the stove, locked the door, etc.?

D. ☐ Do you generally find it hard to get the meaning from reading newspapers and books?

E. ☐ Do you often have problems concentrating?

F. ☐ Do you often feel depressed without any particular reason?

G. ☐ Are you abnormally tired?

H. ☐ Are you less interested in sex than you think is normal?

I. ☐ Do you have palpitations of the heart even when you don't exert yourself?

J. ☐ Do you sometimes feel an oppression in your chest?

K. ☐ Do you sweat without any particular reason?

L. ☐ Do you have a headache at least once a week?

M. ☐ Do you often have painful tingling in some parts of your body?

N. ☐ Do you have problems buttoning and unbuttoning?

O. ☐ Are you having trouble sleeping?

P. ☐ Do you find your mood changes frequently without cause?

Q. ☐ Do you find that noise bothers you more than in the past?

9. Have you taken prescription drugs (i.e. prescribed by your doctor) in **the past 12 months**?

☐ Yes, I have taken prescription drugs for: _____ *Name of drug:* _____

☐ No

10. Have you ever been diagnosed as having a learning disability or attention deficit disorder by a doctor/other health professional?

☐ Yes

☐ No

☐ Don't know

11. How many hours sleep do you usually get (counting naps as well)? _____ *hours*

12. How often do you get enough sleep?

- ☐ Never
- ☐ Rarely
- ☐ Often
- ☐ Always

13. How often do you wake up feeling refreshed?

- ☐ Never
- ☐ Rarely
- ☐ Often
- ☐ Always

QUESTIONS ABOUT NEUROLOGICAL SYMPTOMS

Please respond to each of the following questions by indicating how often in recent **months** you have experienced a particular symptom.

For each question there are four possible answers:

Seldom or Never Sometimes Often Very often

Eg: if you have not experienced this symptom in recent months, **tick** the alternative "seldom or never".

If you have experienced this symptom very often in recent months, **tick** "very often".

If you are uncertain how often you have experienced a certain complaint, the answer that first comes into your mind is usually the best.

Tick only **one** of the four options.

When symptoms occur sometimes, often, or very often we would also like to know for how many years you have experienced these symptoms.

14. How often have you during recent months experienced any of the following and for how many years you have had these symptoms?

	Seldom or never	Sometimes	Often	Very often	How many years?
Dropping things unintentionally					
Weakness of your arms and feet					
Decreased sensation in arms and legs					
Numbness or heaviness in your arms or legs					
Tingling in your arms or legs					
Problems with balance					
Changes in sense of smell or taste					
Decreased sensation on your face					
Difficulties controlling your hand movements (i.e. how often do you notice your hands are more clumsy?)					
Slowness in carrying out your daily activities					
Trembling of hands					
Headache					
Sweating for no obvious reason					
Nausea (i.e. do you feel sick in your stomach?)					
Stomach pains					
Dizziness					

	Seldom or never	Sometimes	Often	Very often	How many years?
Shortness of breath without physical exertion					
Heart fluttering (palpitations)					
Ringing in your ears (tinnitus)					
Feeling of general exhaustion					
Loss of sexual interest					
Lowered alcohol tolerance (i.e. have you noticed it takes less drinks than before to get drunk?)					
Diarrhoea					
Constipation					
Loss of appetite					
Feeling of a tight band around your head					
Difficulty getting started at work					
Feeling irritable					
Feeling depressed					
Feeling impatient					
Being upset by trivial things (i.e. do you find little things upset you?)					
Feeling restless					
Rapid changes in mood					
Feeling of detachment (i.e. do you feel out of touch with your surroundings?)					
Lack of drive (i.e. lack of energy, enthusiasm)					
Lack of interest in social activities					
Difficulty in controlling anger					
Forgetfulness					
Having to write notes to remember things					
Forgetting what you were about to say or do					
Difficulty in concentrating					
Daydreaming					
Feeling confused when you try to concentrate					
Difficulty remembering names and dates					
Absent-mindedness					
Difficulty remembering what you have read or seen on TV					

	Seldom or never	Sometimes	Often	Very often	How many years?
Other people complaining about your memory					
Falling asleep when not in bed					
Unusual tiredness in the evening					
Sleepiness					

Note – How often in **recent months**	Seldom or never	Sometimes	Often	Very often	How many years?
Feeling tired when you wake up					
Lack of energy					
General weariness (or tiredness)					
Needing more sleep than you used to					
Difficulty falling asleep					
Broken sleep					
Waking up too early					
Nightmares					
Snoring someone else has complained about					

15. How often **during recent months** have you experienced any of the following symptoms **during or directly after work**?

	Seldom or never	Sometimes	Often	Very often	How many years?
Irritation of the eyes					
Feeling drunk without drinking alcohol					
Dryness of the mouth or throat					
Throat irritation					
A runny nose					
An unpleasant taste in your mouth					

16. Please indicate how sensitive you usually are to the following conditions:

For example, if you feel you are very sensitive to bright lights, circle the options "strongly agree", but if you are not at all sensitive to bright lights, circle "strongly disagree".

I am generally sensitive to:	**Strongly disagree**	**Disagree**	**Agree**	**Strongly agree**
Bright lights				
Traffic noise, loud music or other loud noises				
Strong smells				
Rough fabrics next to my skin				
Heat				
Cold				

17. Please respond to the statements below, using the following categories (**tick only <u>ONE</u> option**):

	Strongly disagree	Disagree	Agree	Strongly agree
I am generally a nervous person				
I think I am generally less capable than others in overcoming my difficulties				
I worry a lot about trivial things.				
I often feel that something bad may happen at any moment.				
I often feel that even trivial problems are too much for me.				
I usually feel insecure.				

18. Please answer the following questions (**tick only <u>ONE</u> option**):

	Very good	**Good**	**Poor**	**Very poor**
How good is your health?				
How is your health now, compared with what it was 5 years ago?				
How do you feel about your life in general?				
How do you feel about your life now, compared to 5 years ago?				

QUESTIONS ABOUT RESPIRATORY HEALTH

19. Have you had wheezing or whistling in your chest at any time **in the past 12 months**?

- ☐ Yes
- ☐ No **GO TO QUESTION 30**

20. Have you been at all breathless when the wheezing noise was present?

- ☐ Yes
- ☐ No

21. Have you had this wheezing or whistling in the chest when you did not have a cold?

- ☐ Yes
- ☐ No

22. How many attacks of wheezing or whistling have you had **in the past 12 months**?

- ☐ None
- ☐ 1-3 times
- ☐ 4-12 times
- ☐ More than 12 times

23. Have you woken up with a feeling of tightness in your chest at any time **in the past 12 months**?

- ☐ Yes
- ☐ No

24. Have you been woken by an attack of shortness of breath at any time **in the past 12 months**?

- ☐ Yes
- ☐ No

25. Have you been woken by an attack of coughing at any time **in the past 12 months**?

- ☐ Yes
- ☐ No

26. Have you **ever** had asthma?

- ☐ Yes
- ☐ No **GO TO QUESTION 39**

27. Was the diagnosis confirmed by a doctor?

- ☐ Yes
- ☐ No

28. How old were you when you had your **first** attack of asthma?

☐ Years

29. How old were you when you had your **last** attack of asthma?

☐ Years

30. Have you had an attack of asthma **in the past 12 months**?

- ☐ Yes
- ☐ No

31. Are you **currently** taking any medicine (including inhalers, aerosols or tablets) for asthma?

- ☐ Yes
- ☐ No

32. Do you cough almost daily for at least part of the year?

- ☐ Yes
- ☐ No **GO TO QUESTION 43**

33. How many month(s) a year do you have this cough?

☐ Month(s) a year

34. How many consecutive years have you had this cough?

☐ Years

35. Do you usually have this cough in winter?

☐ Yes

☐ No

36. Do you cough up phlegm almost daily for at least part of the year?

☐ Yes

☐ No **GO TO QUESTION 47**

37. How many months a year do you have this cough (with phlegm)?

☐ Month(s) a year

38. How many consecutive years have you had this cough (with phlegm)?

☐ Years

39. Do you usually have this cough (with phlegm) in winter?

☐ Yes

☐ No

40. In the <u>past 12 months</u>, how often have you been unable to work because of respiratory symptoms i.e. cough, phlegm, wheezing/whistling or shortness of breath?

☐ Never

☐ 1-7 times

☐ 8-30 times

☐ At least 31 days

☐ Don't know

41. How often, during the <u>past 12 months</u> (or if you had this job for less than a year, how often since you started), have you had one or more of the following symptoms?

☛ *(Please indicate whether symptoms lessen or disappear during weekends and holidays)*

Symptoms	How often?				Lessen or disappear during weekends and holidays?	
	Daily/ almost daily	1-2 times per week	1-2 times per month	Never/ seldom	No	Yes
Dry cough	☐	☐	☐	☐	☐	☐
Cough with phlegm	☐	☐	☐	☐	☐	☐
Wheezing in the chest	☐	☐	☐	☐	☐	☐
Breathlessness with wheezing	☐	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐	☐
Chest tightness	☐	☐	☐	☐	☐	☐

GENERAL QUESTIONS ABOUT YOUR WORK ENVIRONMENT

42. What type of ventilation does your work area have? *(tick appropriate boxes)*

- ☐ No ventilation
- ☐ Open doors and windows
- ☐ Ventilation fan ducted to outside
- ☐ Air conditioning
- ☐ Booth with fan and air filter
- ☐ Other: _____

43. How effective is the ventilation of your work area? *(tick appropriate boxes)*

- ☐ Not at all effective
- ☐ Moderately effective
- ☐ Very effective
- ☐ Don't know

44.3 Do you work around someone who is spray painting?

- ☐ No
- ☐ Yes

Spray painting/panel beating

45. What proportion of your time at work do you spend spray painting/preparing for spray painting/panelbeater?

- ☐ 5 days a week (i.e. all your working time)
- ☐ 3-4 days a week
- ☐ 1-2 days a week
- ☐ 2-3 days a month
- ☐ 1 day a month
- ☐ Not applicable

46.	On a typical day, how much time do you spend spray painting objects (e.g. cars or furniture)? ☐ Hours ☐ Not applicable
47.	On a typical day, how much time do you spend sanding, filling and chiseling objects (e.g. vehicles)? ☐ Hours ☐ Not applicable
48.	On a typical day, how much time do you spend masking out? ☐ Hours
49.	On a typical day, how much time do you spend mixing paints? ☐ Hours ☐ Not applicable
50.	On a typical day, how much time do you spend cleaning grease and dirt of objects to be spray painted ? ☐ Hours ☐ Not applicable
51.	What sort of cleaners do you normally use for degreasing/cleaning? _____ ☐ Not applicable
52.	On a typical day, how much time do you spend talking to clients and/or doing administrative duties? ☐ Hours

53. On a typical day, how many litres of paint do you use?

☐ Litres

☐ Not applicable

54. What kind of paints do you use?

☐ Mostly water based paints *(i.e. more than 75% of the time)*

☐ Mostly solvent based paints *(i.e. more than 75% of the time)*

☐ Both water and solvent based paints

☐ Not applicable

Do you use "two-pack" Isocyanate-based paints?

☐ No

55. ☐ Yes → *See below*

If YES, how often do you use 'two-pack' isocyanate-based paints?

☐ seldom

☐ Sometimes

☐ Often

☐ Very often

Mixing paint

56. Do you mix up paint in a designated paint mixing room?

- ☐ Yes
- ☐ No → *see below*

If NO, please specify where paints are mixed up for spray painting (e.g. corner of the general workshop, etc)

*(please specify)*_____

57. Are other people working in the vicinity of where you mix up paint?

- ☐ Yes
- ☐ No

58. What type of ventilation does the room/area where the paints are mixed up have? *(tick appropriate boxes)*

- ☐ No ventilation
- ☐ Open doors and windows
- ☐ Ventilation fan ducted to outside
- ☐ Air conditioning
- ☐ Other: *(please specify)*_______

Spray painting

59. Do you use a spray painting booth when spray painting?

- ☐ Yes
- ☐ No → GO TO QUESTION 71

60. What type of spray painting booth do you use?

- ☐ Bench-type spray booth
- ☐ Walk-in spray booth (extracted room)

61. Is the spray painting booth you spray in:

- ☐ Home made?
- ☐ Manufactured?
- ☐ Don't know

62. What length of time do you allow for paint/solvent vapours to be cleared from the booth by the extraction system after you have finished spraying, before you remove your protective equipment?

- ☐ No time at all
- ☐ Less than a minute
- ☐ Less than three minutes
- ☐ More than three minutes
- ☐ I remove my PPE only once I am outside the booth
- ☐ Not applicable

63. Do you ever remove your hood/mask in the booth briefly to check a partially or fully completed job?

- ☐ Yes
- ☐ No

64. What types of vehicles/objects are you involved with spray painting? (tick more than one answer if applicable)

- ☐ Cars
- ☐ Trucks
- ☐ Buses
- ☐ Other Heavy Machinery *Please specify*_____
- ☐ Other *Please specify*_____

65. Do you only carry out 'touch up" spray painting work?

- ☐ Yes
- ☐ No

66. Does any of the spray painting conducted at your work take place outside a spray booth?

- ☐ No, never → IF NEVER GO TO QUESTION 77
- ☐ Seldom
- ☐ Sometimes
- ☐ Often
- ☐ Very often

67. Does any 'two-pack' isocyanate-based spray painting conducted at your work take place outside a spray booth?

- ☐ No, never
- ☐ Seldom
- ☐ Sometimes
- ☐ Often
- ☐ Very often

68. When spray painting is conducted outside the booth, is the spraying area:

- ☐ Under cover (e.g. in the corner of the workshop)?
- ☐ In the open air (e.g.outside in the yard)?

69. Under what circumstances is spray painting done outside of the spray booth?

- ☐ Item too large for booth
- ☐ Spray booth not working
- ☐ Easier/faster to spray item outside of booth
- ☐ Other

*Please specify:*_____

Cleaning up

70. Do you ever use thinners/another solvent to clean your hands/other body parts?

☐ No, never

☐ Yes *(Please specify which solvent you use)*_____

If YES, How often?

☐ Seldom

☐ Sometimes

☐ Often

☐ Very often

71. When you are cleaning your gun, how do you clean it?

☐ In an enclosed gun washer

☐ In an un-enclosed gun washer

☐ Spray into a fan on the floor/elsewhere

☐ Other → *(Please describe cleaning process)*_____

_____

72. If you clean you gun in an enclosed or un-enclosed gun washer, is this unit extracted?

☐ Yes

☐ No

☐ Don't know

Please specify what you use to clean you gun after spraying solvent-based paints (*e.g. thinners, spirits etc*)

Use of Personal Protective Equipment (PPE)

Please indicate for which tasks in the column headings you use each of the listed items of protective equipment

(*note to interviewers – work down columns i.e. ask about protective equipment use while sanding/chiseling then degreasing/cleaning etc. Also ask about "other" tasks or PPE items they may wear)*

73.	Sanding/ Chiseling prep.	degreasing/cleaning prep.	Masking out	Mixing paints	Spraying inside booth	Spraying outside booth	Spraying "two-pack" Isocyanate paints	Cleaning (Gun etc)	Other *(Please specify)*
Goggles	☐	☐	☐	☐	☐	☐	☐	☐	
Footwear	☐	☐	☐	☐	☐	☐	☐	☐	
Apron	☐	☐	☐	☐	☐	☐	☐	☐	
Disposable mask	☐	☐	☐	☐	☐	☐	☐	☐	
Filter cartridge respirator	☐	☐	☐	☐	☐	☐	☐	☐	
Air line respirator	☐	☐	☐	☐	☐	☐	☐	☐	
Rubber or plastic gloves	☐	☐	☐	☐	☐	☐	☐	☐	
Overalls	☐	☐	☐	☐	☐	☐	☐	☐	
Full spraysuit	☐	☐	☐	☐	☐	☐	☐	☐	
Other *(Please specify)*	_____	_____	_____	_____	_____	_____	_____	_____	

74. Which of the following types of respirator do you wear (*tick appropriate boxes)*

- ☐ Full-mask airline/air-fed respirator
- ☐ Half-mask airline/air-fed respirator
- ☐ Full-mask cartridge respirator
- ☐ Half-mask cartridge respirator

How often do you wear a respirator (cartridge or airline) when:

	Seldom or never	Sometimes	Often	Very often	Always
Mixing up paint					
Spray Painting					
Cleaning up (gun etc)					

75. Do you have your <u>own</u> cartridge respirator?

- ☐ Yes
- ☐ No

76. What type of <u>cartridge filter</u> is fitted to the respirator you use? *(<u>does not concern</u> disposable masks)*

- ☐ Cartridges designed for spray painting/solvent use (as per manufacturers guidelines)
- ☐ P1
- ☐ P2
- ☐ P3
- ☐ Other *(Please specify)*_____
- ☐ Don't know
- ☐ Not applicable

77. Where do you store your respirator when it's not in use?

- ☐ In the main workshop
- ☐ In the paint mixing/paint storage room
- ☐ In a designated cupboard/locker in the main workshop
- ☐ In the paint/solvent storage area
- ☐ Other *(Please specify)*_____
- ☐ Not Applicable

78. Where are the replacement filter cartridges for the respirators stored?

- ☐ In the main workshop
- ☐ In the paint mixing/paint storage room
- ☐ In a designated cupboard/locker in the main workshop
- ☐ In the paint/solvent storage area
- ☐ Other *(Please specify)*_____
- ☐ Not Applicable

79. How often are the cartridges changed in the respirator you use?

- ☐ Daily
- ☐ Once a week
- ☐ 1 – 2 times per month
- ☐ As and when required (i.e. by smell, weight)
- ☐ Other *(Please specify)*_____
- ☐ Not applicable

80. How often, when wearing a respirator of any kind, do you notice the smell of paint/solvent when spraying/mixing paint or cleaning with solvents (tools etc)?

- ☐ Never
- ☐ Seldom
- ☐ Sometimes
- ☐ Often
- ☐ Very often

81. How often do you wear gloves when:

	Seldom or never	Sometimes	Often	Very often	Always
Mixing up paint					
Spray Painting					
Cleaning up (gun etc)					

82. When you are doing any type of spray painting, is any of your skin exposed?

☐ No

☐ Yes *(Please specify what is exposed)*_____

If YES, How often?

☐ Rarely

☐ Sometimes

☐ Often

☐ Every time I spray paint

Hobbies and other jobs

Do you have hobbies that involve exposure to solvents *(e.g. work that involves solvents for cleaning, cutting fluids, spray painting, use of varnishes, lacquers or epoxies*)?

☐ No

☐ Yes → *See below*

If YES, how much time do you devote to this hobby?

☐ Hours per ☐

If YES, Please specify below what products containing solvents you use for your hobby

84. In addition to your current job, do you have another job at present that involves exposure to solvents?

☐ Yes → *please specify what this job is:*_____

☐ No

If YES, Please specify below what products containing solvents you use for your other job

85. How often do you wear the following items of protective equipment when using solvents/solvent-based products for your hobby/other job?

	Seldom or never	Sometimes	Often	Very often	Always
Respirator					
gloves					

QUESTIONS ON SMOKING, ALCOHOL AND EDUCATION

Smoking

86. Have you smoked more than 5 packs of cigarettes in total in your whole life?

- ☐ Yes
- ☐ No GO TO QUESTION 98

87. Do you still smoke?

- ☐ Yes
- ☐ No At what age did you quit smoking? ☐

88. How many cigarettes per day do you or did you smoke?

☐ Cigarettes per day

89. At what age did you start smoking?

☐ Years

Alcohol

90. Throughout your working life to date, on average how often have you consumed alcohol?

- ☐ Never
- ☐ Less than once a month
- ☐ 1-2 times a week
- ☐ 3-5 times a week
- ☐ Daily

91. How many of the following alcoholic drinks would you have consumed over a normal working week? *(total over the whole week)*?

- ☐ Bottles of beer *(number)*
- ☐ Glasses of wine *(number)*
- ☐ Small glasses of spirits *(number)*

92. How often do you currently consume alcohol?

- ☐ Never
- ☐ Less than once a month
- ☐ 1-2 times a week
- ☐ 3-5 times a week
- ☐ Daily

93. How many of the following alcoholic drinks do you currently consume over a normal working week? *(total over the whole week)*?

- ☐ Bottles of beer *(number)*
- ☐ Glasses of wine *(number)*
- ☐ Small glasses of spirits *(number)*

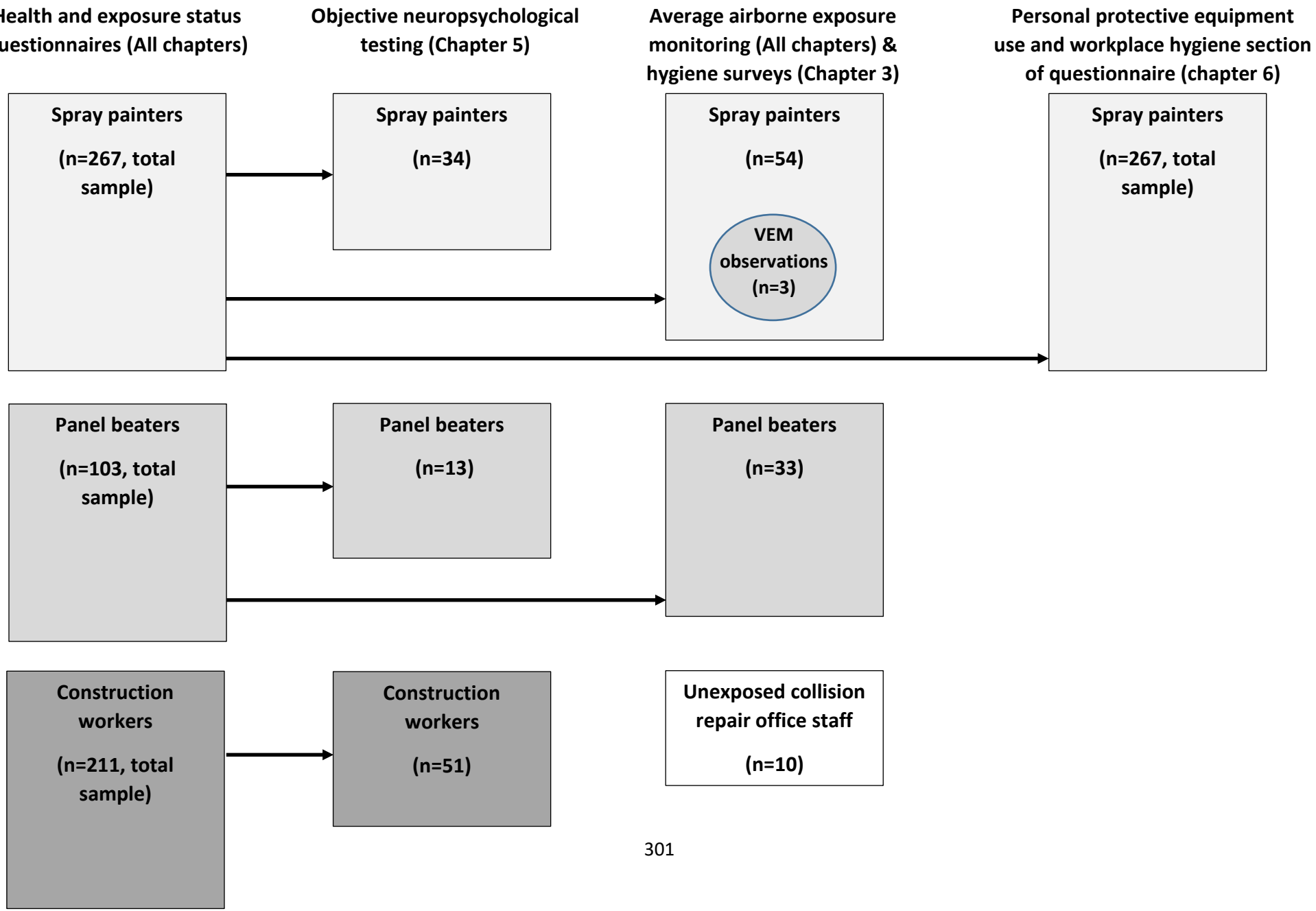
Education

94. What is the highest level of education you received?

- ☐ Primary school
- ☐ Secondary school *(college)*
- ☐ University or other form of tertiary education

Thank you for your time answering this questionnaire. Do you have anything you would like to add or any comments?

Appendix 2: Flow diagram of participants included in the results chapters (3, 4, 5 and 6) in this thesis.



DRC 16

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: Samuel John Keer

Name/Title of Principal Supervisor: Prof. Jeroen Douwes

Name of Published Research Output and full reference:

Keer, S., Taptiklis, P., Glass, B., McLean, D., McGlothlin, J.D., and Douwes, J., 2018. Determinants of airborne solvent exposure in the collision repair industry. Annals of Work Exposures and Health, 2018, 62(7) 871-883.

In which Chapter is the Published Work: Chapter 3

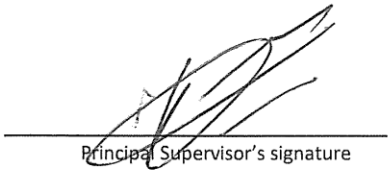
Please indicate either:

- 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

11/6/18
Date



Principal Supervisor's signature

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In which Chapter is the Published Work: Chapter 4

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Candidate's Signature — Date: 11/6/18

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In which Chapter is the Published Work: Chapter 5

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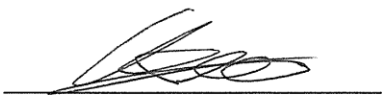
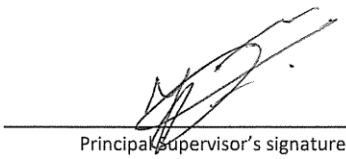


Candidate's Signature

11/6/18.

Date



Principal Supervisor's signature

11/6/18

Date

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Keer, S., McLean, D., Glass, B. and Douwes, J., 2018. Effects of Personal Protective Equipment Use and Good Workplace Hygiene on Symptoms of Neurotoxicity in Solvent-Exposed Vehicle Spray Painters. Annals of Work Exposures and Health, 62(3), pp.307-320.

In which Chapter is the Published Work: Chapter 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 — Date: 11/6/18

Principal Supervisor's signature — Date: 11-6-18

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Health and Disability Ethics Committees

Multi-region Ethics Committee
Ministry of Health
No. 1 The Terrace
PO Box 5013
Wellington 6145
Phone (04) 816 2403
(04) 816 2646
Fax (04) 496 2343
Email: multiregion_ethicscommittee@moh.govt.nz

20 September 2011

Professor Jeroen Douwes
Centre for Public Health Research
Massey University
Private Bag 756
Wellington

Dear Professor Douwes -

Re:	Ethics ref:	**MEC/10/08/081** (please quote in all correspondence)
	Study title:	Neurotoxic effects of occupational solvent exposure
	Investigators:	Professor Jeroen Douwes, Professor Neil Pearce, Professor Bill Glass, Dr David McLean, Mr Brad Prezant, Professor Diana Echeverria, Dr Wendyl D'Souza, Ms Tania Slater
	Approved Localities:	Centre for Public Health Research, Massey University, Wellington Campus

This study was given ethical approval by the Multi-region Ethics Committee on **20th September 2011.**

Approved Documents

- National Application Form
- Signed Part 4 declaration for Jeroen Douwes
- HRC reports and rebuttal
- Study Protocol
- Consent Form - revised (no version/date)
- Questionnaire - revised (no version/date)
- Evidence of Maori Consultation - Letter signed and dated 3 Aug 2010 by Chris Cunningham - Massey university Research Centre for Maori Health and Development
- Signed Locality Assessment for the Centre for Public Health Research signed by Professor Pearce
- Signed locality Assessment for the Centre for Public Health Research signed by the current director
- Participant Information Sheet for Carpenters, version 2, dated 16 Sep 2011
- Participant Information Sheet for Spray painters, version 2, dated 16 Sep 2011

This approval is valid until **20th September 2016**, provided that Annual Progress Reports are submitted (see below).

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment
- information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports

The first Annual Progress Report for this study is due to the Committee by **20th September 2012**. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

Statement of compliance

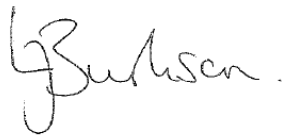
The committee is constituted in accordance with its Terms of Reference. It complies with the *Operational Standard for Ethics Committees* and the principles of international good clinical practice.

The committee is approved by the Health Research Council's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990.

We wish you all the best with your study.

Please do not hesitate to contact me should you have any queries.

Yours sincerely



Laura Jayne Burlison
Administrator
Multi-Region Ethics Committee
Email: multiregion_ethicscommittee@MOH.govt.nz