CHILDHOOD LEAD EXPOSURE: EFFECTIVENESS OF CLEANING INTERVENTION AND INFLUENCES OF SEASONALITY AND HOME FLOOR-SURFACING TYPES

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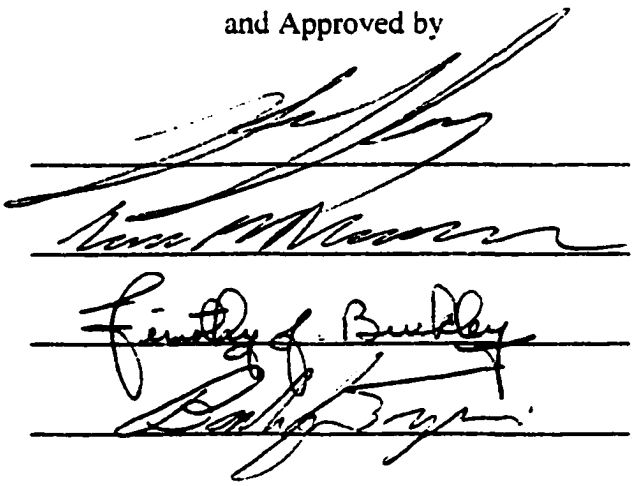

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ABSTRACT OF THE DISSERTATION

Childhood Lead Exposure: Effectiveness of Cleaning Intervention and Influences of Seasonality and Home Floor-Surfacing Types

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The dissertation presents the effectiveness of a cleaning intervention and examines the influences of seasonality and home floor-surfacing types on childhood lead exposure. Dust wipe and vacuum samples and blood specimens, which were collected in the Childhood Lead Exposure Assessment and Reduction Study (CLEARS) in Jersey City, New Jersey, were used and analyzed for the research. In addition the thesis also includes the comparison of two levels of childhood lead exposures, in which partial dust and blood data collected in the Treatment of Lead-exposed Children (TLC) Trial were used to compare with the CLEARS data.

The CLEARS participating homes were randomized to the Lead Intervention Group and Accident Prevention Group (control) to examine the effectiveness of the cleaning intervention. During the cleaning intervention, lead loading of the wipe samples in the Lead Intervention homes was found to be 37% and 35% lower for the second and third visits, respectively, than that in the Accident Prevention homes ($p = 0.001$ and 0.011). Dust loading and lead loading of the vacuum samples in the Lead Intervention homes showed a significant decline from the first visits through the third visits, while no decline was found for the Accident Prevention homes. The results suggested that the

cleaning intervention should be effective to reduce dust lead levels in the household. However, floor surfacing (carpeted or linoleum tiles paved) in the home had an impact on the efficacy of the cleaning intervention and the childhood lead exposure. The ANOVA showed that a significant decline of mean blood lead concentration was observed in the uncarpeted households during the cleaning intervention, but no significant difference was found in the carpeted households.

In the seasonality study, the geometric mean blood lead concentrations were 10.44 and 8.61 μg/dl for the Summer and Winter groups, respectively ($p = 0.004$). The dust lead levels (floor lead loading, sill lead loading and carpet lead concentration), consistent with the blood lead levels, were highest in June, July and August. The stepwise linear regression model suggested that the seasonality of blood lead levels in these children may result mainly from the seasonal distributions of dust lead levels in the home.

The CLEARS and TLC Trial presented two different levels of lead exposures, 10-25 μg/dl and 20-44 μg/dl, respectively. The regression model showed that only floor lead loading was associated with blood lead concentration for the lead exposure in CLEARS; however, the CLEARS regression lines was not appropriately available to the TLC data. The result indicated that high lead exposure in the TLC Trial might have other sources of high lead in the home. This thesis concludes that the childhood lead exposure in the urban areas of New Jersey, showing the changes for cleaning intervention and seasonality, is based on the association of blood lead and dust lead.

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ABBREVIATIONS

ANOVA	Analysis of variance
ATSDR	Agency for Toxic Substances and Disease Registry
CDC	Centers for disease Control and Prevention
CLEARS	Childhood Lead Exposure Assessment and Reduction Study
EAA	Electrothermal atomization atomic absorption spectroscopy
EPA	Environmental Protection Agency
FAA	Flame atomic absorption spectroscopy
GFAA	Graphite furnace atomic absorption spectrophotometer
GM	Geometric mean
GSD	Geometric standard deviation
HUD	Department of Housing and Urban Development
ICP-MS	Inductively coupled plasma-mass spectroscopy
LWW	Lioy-Weisel-Wainman dust wipe sampler
PbB	Blood lead level
PbC	Lead concentration
PbD	Dust lead level
PbL	Lead loading
TLC	Treatment of Lead-Exposed Children Trial
XRF	X-Ray Fluorescence detector

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CHAPTER 1: INTRODUCTION

1.1 Childhood Lead Exposure

Lead is ubiquitous in the human environment as a result of hundreds of years of industrialization. It was widely used in industrial activities, such as ammunition manufacturing, battery manufacturing, paint production, and gasoline refining. Lead is a toxicant that may deleteriously affect the nervous, hematopoietic, endocrine, renal, and reproductive systems (ATSDR, 1993). Childhood lead exposure is of concern, because children absorb lead more readily than do adults and the developing nervous systems are particularly susceptible to the toxic effects of lead (ATSDR, 1988; CDC, 1991). In 1998, the Centers for Disease Control and Prevention (CDC) defines an elevated blood lead level for children as blood lead concentration above 10 μg/dl.

Lead was used as gasoline additives and the burning of gasoline was a large single source of lead in the environment (ATSDR, 1993). After the removal of lead from gasoline in the mid-1970s, the blood lead levels (PbBs) in the U.S. population, especially in the subpopulation of preschool children, were significantly reduced. Between 1976 and 1991 the geometric mean PbBs in preschool children declined from 13.7 to 3.2 μg/dl for non-Hispanic white children and from 20.2 to 5.6 μg/dl for non-Hispanic black children (Pirkle *et al.*, 1994). The latest results indicate that, throughout 1994, the geometric mean PbBs have even dropped to 2.3 and 4.3 μg/dl for non-Hispanic white and black children, respectively (CDC-MMWR, 1997). Despite the major PbB decline, there are nearly 1

million children aged 1 to 5 years old who still have PbBs above 10 μg/dl (CDC-MMWR, 1997).

Lead-laden household dust is considered to be the primary source of childhood lead exposure. Ingestion is the major pathway of lead exposure due to children's frequent hand-to-mouth behavior (HUD, 1995). A number of studies have shown that the elevated PbBs in preschool children were strongly associated with elevated lead levels in house dust (PbDs), in term of either lead loading (mg/m^2 or $\mu g/ft^2$) or lead concentration (μg/g) (Charney *et al.*, 1983; Bornschein *et al.*, 1986; Thornton *et al.*, 1990; Davies *et al.*, 1991; Clark *et al.*, 1991; Cambra and Alonso, 1995; Lanphear *et al.*, 1996a; Rhoads *et al.*, 1999). Besides the studies of blood lead-dust lead relationships, other lead exposure studies, such as lead source apportionment (Hunt *et al.*, 1992; Hunt *et al.*, 1993; Adgate *et al.*, 1998), lead-based paint abatement (Farfel and Chisolm, 1990; Farfel *et al.*, 1994a), lead-laden dust sampling methodology (Que Hee *et al.*, 1985; Lioy *et al.*, 1993; Farfel *et al.*, 1994b; Millson *et al.*, 1994; Adgate *et al.*, 1995; Lanphear *et al.*, 1995; Wang *et al.*, 1995; Reynolds *et al.*, 1997; Rich *et al.*, 1999), and dust control intervention (Charney *et al.*, 1983; Ewers *et al.*, 1994; Hilts *et al.*, 1995; Lanphear *et al.*, 1996b; Hilts *et al.*, 1998; Lioy *et al.*, 1998), have been widely performed in the recent years.

Lead in household dust is mixture of multiple interior and exterior proximate and ultimate sources of lead. Lead-based paint is recognized as the major lead source in old houses (Clark *et al.* 1985, Charney *et al.* 1980, Charney *et al.* 1983). Exterior sources, including street dust, outdoor soils and airborne lead-bearing particles, are considered to be the significant contributors to house dust in urban areas. Some previous studies demonstrated that exterior soil and dust had an impact on childhood lead exposure

(Yankel *et al.* 1977, Bornschein *et al.* 1985a). Alternatively, source apportionment of lead in house dust conducted using automated scanning electron microscopy indicated that exterior sources (street dust/soil) and lead-based paint appeared to be major contributors to lead-laden dust in the home environment (Hunt *et al.*, 1992; Hunt *et al.*, 1993). A recent source apportionment study of lead, performing chemical mass balance models for a lead intervention program (CLEARS), demonstrated that nearly 50% of lead in household dust came from street dust/soil, and 33% and 17% came from lead-based paint and air-borne particles, respectively (Adgate *et al.*, 1998).

Lead-based paint is a source of high-dose lead poisoning, since it usually contains 5-40% lead (50,000-400,000 ppm) (ATSDR, 1993). It is estimated that approximately 57 million houses in the United States built before 1978, when use of lead-based interior paint was banned, contain lead-based paint in the houses (Lead-Based Paint Hazard Reduction and Financing Task Force, 1995). In the lead-painted houses, flaking paint chips or fragments off the walls, ceilings or windowsills may be spread over the home environment, and become an acute threat to preschool children's health. Residential lead abatement is necessary to reduce children's lead exposure. Various levels of lead abatements, including removal, cleanup and disposal of lead paint, have been suggested and the efficacy has been investigated by Farfel and Chisolm (1991), and Farfel *et al.* (1994). Since 1993, the U.S. Department of Housing and Urban Development (HUD) has been implementing the Lead-Based Paint Hazard Control Grant Program in order to reduce lead-based paint hazards in the houses built before 1978. Until it is removed or encapsulated, lead-based paint will remain a threat to the health of young children.

In houses with no lead-based paint, children's exposure to lead is still of concern since there are many urban children whose PbBs are above 10 μg/dl. The exterior lead is a significant proximate source of the lead exposure. Exterior sources of lead, street dust/garden soil and airborne lead particles, enter the indoor environment via human or pet activities and air ventilation. Most lead-contaminated soils in urban areas come from leaded paint and landfills, which contain waste from lead ore mining, ammunition manufacturing, and industrial activities. When lead was used as a gasoline additive, it was spread extensively via exhausts and deposited in street dust. Although prohibiting the leaded gasoline use has reduced airborne lead production significantly (ATSDR, 1993), in urban areas, the lead particles previously released from automobile exhausts and accumulated in the environment, remain available for contact and exposure.

Exposure metrics of microenvironments, lead concentration (μg/g), lead loading (mg/m^2 or $\mu g/ft^2$), and dust loading (g/m^2 or g/ft^2), have been used in the studies of lead exposure. Lead loading was widely used in most studies (Charney *et al.*, 1983; Bornschein *et al.*, 1986; Davies *et al.*, 1991; Clark *et al.*, 1991; Adgate *et al.*, 1995; Lanphear *et al.*, 1996b; Freeman *et al.*, 1996; Lioy *et al.*, 1998), because it not only was found most correlated with blood lead concentration but also could be derived without weighing dust mass on sampling media. However, lead concentration was also used in some studies to indicate dust lead levels in the home (Laxen *et al.*, 1987) or lead content in soils (Lanphear *et al.*, 1996a), while dust loading was used for examination of a cleaning intervention (Lioy *et al.*, 1998). The purpose of lead exposure studies is to reduce lead levels in household dust and prevent children from experiencing lead poisoning. To achieve that goal, the potential lead sources need to be identified and the

associations between dust lead and blood lead have to be well understood and examined in microenvironmental approaches. Dust control intervention is considered an effective tool to reduce lead levels present in house dust and in children's blood (Charney *et al.*, 1983; Hilts *et al.*, 1995; Hilts *et al.*, 1998). This thesis, mostly based on a dust control intervention program, presents the results of childhood lead exposure in urban areas.

This dissertation examines whether a cleaning intervention is effective in reducing the residential dust lead levels for children experiencing low to mild levels of lead exposure. Following the examination of a cleaning intervention, other lead exposure issues include: the seasonality of lead exposure involving sources of lead, the influence of floor surfacing in the home on lead exposure, and the comparison between two urban lead exposures with different ranges of elevated blood lead levels.

1.2 Lead Intervention Strategies

Treatment of lead poisoned children varies with the levels of lead poisoning. At low to mild levels of poisoning (10-25 μg/dl) lead intervention focuses on dust control of the residential environment, while at high lead levels (20-44 μg/dl) lead paint abatement and, sometimes, medication regimes are imposed. The Childhood Lead Exposure Assessment and Reduction Study (CLEARS) and the Treatment of Lead-Exposed Children (TLC) Trial, were designed for the low to mild level and the high level, respectively:

- The CLEARS was a controlled trial to get a better understanding of children's exposure to lead and to test whether a cleaning and education protocol resulted in blood lead and dust lead reduction (Rhoads and Lioy, 1992). The families, most of

which were located in Jersey City, all had evidence of lead exposure in the home. The CLEARS focused on documenting and reducing their exposures through education and assistance with lead dust control. Actual PbBs in the children (age 6-32 months) ranged from 3 to 28 μg/dl at the outset of the study. Blood Specimens and dust samples, including wipe samples from floors and windowsills, and vacuum samples from carpets or rugs, were collected as microenvironmental samples to examine the efficacy of lead interventions. Portions of blood specimens and environmental dust samples in CLEARS were used for examining the influences of seasonality and floor-surfacing types on the lead exposure.

- The TLC Trial, a randomized clinical trial, was designed to assess the effects of lead chelation with succimer in children aged 12 to 32 months with baseline blood lead levels between 20 and 44 μg/dl. The developmental status of each child was assessed at baseline and followed for three years following treatment with chelating agent, (succimer) or with placebo (TLC protocol, 1994). Dust sampling, including wipe and vacuum sampling, provided the information needed to determine the PbDs of children's residential environments, which were scattered within the Newark area of New Jersey. Blood lead and dust lead data of the TLC Trial were used, along with those of CLEARS, to compare the blood lead-dust lead relationships for the two ranges of lead-poisoning, 10-25 μg/dl (CLEARS) and 20-44 μg/dl (TLC Trial).

1.3 Research Responsibilities

The CLEARS

- Field sampling: LWW wipe sampling, vacuum sampling, street dust/soil sampling, and airborne dust sampling.

- Sample analysis: pre- and post sampling preparation, acidic digestion of wipe and vacuum samples, wipe and vacuum sample analysis on FAA and ICP-MS, data processing, quality control/quality assurance, and statistical analysis of blood and dust data.

The TLC Trial

- Dust sampling: designing of the original and modified LWW sampler comparison.
- Sample analysis: the same work as CLEARS.

1.4 Hypothesis

Since many previous lead studies have indicated that PbBs in preschool children are associated with PbDs in the household, the changes in either blood or dust lead levels are supposed to result in the same changes in the other lead levels. The research hypotheses for this thesis are established as:

- A vigorous cleaning intervention can be effective in reducing PbDs in children's residential environments.
- Seasonal variation of lead poisoning in children may result from the same seasonal patterns of PbD subsets in the home environment.
- The types of home floor surfacing, bare floors and carpets, may yield different results for the cleaning intervention as well as childhood lead exposure due to the different retention characteristics for dust.
- Lead exposure trials with different blood lead concentration ranges may appear different PbD compositions.

1.5 Specific Aims

To examine the research hypotheses of childhood lead exposure, the effectiveness of the lead intervention in CLEARS has to be elucidated prior to other analyses. With the completion of the cleaning intervention study, the portion of data that are not affected by the cleaning intervention can be used to perform the studies of blood lead-dust lead

relationships (e.g. seasonality and floor-surfacing study). When the blood lead-dust lead relationships for CLEARS are established, the relationships for the TLC Trial can be examined to complete the comparisons of two urban childhood lead exposure studies. The research specific aims associated with the hypotheses are:

1.5.1 Examination of Lead Intervention Study

- Examine the distributions of collected sample types for statistical analysis.
- Compare PbDs in lead concentration, lead loading and dust loading for wipe and vacuum data at each home visit between the Lead Intervention Group and Accident Prevention Group.
- Compare micro-environmental PbDs in the three dust variables for wipe and vacuum data between three home visits within the two intervention groups.
- Estimate the effect of cleaning on reducing PbDs in various types of samples.

1.5.2 Seasonality of Childhood Lead Exposure

- Categorize blood lead and dust lead data with no cleaning intervention effect into seasonal groups by monthly temperature.
- Examine the relationships between PbBs and PbDs and examine the correlation between the different dust variables: lead concentration, lead loading and dust loading for floor, sill and carpet samples, and blood lead concentration.
- Compare PbBs and PbDs between seasonal groups.
- Develop regression models for PbBs and PbDs and test the significance of season factors in the models.
- Examine the implications of seasonality for lead exposure.

1.5.3 Influences of Home Floor Surfacing on Lead Exposure

- Re-organize blood lead data by carpeted or uncarpeted status in the home.
- Re-examine the cleaning effect on blood lead concentration differentiated by carpeted or uncarpeted houses.
- Evaluate the significance of floor surfacing to lead exposure.

1.5.4 Comparisons of Two Urban Lead Exposures

- Compare the original and modified LWW wipe samplings used in CLEARS and the TLC Trial.
- Develop regression models of PbBs and PbDs for CLEARS, the TLC Trial, and the combination of the two studies.
- Evaluate the PbB-PbD relationships for the two different levels of lead poisoning.

1.6 Data Selection

All the results presented in this thesis used the data collected as part of CLEARS and the TLC Trial. Each study had a specific criterion of data selection and process to test the hypothesis. The data selections for the hypothesis tests are:

1.6.1 Lead Intervention Study

All of the dust data from the consenting subjects in CLEARS were included and analyzed for the descriptive statistics. Dust data labeled with valid visit numbers in the Lead Intervention or Accident Prevention groups were used for the comparisons between the two intervention groups (t-test). Data that contained all three home visits at the same sampling locations were used to compare the dust lead levels between home visits (repeated-measures design and one-way ANOVA).

1.6.2 Seasonality of Lead Exposure

To examine the seasonal influences on lead exposure, the blood and dust data should not be affected by any known intervention (e.g. cleaning effect). Thus, the data obtained from Accident Prevention homes, which did not receive the cleaning intervention, were eligible for the analysis. The blood and dust data were categorized into seasonal groups and respective subsets for mean comparisons (t-test). Only the datasets

with correspondence between blood and dust samples were used for correlation analysis and stepwise multiple linear regression.

1.6.3 Floor-Surfacing Types on Lead Exposure

The data selected for this part of study was based on the work of Rhoads *et al.* (1999), who reported 46 and 53 children with the baseline (first visit) and final (third visit) blood data for the Lead Intervention and Accident Prevention groups, respectively. The blood data for the second visit, which were not used in Rhoads *et al.*'s work, were added to the study, but some subjects were removed due to missing the second-visit data. For the purpose of a nested factorial design of ANOVA, the blood data, after being divided into the carpeted and uncarpeted subgroups, were randomly selected to have equal sample number for the two floor-surfacing subgroups in either intervention group (21 for Lead Intervention homes and 17 for Accident Prevention homes). Repeated-measures design of ANOVA was used to compare PbBs between home visits within either floor-surfacing subgroup for the Lead intervention homes or the Accident Prevention homes.

1.6.4 Comparisons of Two Lead Exposure Studies

The database used for CLEARS in this part of study was same as the one in the seasonality study. The pre-cleaning database of blood and dust samples in the TLC Trial was used for the comparisons. Since the vacuum sample size in the TLC Trial was much fewer than that in CLEARS, the comparisons of the two lead exposures did not include vacuum data of the CLEARS database used in the seasonality study.

1.7 Structure of Thesis

Chapters 2-5 in the thesis presents an investigation of the previously cited hypotheses. These chapters were written independently to address the issues associated with each specific aim in the order listed above. Chapter 2 addresses the effect of cleaning intervention in reducing PbDs in the household and describes most sampling and analysis methods for the following chapters. Chapter 3 addresses the seasonal influences on childhood lead exposure. Chapter 4 addresses the re-examination of cleaning intervention effect on different floor-surfacing types in the home environment. Chapter 5 addresses the comparisons of the original and modified LWW samplings and the relationships between PbBs and PbDs for two ranges of blood lead concentrations. Conclusions of this thesis and recommendations for future research are described in Chapter 6 and Chapter 7, respectively.

CHAPTER 2: THE EFFECTIVENESS OF A CLEANING INTERVENTION ON CHILDHOOD LEAD EXPOSURE

2.1 Introduction

Household dust deposited on rugs and various flat surfaces in the home, as a metric of potential exposure to specific environmental contaminants (e.g. lead, chromium and pesticides), has aroused the attentions of environmental scientists and hygienists in the recent years. A number of studies have shown that household dust was associated with toxic chemical exposure (Sayre and Katzel, 1979; Bornschein *et al.*, 1985b; Roberts *et al.*, 1991a; Lioy *et al.*, 1992; Ewers *et al.*, 1994; Roberts *et al.*, 1995). Based on the relationship between house dust and chemical exposure, the Childhood Lead Exposure Assessment and Reduction Study (CLEARS) was designed as a systematic attempt to determine if a vigorous cleaning program could be employed to reduce children's elevated blood lead levels (PbBs). Eligible children for CLEARS were randomized to the Lead Intervention Group, which received periodic cleaning intervention work in the home, and the Accident Prevention Group, which was treated as a control group and given accident prevention education only.

It appeared that dust lead levels (PbDs) in the household would be the best indicators of exposure since no major active sources of airborne lead were present in the area (geometric mean: 32 ng/m^3), and the lead levels in the drinking water was low (geometric mean: 3.4 ppb) (Rhoads *et al.*, 1999). In particular, the chromium study done in Jersey City appeared to show that changes in house dust loadings were the best indicators of chromium reduction after remediation of hazardous wastes laden soil around

a home or neighborhood (Lioy *et al.*, 1992). Therefore, dust lead data collected from wipe and vacuum techniques, which were previously used in the chromium study, were used to assess PbDs in the home environment. In this chapter, the efficacy of cleaning intervention in reducing PbDs in the home environment, as part of CLEARS, was examined. The effectiveness of the program in reducing PbBs was described in a paper by Rhoads *et al.* (1999).

2.2 Background

The CLEARS was conducted from June of 1992 through September of 1995 in the urban area of Jersey City, New Jersey (Rhoads and Lioy, 1992). Children enrolled in CLEARS ranged in age from 6 months to 3 years old. They were recruited from neighborhood clinics, the Jersey City Childhood Lead Poisoning Prevention Program, and by referral from private physicians and other community sources (Rhoads *et al.*, 1999). Subjects were eligible for participation if they met at least one of the following criteria: (1) reported blood lead values between 8 and 20 μg/dl (0.39-0.97 μmol/l), (2) identified lead on the surfaces within the residence (X-ray fluorescence reading > 2.0 mg-Pb/cm^2 or in house dust > 1500 μg/g), or (3) an older sibling in the residence with a blood lead > 10 μg/dl. Primary interior and exterior activity areas were identified through discussions with care-givers about where the participating child spent time, and from visual clues observed by the CLEARS technicians. After informed consent was received, subjects were randomized to the Lead Intervention Group (Lead) or the Accident Prevention Group (Accident) and their residences were visited 3 times at 4-6 month

intervals. Blood and dust samples were collected at home visits to provide evidences of the effectiveness of the intervention.

2.3 Methods

2.3.1 Sample Collection

Dust sampling included both wipe and vacuum techniques, and each was completed in the participating CLEARS homes. Interior activity areas sampled were those mostly likely to be used by children (e.g. living rooms, bedrooms, kitchens, and windowsills), and were sampled to establish a metric of residential lead exposure (Freeman *et al.*, 1996). The Lioy-Weisel-Wainman (LWW) dust wipe sampler was used to collect dust on floors and windowsills. The LWW sampler (original) employed a set of three round polyethylene filters mounted on a replaceable non-skid rubber surface attached to the sampling block (Figure 2.1). Most samples were collected with a 100 cm^2 template while some samples, located on narrow surfaces, were collected with a 50 cm^2 template. When sampling, technicians put some droplets of de-ionized water on the non-skid rubber pad, and wetted and placed a polyethylene filter on the pad with a pair of forceps. Then the sampling block with the wetted filter was placed and moved back and forth within the template on sampling surfaces. Same sampling procedure was conducted for the rest of filters. The collection efficiencies of the LWW sampling kit were approximately 100% and 87% for floor and windowsills, respectively (Lioy *et al.*, 1993). Side-by-side wipe samples were collected with every tenth sample using an area with similar surface characteristics and adjacent to the first sampling location. It was found that coefficients of variation (CV) were 19% and 10% for the values of dust loading

(g/m^2) on floors and sills, respectively, and were 23% and 43% for lead loading (mg/m^2) on floors and sills, respectively (Adgate *et al.*, 1995).

A Data Vac II (Metropolitan Vacuum Cleaner Co., Suffern, NY) was modified to collect dust on carpet or rug with an in-line filter placed in the vacuum hose. The technique was previously described by Wang *et al.* (1995). The carpets were sampled by moving the vacuum nozzle back and forth three times in an overlapping pattern within a 0.25 m^2 template. The vacuum had a flow rate of 1.7 m^3/min, and an inlet velocity of 13.5 m/sec. Collection efficiency of the vacuuming technique was dependent of carpet type, relative humidity (RH) and dust quantity, and data were adjusted using the algorithm developed by Wang *et al.* (1995).

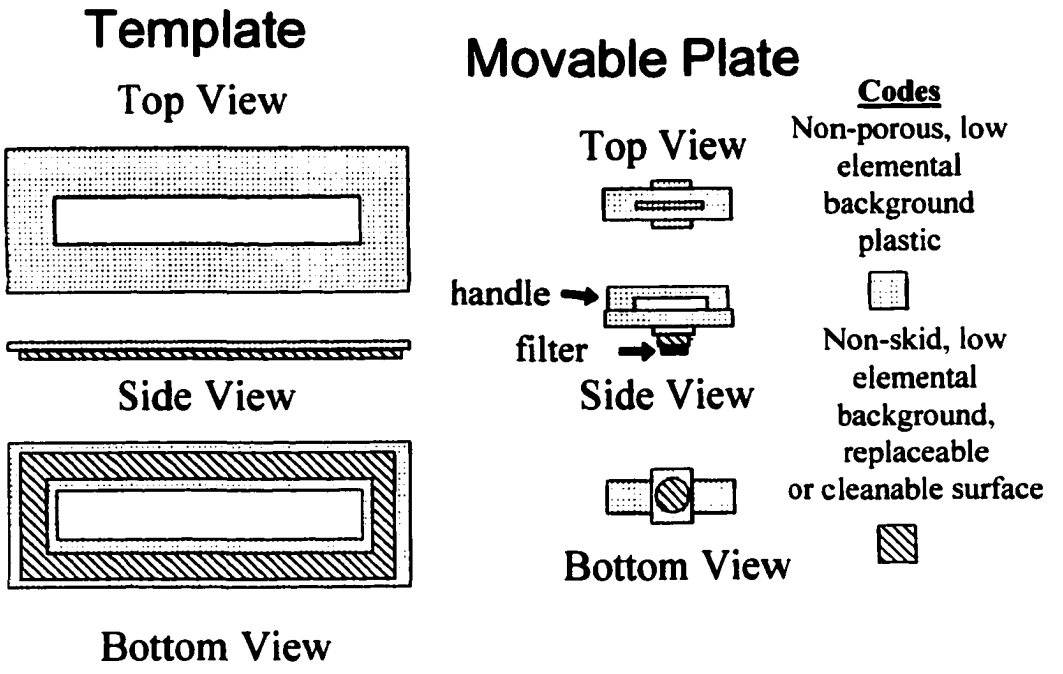

Figure 2.1 The LWW Wipe Sampler (Original).

2.3.2 Sample Analysis

All samples were microwave digested in 19% (v/v) spectrograde (wipe) or reagent grade (vacuum) nitric acid following a protocol of U.S. Environmental Protection Agency (USEPA 1991). Vacuum samples were analyzed by using flame atomic absorption spectroscopy (FAA, Perkin Elmer Model 3100) at the wavelength of 283.3 nm. A graphite furnace atomic absorption spectrophotometer (GFAA, Perkin Elmer) or inductively coupled plasma-mass spectroscopy (ICP-MS, Fisons Instrument VG PlasmaQuad) was used to analyze wipe samples (Adgate *et al.*, 1995). Calibration standards were checked on every 10th sample run for quality control; NIST (National Institute of Standards and Technology) reference material 981 and 2711 (wipe), and 2710 (vacuum) were used for the quality assurance analyses. Sample digestion blanks, reagent blanks and lead solution spikes were included in all analytical runs. The detection limits were approximately 0.5 ppm and 10 ppb for the FAA and GFAA, respectively, and the ICP-MS had a detection limit of 1 ppb. Detection limit depends on the ratio of the magnitude of the analytical signal to the size of the statistical fluctuations in the blank signal (Appendix 7). The detection limits used here, known as an operational detection limit, were the minimum concentrations that could be detected. For both the wipe and vacuum samples acceptable instrument error was within ± 20%, although most QC analyses were within ± 10%.

2.3.3 Cleaning Protocol

Families in the Lead Intervention Group received lead dust control service every two weeks over a 12-18 month period after the first home visits. Home dust control was

carried out by a CLEARS crew of two persons, who were trained in practical ways to reduce lead contamination in the home. The home cleaning staff discussed the play and activity habits of each young child with the mother, and special care was given to clean dust in these areas. Floors and smooth surfaces were cleaned with a low phosphate detergent (Spic and Span®), while rugs and carpets were cleaned with a high efficiency particulate air (HEPA) filter vacuum cleaner. Efforts were made to involve the family in the cleaning to give them a degree of control in this important area of their home life. In addition, family members were encouraged to remove loose paint in accessible areas, and make repairs with simple wet scraping and repainting of surfaces.

2.3.4 Data Analysis

All the wipe and vacuum data were log-transformed prior to statistical analysis, since the wipe and vacuum samples, in terms of lead concentration, lead loading and dust loading, appeared to be log-normally distributed (Figure 2.2 and 2.3). Independent-samples t-tests were used to compare mean lead concentrations, lead loadings or dust loadings for all available wipe and vacuum samples between the Accident and Lead groups at each home visit. Repeated-measures design of analysis of variance (ANOVA) was performed for wipe and vacuum samples which were collected at the same sampling locations three times for the Accident and the Lead group. The ANOVA design is stated as:

$$Y_{ijk} = \mu + S_i + V_j + SV_{ij}$$

where

Y represents the measured variable, lead concentration, lead loading or dust loading of wipe or vacuum samples.
μ represents the true value.
S is the between-subjects effect.
V is the effect of treatment among three home visits (cleaning intervention for Lead group and prevention education for Accident group).
SV is the interaction effect of S and V.

The V effect was tested against SV to indicate the significant differences in lead concentration, lead loading or dust loading for wipe or vacuum samples between home visits. The null hypothesis is stated as:

$$H_O : PbD_{V1} = PbD_{V2} = PbD_{V3}$$
$$H_A : PbD \text{ not equal for three home visits}$$

One-way ANOVA, using the least-significant difference (LSD) multiple mean comparison test, was performed for the sample sets with significant V effect (significant difference between three home visits) to clarify where the significant difference(s) occurred between three home visits.

2.4 Results

The entire CLEARS micro-environmental data set was used to first describe the overall distribution patterns of dust and lead in the residences selected as part of both participant groups. The summary statistics for the ensemble of all the wipe samples had a geometric mean lead concentration of 603 μg/g (Table 2.1) with the highest concentration above 7,500 μg/g (Figure 2.2). The geometric mean dust leading and lead loading were 0.47 g/m^2 and 0.28 mg/m^2, respectively. Among the three distributions for wipe samples, lead loading had the highest geometric standard deviation (Table 2.1 and Figure 2.2).

The vacuum samples from the carpets or rugs showed a different result (Table 2.1 and Figure 2.3). The mean lead concentration was 502 μg/g with the peak value of 35,600 μg/g. The mean dust loading and lead loading (6.65 g/m^2 and 3.35 mg/m^2, respectively) were much higher than those for the wipe samples, implying that carpets or rugs were a huge dust and lead sink in the residential environments.

Table 2.1 General Log Normal Distribution Parameters for all Wipe Samples and Vacuum Samples Obtained during the course of CLEARS: Dust Loading, Lead Loading, and Lead Concentration.

Vacuum Samples	n	GM	GSD
Dust Loading	516	6.65 g/m^2	3.3
Lead Loading	516	3.35 mg/m^2	5.0
Lead Concentration	516	502 μg/g	3.0

Wipe Samples	n	GM	GSD
Dust Loading	1731	0.47 g/m^2	2.9
Lead Loading	1733	0.28 mg/m^2	4.5
Lead Concentration	1731	603 μg/g	3.0

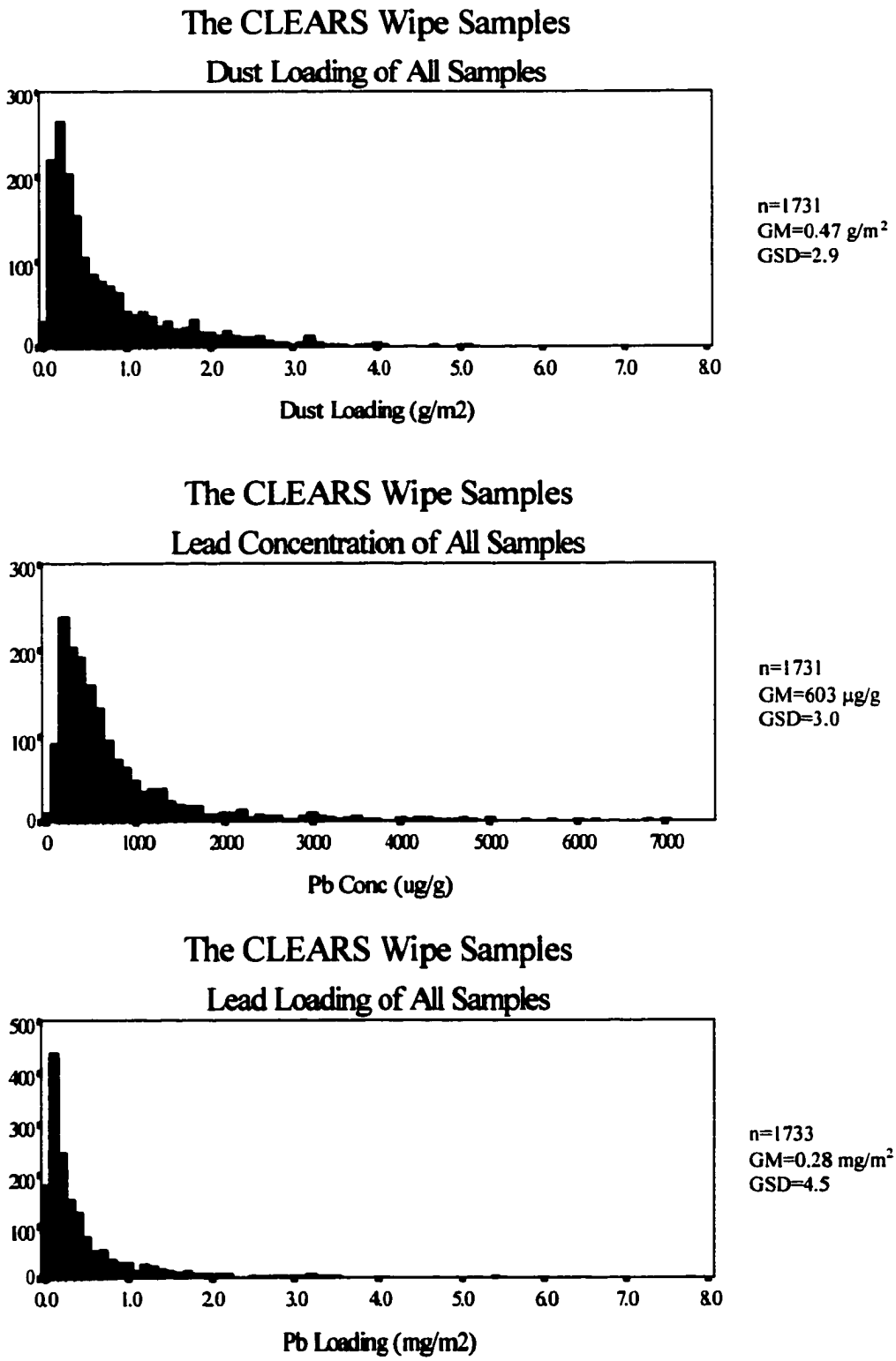

Figure 2.2 Distributions of the CLEARS Wipe Samples.

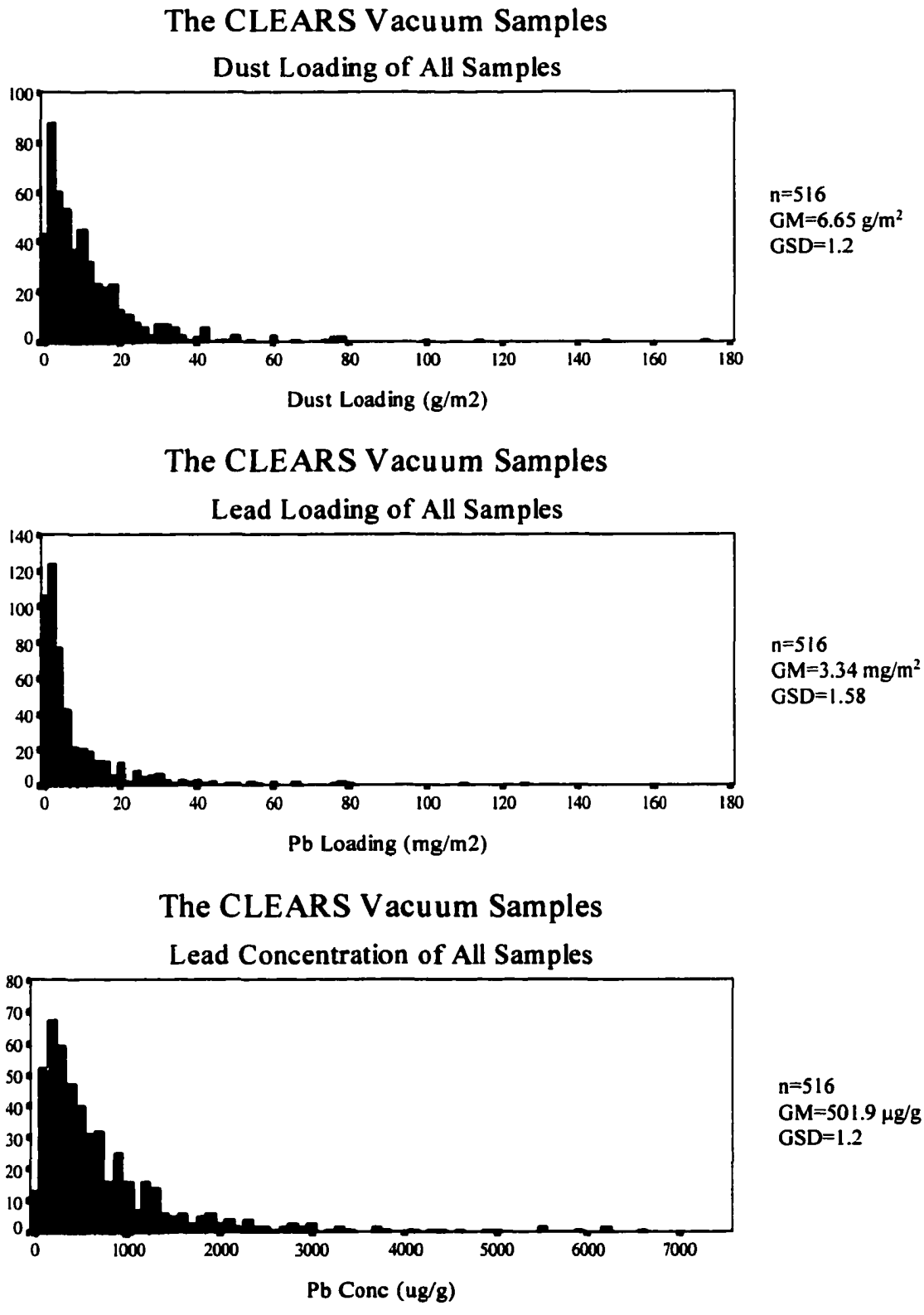

Figure 2.3 Distributions of the CLEARS Vacuum Samples.

2.4.1 Sampling Results from All Participating Homes

2.4.1.1 Wipe samples

Data for homes with at least two sampling visits were first examined for the Accident and Lead groups. Lead concentration, lead loading and dust loading derived from wipe samples taken in each residence during sampling visits 1, 2 and 3 are shown in Table 2.2a. The geometric mean lead concentrations and lead loadings measured during the second and third sampling visit in the Lead Intervention homes were lower than the levels observed in the Accident Prevention homes. Between the two intervention groups, the lead loading values were lowered by 37% and 35% for the second and third visit, respectively, and the lead concentrations were reduced by 27% and 24%, respectively. These results were analyzed for statistical significance using a t-test on the logarithms of the distributions. The mean lead loading in the Accident group was significantly different from that in the Lead group with p values of 0.001 and 0.011 for the second and third visit, respectively, while the mean lead concentrations were significantly different with p values of 0.006 and 0.016. The percent declines between the second and third visit data, however, are not directly comparable since not all homes had three sampling visits. The dust loading were lower but not statistically lower in the Lead Intervention homes, as compared to the Accident Prevention homes after the second and third visits.

Table 2.2 The Distributional Statistics for Wipe Samples and Vacuum Samples of Homes Participating in the Accident Prevention (Lead Controls) and Lead Cleaning Intervention Groups of CLEARS: Having Two or Three Visits for Sampling.

		VISIT 1			VISIT 2			VISIT 3		
		N	GM	GSD	N	GM	GSD	N	GM	GSD
A)	Wipe Sampling (Total - Undifferentiated by Room Type)									
	1. Cleaning Intervention									
	Dust Loading (g/m^2)	201	0.49	3.0	201	0.41	2.9	113	0.35	2.6
	Lead Loading (mg/m^2)	201	0.31	4.7	201	0.24	4.1	113	0.17	3.7
	Lead Concentration ($\mu g/g$)	201	633	3.4	201	570	3.2	113	484	2.7
	2. Accident Prevention									
	Dust Loading	203	0.46	3.0	200	0.49	2.9	138	0.40	2.9
	Lead Loading	203	0.31	4.0	200	0.38	4.7	138	0.26	4.1
	Lead Concentration	203	673	2.7	200	783	3.1	138	652	2.5
B)	Vacuum Sampling									
	1. Cleaning Intervention									
	Dust Loading	80	9.00	2.9	72	5.78	3.1	35	2.90	3.4
	Lead Loading	80	4.47	4.0	72	2.80	5.0	35	1.53	4.2
	Lead Concentration	80	497	2.9	72	485	3.2	35	526	2.6
	2. Accident Prevention									
	Dust Loading	80*	6.35	3.1	81	6.12	3.9	36	7.64	4.3
	Lead Loading	80	3.51	3.6	81	2.51	5.6	36	2.98	6.0
	Lead Concentration	80	553	2.8	81	410	2.3	36	390	3.0

Key: GM = Geometric Mean
GSD = Geometric Standard Deviation

* = One Mass Sample Lost

2.4.1.2 Vacuum samples

The vacuum sample results obtained from the Accident Prevention homes showed slight decreases in lead concentration for the second and third visits, while those from the Lead Intervention homes remained at the same levels (Table 2.2b). The mean dust loading and lead loading for the Lead group, however, were higher than those for the Accident group at the baseline levels (first visits). The mean dust loadings and lead loadings showed a decreasing trend for the Lead Intervention homes from the first visit to the third visit, while no significant changes were observed for the Accident homes. For the third visit, the mean dust loading in the Lead group was lower with statistical significance ($p = 0.004$). The mean lead loading in the Lead group was also lower for the third visit, but it was not significantly different from that in the Accident group ($p = 0.087$). The significant decline of dust loading in the Lead group from the first visit to the third visit indicated the effectiveness of the HEPA filter vacuum cleaner in removing dust from carpets or rugs.

2.4.2 Results for the Subset of Homes with Three Sampling Visits

To obtain a better picture of the efficacy of the Lead Intervention throughout CLEARS, the data were stratified to include only those homes in which three sampling visits were made over the course of one-year Lead Intervention. Wipe samples were categorized into several subsets according to the sampling locations in the participating homes in the Accident and Lead groups, whereas vacuum samples were not sub-divided since the sampling populations were low. The geometric means and standard deviations of the distribution analyses and the significances of repeated-measured designs for the

refined dust loading, lead loading and lead concentration data set are shown in Tables 2.3, 2.4 and 2.5, respectively.

2.4.2.1 Dust loading of wipe and vacuum samples

The comparisons of mean dust loadings between the three home visits were first examined to assess the effectiveness of the cleaning intervention. Repeated-measures design of ANOVA for the Lead Intervention homes demonstrated that the vacuum samples had a statistically significant decrease in dust loading among the three visits ($p < 0.001$), and the wipe samples derived from the windowsills also appeared a significant decline ($p < 0.001$). The 31 vacuum samples yielded a 70% decline over the three visits and were illustrated in Figure 2.4. A one-way ANOVA showed significantly different ($p = 0.05$) between any two out of the three visits for the vacuum samples, and different between the first visit and the second or third visit for the sill samples. There was a slight decrease in the bedroom subset and an increase in the living room subset, but they were not significantly different ($p = 0.082$ and 0.061, respectively). No significant change was observed in the kitchen subset. One observation in the Lead Intervention homes was that the dust loading in the bedroom and on the windowsills decreased to approximately 0.3 g/m^2, which was similar to the value obtained in the kitchen subset throughout the intervention.

In the Accident Prevention homes, there were no significant differences observed among the three visits in any subset of wipe or vacuum samples. Compared to no changes in the Accident Prevention homes (control group), the cleaning intervention in the Lead Intervention homes could be considered effective in reducing household dust.

Table 2.3 Dust Loading on Carpets and Surfaces for All Residences with Sampling Conducted Three Times Sequentially Over the Course of CLEARS in Either the Lead Intervention or the Accident Prevention Homes.

Vacuum Sampling					Wipe Sampling				
Accident Prevention (g/m^2)					Accident Prevention (g/m^2)				
Visit #	n	GM	GSD	p	Visit #	n	GM	GSD	p
					Bedroom				
1	33	4.89	3.3	0.185	1	27	0.37	2.7	0.445
2	33	5.57	5.0		2	27	0.43	3.3	
3	33	6.88	4.4		3	27	0.36	2.5	
					Living Room				
					1	21	0.29	3.3	0.790
					2	21	0.31	2.7	
					3	21	0.33	2.5	
					Windowsill				
					1	35	0.66	2.9	0.446
					2	35	0.56	2.8	
					3	35	0.53	2.8	
					Kitchen				
					1	17	0.34	2.5	0.811
					2	17	0.34	2.0	
					3	17	0.29	4.1	
Lead Intervention (g/m^2)					Lead Intervention (g/m^2)				
Visit #	n	GM	GSD		Visit #	n	GM	GSD	
					Bedroom				
1	31	10.70	2.7	< 0.001	1	22	0.49	2.6	0.082
2	31	5.70	3.3		2	22	0.32	2.4	
3	31	3.10	3.3		3	22	0.32	2.8	
					Living Room				
					1	14	0.30	3.9	0.061
					2	14	0.50	2.6	
					3	14	0.60	2.1	
Note: GM: Geometric Mean					Windowsill				
GSD: Geometric Standard Deviation					1	27	0.75	2.2	< 0.001
					2	27	0.32	3.0	
					3	27	0.29	2.2	
					Kitchen				
					1	21	0.33	2.2	0.857
					2	21	0.29	2.7	
					3	21	0.30	2.7	

Table 2.4 Lead Loading on Carpets and Surfaces for All Residences with Sampling Conducted Three Times Sequentially Over the Course of CLEARS in Either the Lead Intervention or the Accident Prevention Homes.

Vacuum Sampling					Wipe Sampling				
Accident Prevention (mg/m^2)					Accident Prevention (mg/m^2)				
Visit #	n	GM	GSD	p	Visit #	n	GM	GSD	p
					Bedroom				
1	33	3.21	3.3	0.775	1	27	0.21	2.2	0.016
2	33	2.74	5.0		2	27	0.35	3.7	
3	33	2.69	6.0		3	27	0.20	2.5	
					Living Room				
					1	21	0.15	4.1	0.571
					2	21	0.18	3.0	
					3	21	0.19	2.7	
					Windowsill				
					1	35	0.52	3.7	0.982
					2	35	0.55	4.7	
					3	35	0.53	4.7	
					Kitchen				
					1	17	0.23	3.0	0.172
					2	17	0.34	2.0	
					3	17	0.13	4.5	
Lead Intervention (mg/m^2)					Lead Intervention (mg/m^2)				
Visit #	n	GM	GSD	Prop.	Visit #	n	GM	GSD	Prop.
					Bedroom				
1	31	4.94	3.7	0.001	1	22	0.24	4.2	< 0.001
2	31	3.72	5.6		2	22	0.13	3.6	
3	31	1.71	4.1		3	22	0.12	3.5	
					Living Room				
					1	14	0.16	3.4	0.713
					2	14	0.15	2.4	
					3	14	0.18	2.3	
Note: GM: Geometric Mean					Windowsill				
GSD: Geometric Standard Deviation					1	27	0.69	4.9	< 0.001
					2	27	0.26	3.6	
					3	27	0.18	4.0	
					Kitchen				
					1	21	0.13	5.0	0.941
					2	21	0.13	4.1	
					3	21	0.12	3.3	

Table 2.5 Lead Concentration on Carpets and Surfaces for All Residences with Sampling Conducted Three Times Sequentially Over the Course of CLEARS in Either the Lead Intervention or the Accident Prevention Homes.

Vacuum Sampling					Wipe Sampling				
Accident Prevention (μg/g)					Accident Prevention (μg/g)				
Visit #	n	GM	GSD	p	Visit #	n	GM	GSD	p
					Bedroom				
1	33	657	2.5	0.055	1	27	559	1.8	0.114
2	33	492	3.3		2	27	822	3.0	
3	33	391	3.0		3	27	564	2.0	
					Living Room				
					1	21	514	2.7	0.785
					2	21	589	1.8	
					3	21	569	1.8	
					Windowsill				
					1	35	786	3.0	0.414
					2	35	967	4.2	
					3	35	1008	2.9	
					Kitchen				
					1	17	710	1.6	0.116
					2	17	615	2.7	
					3	17	478	2.5	
Lead Intervention (μg/g)					Lead Intervention (μg/g)				
Visit #	n	GM	GSD	Prop.	Visit #	n	GM	GSD	Prop.
					Bedroom				
1	31	464	3.0	0.375	1	22	660	3.3	0.033
2	31	661	3.7		2	22	385	2.2	
3	31	545	2.7		3	22	382	2.0	
					Living Room				
					1	14	540	3.7	0.039
					2	14	275	2.0	
					3	14	320	1.9	
Note: GM: Geometric Mean					Windowsill				
GSD: Geometric Standard Deviation					1	27	915	4.2	0.335
					2	27	836	3.8	
					3	27	642	4.2	
					Kitchen				
					1	21	411	3.3	0.978
					2	21	428	2.2	
					3	21	408	2.2	

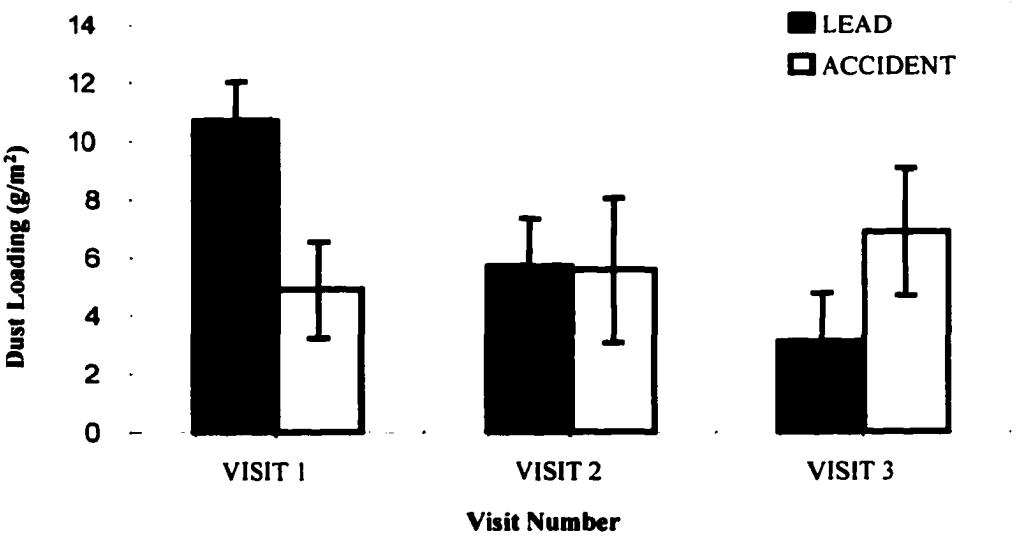

Figure 2.4 Geometric Mean Dust Loadings of Vacuum Samples for Houses Visited 3 Times.

2.4.2.2 Lead loading of wipe and vacuum samples

Lead loading, which was considered the indicator of blood lead levels for childhood lead exposure, followed the patterns of dust loading for the Accident and Lead groups. The wipe and vacuum samples in the Accident Prevention homes did not yield significant differences in lead loading between the three visits except those in the bedroom subset ($p = 0.016$). The occurrence of a peak value at the second visit might be due to some unusual contributions of lead materials to household dust. In the Lead Intervention homes, repeated-measures designs also yielded statistical significances in lead loading for the vacuum and windowsill samples ($p = 0.001$ and < 0.001, respectively). In addition, the bedroom samples, which did not had significant difference in dust loading, were significantly different in lead loading between the three visits ($p < 0.001$). There were 65%, 50% and 74% declines in lead loading for the vacuum samples, the bedroom and windowsill samples, respectively, as compared with the first and third visits. A one-way ANOVA showed a significant difference ($p = 0.05$) between the first or second visit and the third visit for the vacuum samples, and a significant difference between the first visit and the second or third visit. However, the difference between the first and third visits in the bedroom subset was found significant only at the significance level of 0.1. The lead loading in the living rooms and kitchens, as the patterns in dust loading, did not show any significant changes between the home visits.

2.4.2.3 Lead concentration of wipe and vacuum samples

The lead concentrations illustrated a different pattern. There were no statistical significances found between the three visits in the Accident Prevention homes, although some types of samples showed decreasing or increasing trends. In the Lead Intervention

homes, unlike the results for dust loading and lead loading, no statistical significances in lead concentration were found for the vacuum samples or the windowsill samples. However, there was a statistical significance in lead concentration observed for the samples derived from the bedrooms and living rooms with p values of 0.033 and 0.039, respectively. It seemed to the two types of samples that the lead concentrations were significantly reduced right after the cleaning intervention was implemented. None of the homes in either the Accident Prevention or the Lead Intervention portion of the study participated in a long term remediation program while samples were being taken during CLEARS. Therefore, the primary means for reducing the concentration were either dilution from another origin, or the lack of current input from a source that had historically contributed to the lead loading. Increases could be associated with a new source, increased flux from a current source of lead, or the selective removal of recently accumulated dust with low lead content. Seasonal different sources of lead might be considered one of the reasons which altered lead concentrations in household dust (described in Chapter 3).

2.5 Discussion

The analysis of the vacuum and wipe sampling data, and the comparisons between the Lead Intervention program homes and the Accident Prevention homes in the CLEARS indicated that a thorough cleaning program conducted over the course of a year would reduce the geometric mean dust loading and lead loading. This is true for both vacuuming of carpets or rugs, and cleaning of exposed surfaces. For the carpets or rugs, the decrease in lead and dust loading was substantial (> 75%) and progressed throughout

the study. The result was consistent with the preliminary studies of Roberts *et al.* (1995b) who indicated that intensive cleaning was necessary to begin to remove lead deeply embedded in a carpet or rug. However, the result did not support the work of Ewer *et al.* (1994) who indicated that vacuuming did poorly in removing embedded lead from used rugs.

For the exposed surfaces, the decrease in dust and lead loadings for windowsill and bedroom samples was significant at the second visit as compared to the baseline level, but the decrease between the second and third visits was minimal. This might imply that one time cleaning intervention work was effective in reducing the PbDs of the exposed surfaces to the background level, and that regular lead sources did not contribute much contamination by the next cleaning intervention. There were, however, no significant differences found for the samples obtained in the living rooms or kitchens between the home visits. It is probably because living rooms and kitchens are very frequently used areas in the home environments, and the leaded dust was not easily deposited on the surfaces. Therefore, the PbDs on those surfaces remained as low as the background level, and did not have significant changes with application of the cleaning intervention.

The lead concentration results appeared different. In the Lead Intervention homes, wipe samples showed a significant decrease in lead concentration over time in the bedroom and living room subsets ($p = 0.033$ and 0.039, respectively). The suggestion here is the presence of historically high lead content materials on the surfaces prior to the first sampling visit, and before the start of the home Lead Intervention. The values could have been derived from a particular source (e.g. automotive exhaust) or series of events

that deposited led enriched dust (e.g. deterioration of a wall or periodic tracking of lead indoors). In other sample subsets of the Lead group and all sample subsets of the Accident group, lead concentrations between the three visits were not significantly different. They agreed with the fact that no homes in the two intervention groups participated in a long-term remediation program. Seasonally different sources of lead might result in a slight decrease in lead concentration for some sample subsets (e.g. vacuum samples in the Accident Prevention homes), because samples included for the three visits were not derived from the same seasonal patterns.

Based upon the micro-environmental sampling and analysis of lead in house dust, it is apparent that a Lead Intervention will significantly reduce the geometric mean lead loadings in rugs and on surfaces that can be touched by a child. This should result in less lead adhering to a child's skin, objects used for play, or food consumed while at play (National Research Council, 1993). Thus, it would be possible to have the actual exposure and internal dose decline in the children participating in CLEARS Lead Intervention group. This has been documented in a manuscript by Rhoads *et al.* (1999) for children participating in the Lead Intervention. There was a mean reduction in blood lead values of 2.2 μg/dl for the children from the Lead Intervention homes and < 0.17 μg/dl for those in the Accident Prevention homes. Further investigation for the cleaning effect in reducing children's blood lead concentrations on various floor-surfacing homes (e.g. carpeted or bare-floor paved) will be described in Chapter 4.

The study also showed that a consistent cleaning protocol, and, as a logical extension, prevention of exposure must focus on cleaning locations where a child participates in indoor activities, and contacts lead burdened surfaces. Further, rugs and

other freely accessible surfaces must be cleaned or periodically replaced to reduce the total potential lead burden in a child. This is necessary since it is possible that contamination on surfaces, such as tables, cannot be effectively reduced below a baseline value, which would be some function of the general characteristics of the home environment. This point is supported by (1) the difficulty in reducing the geometric mean lead loading of the wipe samples below 0.12 mg/m^2 in the kitchens and the living rooms of the Lead Intervention homes, and (2) reductions in the bedrooms and on the windowsills had trends toward the mean of 0.12 mg/m^2. A similar phenomenon was observed for dust loading.

Finally, two aspects of the CLEARS protocol suggest that it should be possible to implement a modified strategy for use by families with lead burdened homes to reduce exposure. First, the personnel trained for the CLEARS were not scientists or laboratory technicians. Second, the CLEARS employed many readily available methods and materials to conduct the intervention. The most sophisticated item was the HEPA vacuum cleaner, and in recent years a number of manufacturers are producing commercial models that are in a price range (< $400.00) that is affordable by the general public.

CHAPTER 3: SEASONAL INFLUENCES ON CHILDHOOD LEAD EXPOSURE

3.1 Introduction

Childhood lead exposure was discovered to vary with seasons. Several studies have reported that blood lead levels are higher in the summer months than at other times of year (Hunter, 1977; Hunter, 1978; Stark *et al.*, 1980; Rabinowitz *et al.*, 1985; Rothenberg *et al.*, 1996). Some animal experiments implemented by gavaging lead compounds over various seasons have suggested that solar radiation, through its effect on the biosynthesis of vitamin D, may be the main reason for the seasonality of plumbism (Hunter, 1977; Barton and Huster, 1987). These studies indicate that vitamin D, which promotes calcium absorption, unfortunately, may also promote lead absorption. However, some investigators have found no relationship between vitamin D and blood lead levels (Laraque *et al.*, 1990; Koo *et al.*, 1991), or an inverse relationship (Sorrel and Rosen, 1977; Mahaffey *et al.*, 1982).

The control group in CLEARS, which were not affected by the cleaning intervention and provided blood and dust data over the calendar year, allowed an examination of seasonality of dust lead and blood lead in urban environments. The seasonality in CLEARS might result from different exposure mechanisms during each season. Included would be source strengths, patterns of exposure and the absorption of lead from the gastrointestinal tract. Since the role of vitamin D in affecting internal lead absorption was still ambiguous, the analysis of seasonality in this chapter was focused on sources and patterns of exposure. Data on preschool children's blood lead levels and lead

in household dust present on floor, windowsills and carpets, and children's outdoor activities were divided into seasonal groups. Mean comparisons, correlations and regression analyses for blood lead and dust lead data were performed to investigate the seasonality of childhood lead exposure.

3.2 Background

Only the blood lead and dust lead data collected from the control group of CLEARS were used to determine seasonal relationships. Selection of this database was based on the fact that families in the control group did not receive the cleaning intervention, and the household dust lead and blood lead data did not show significant changes between home visits (Chapter 2; Rhoads *et al.*, 1999). The sample populations yielded 313 blood samples, 177 carpet samples, 413 floor wipe samples, and 214 windowsill samples from 135 children in 67 families. Nineteen families (28.4%) moved during the study, but since those movements were within local areas and they still met the protocol design, they were not removed from the study. Soil and street dust samples (n = 205), representing outdoor lead content, were used to sketch out the lead distribution in the urban area of Jersey City. The blood data were examined for seasonality by plotting monthly blood lead concentrations with corresponding outdoor and indoor temperatures (Figure 3.1). The indoor temperatures were recorded at the home visits. The average outdoor temperature during each month of the study is shown in Table 3.1. The mean temperature for the year, 51 °F, conveniently divided the data into two groups. Data collected from April through September were broadly categorized as the Summer Group; while data collected during the other six months were categorized to the Winter group.

The average temperatures of April and October were on the borderline of the mean of 51 °F, and April was allocated to the Summer group and October was to the Winter group. The data categorization for seasonality was conducted before any preliminary data analysis was attempted.

Table 3.1 The Profile of Average Temperatures during the Period of CLEARS.

Year	Month					
	Jan	Feb	Mar	Apr	May	Jun
1992						66.9
1993	35.3	28.8	36.9	50.7	62.2	69.6
1994	24.1	28.9	39.4	53.8	58.1	72.7
1995	36.3	29.2	43.7	49.9	59.4	69.7
Mean	31.9	29.0	40.0	51.5	59.9	69.7
Year	**Month**					
	Jul	Aug	Sep	Oct	Nov	Dec
1992	72.9	69.6	56.1	50.9	44.4	35.6
1993	76.9	73.7	65.5	52.5	44.2	33.9
1994	77.1	70.4	64.3	52.8	49.2	39.2
1995	76.5	74.6	66.1			
Mean	75.9	72.1	63.0	52.1	45.9	36.2

All values in Fahrenheit scale. Sources from "the Office of the New Jersey State Climatologist," (http://climate.rutgers.edu/stateclim/).

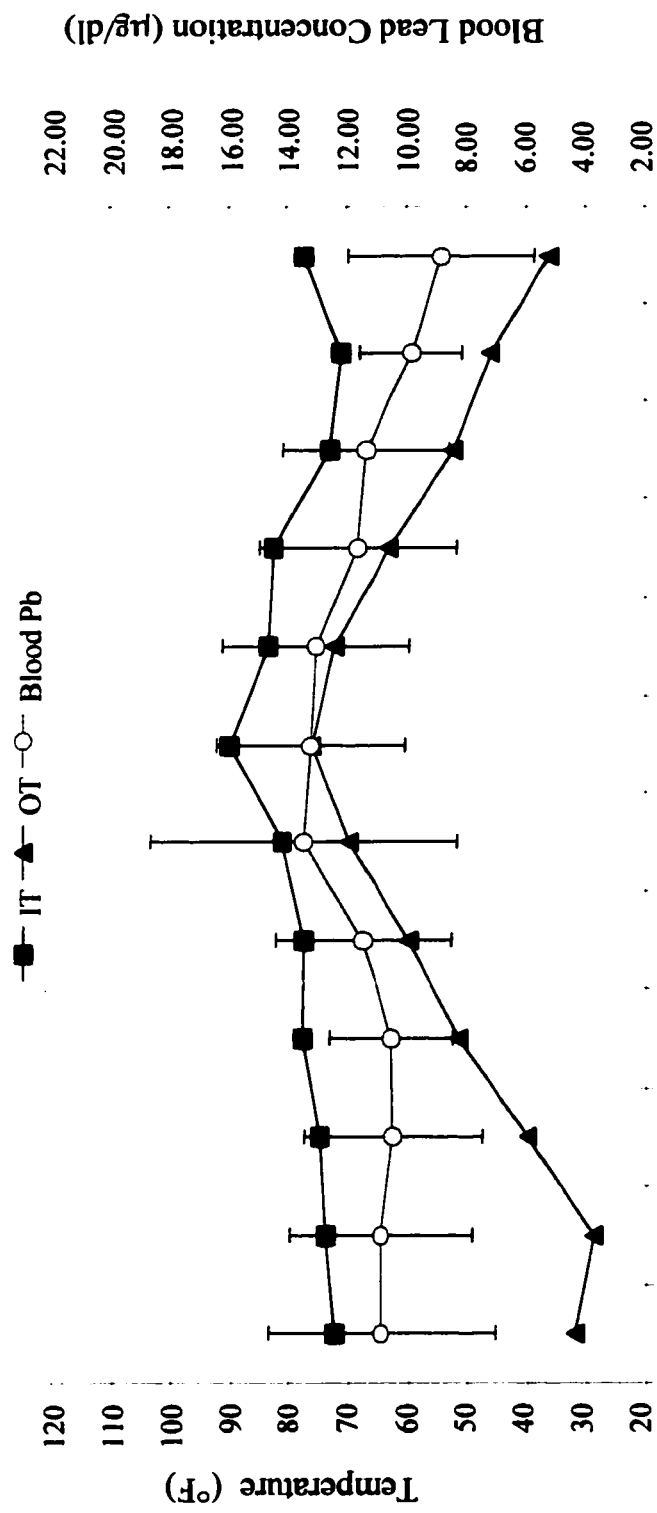

Figure 3.1 Monthly Mean Blood Lead Concentrations vs. Indoor and Outdoor Temperatures (IT and OT). Error Bars Represent Stardard Deviations.

3.3 Methods

The sample collections and analyses for wipe and vacuum sampling in CLEARS were described in Chapter 2.

3.3.1 Sample Collection

3.3.1.1 Blood sampling and handling

Blood specimens were obtained from participating children by venipuncture using needles and vacuum tubes from lots that were pre-checked for blood contamination. Sampling supplies were prepared by the CDC, Nutritional Biochemistry Branch, Atlanta, Georgia. Blood was collected by standard venipuncture into 3-ml lavender-top Vacutainer tubes. We tried to obtain at least 1.5 ml of blood was taken per sampling to assure sufficient quantity for processing and to avoid incomplete mixing with the anticoagulant (EDTA). Specimens were labeled and initialed by the collector immediately after sampling, and were refrigerated at 4 °C during the storage. Samples were air-shipped on ice to Atlanta, GA for analysis at the Nutritional Biochemistry Branch, CDC (Rhoads and Lioy, 1992).

3.3.1.2 Soil and street dust sampling

Soil and street dust samples were collected from child's outdoor primary activity areas (e.g. backyards and parks) and primary entryways outside the households (stairs, steps and sidewalks). At least 10 grams of soil or dust was required for each sample. A paint brush and a dustpan were used to sample and transfer street dust to a labeled zip-lok polyethylene bag. A soil sampling ring (4 inches in diameter and half an inch in width), cut from PVC tubing, was used to circumscribe the soil by pressing it firmly into the

ground, and a small plastic shovel was used to collect the soil and to transfer to a labeled zip-lok bag. The collecting tools were cleaned between samplings to prevent sample contamination. The soil and street dust samples were delivered to the National Exposure Research Laboratory of the United States Environmental Protection Agency, North Carolina for further analyses.

3.3.2 Sample Analysis

3.3.2.1 Blood samples

Blood specimens received by CDC were analyzed for lead content by electrothermal atomization atomic absorption spectrometry (EAA, Perkin Elmer 5000) using a process described by Miller *et al.* (1987). The EAA was used with a deuterium background correction and set at 283.3 nm for lead analysis. The blood samples were carefully handled by the analysts who wore gloves, laboratory coats and safety goggles. A matrix modifier, containing 0.2% (v/v) nitric acid, 0.5% (v/v) Triton X-100, and 0.2% (w/v) ammonium phosphate, was prepared for 10-fold sample dilutions. Two-level bovine and human blood quality control pools (5 and 20 μg/dl) were used during the blood lead analysis. All the biological samples and diluted specimens were disposed in a biohazard autoclave bag at the end of analysis.

3.3.2.2 Soil and street dust samples

Each soil and street dust sample was prepared for analysis by drying to a constant weight, sieving, grinding, and forming a compressed disk. Drying to a constant weight was accomplished by placing the soil or street dust evenly onto a plastic coated paper plate for 24 hours in a ventilated hood. After the drying, the sample was initially sieved

using a #10 mesh (2 mm) sieve. The coarse fraction of the sample, remaining within the sieve, was discarded, while the fine fraction was homogenized and split into ¼ and ¾ fractions. The ¼ fraction of sample was stored for potential CCSEM (Computer Controlled Scanning Electron Microscopy) analysis. The ¾ fraction was then sieved using a #60 mesh (250 μm) sieve. The coarse portion (> 250 μm) was discarded and the fine portion was ground to a fine slurry using a Chemplex Mill™ and analytical grade 2-propanol. The slurry was evaporated under a heat lamp in the hood.

The resulting fine powder was placed into a plastic vial with a plastic bead added, and the sample was placed in a Spex Mill™ for 5 minutes to break up the sample. The contents of the sample were weighed using an analytical balance. A binder (Chemplex Grinding and Briqutting Additive™) was added to the sample 5-10 percent by weight. The binder/sample mix was transferred again to a vial with a plastic bead and homogenized for 5 minutes using the Spex Mill™. The homogenized mixture was transferred to a Bechman™ hydraulic press and compressed to 20 tons to form a 31 mm sample disk. The disk was analyzed for lead content using an energy dispersive X-ray spectrometry (XRF-Kevex™).

3.3.3 Data Analysis

The data for the CLEARS control group were categorized by the previously defined Summer and Winter groups. They were analyzed by two independent approaches: individual samples (IS) and home visits (HV). On the individual-sample basis, every blood or dust sample collected in the CLEARS control group was used as a unit in the statistical analyses regardless of correspondence between the blood and dust

data. The IS-based analyses, which comprised as many valid samples as possible, helped establish the profiles of seasonal variation. When "home visit" was used as a unit in statistical analyses, interest focused on the relationships between blood and dust data. Thus, we only selected data which had corresponding blood and dust samples (i.e. blood and dust samples were collected within a 2-month period for each home visit), and used a representative pair of blood and dust sample results for each home visit. For home visits with multiple blood or dust samples, the geometric means of the all blood or dust data were used in statistical analyses. Unpaired blood or dust data (i.e. no corresponding dust or blood data) were not used in the HV-based analyses.

Data for children's outdoor activity patterns were obtained from the questionnaires of the Jersey City Child Health Study: Food and Eating Habit Survey, which provided the information of foods that participating children ate, dining places (indoor or outdoor), frequency of outdoor activities, and storage and preparation of food. There were 119 questionnaires with complete data of frequency of children's outdoor activities in weekdays and weekends (Figure 3.2). To be consistent with the selection of blood and dust data, only the outdoor activity data obtained in the Accident Prevention homes were used. The outdoor data were categorized into the two major seasonal groups by the dates when the questionnaires were completed, and were statistically analyzed for the examination of outdoor lead exposure.

The IS-based data were selected for comparing blood and dust data between the seasonal groups. The seasonal groupings were further divided into four 3-month subsets according to the temperature profile. June, July and August, which are considered summer, were defined as the Hot set; the other months in the Summer group (April, May

and September) were labeled as the Warm set. December, January and February, the coldest months in a year, were defined as the Cold set; while the other months in the Winter group (March, October and November) were labeled as the Cool set. Since all the blood and dust data appeared log-normally distributed (Figure 2.2, 2.3 and 3.3), they were geometrically transformed prior to conducting statistical analyses. Independent-sample t-tests (2-tailed) were used to examine the significances of means for blood and dust data between the two seasonal groups and their respective subsets.

For each single mean comparison of blood or dust data, a 95% confidence interval was used to determine the significance. Since there were 10 mean comparisons of blood and dust data for seasonality, the chance to observe a single significant difference out of 10 comparisons would be higher than 5%. Thus, for multiple-comparisons analysis, an adjustment called the Bonferroni method was needed to have a 95% joint confidence region over the combination of 10 comparisons. The Bonferroni method was to divide the α level (0.05) for each single comparison by the number of comparisons (10) to have the overall α level equal 0.05.

Spearman correlation analyses were completed for the whole HV-based blood and dust data (floors, sills and carpets). The objective was to determine if there were any significant correlations, and which variable, lead concentration, dust loading or lead loading, had the best associations with blood data. Analyses within the Summer and Winter groups were performed to observe any relationships between blood and dust data for seasonal groupings.

Stepwise multiple linear regression analysis was performed using the HV-based data to determine if any seasonal factors, besides the dust lead levels, would affect

children's blood lead levels. The four seasonal subsets (Hot, Warm, Cool, Cold) and the dust variables (lead concentration, lead loading and dust loading) for floor, sill and carpet samples were used as the independent variables for the regression analysis. The stepwise multiple linear regression model is stated as:

$$Y = B_0 + (B_1S_1 + B_2S_2 + B_3S_3) + (B_4X_1 + B_5X_2 + B_6X_3 + \cdots)$$

where

Y represents log-transformed blood lead concentration.
S represents the seasonal subset (S_1 = Hot, S_2 = Warm, and S_3 = Cool).
X_i represents the entered dust lead variable (lead concentration, lead loading or dust loading). i = 1, 2, 3...
B_0 is the constant, and
B_j is the coefficient of independent dust variable. j = 1, 2, 3...

The seasonal subset in which a pair of blood and dust samples were collected was scored as 1, and the other three subsets would be zeroes. For example, samples in the Hot set and the scores would be 1, 0, and 0 for S_1, S_2, and S_3, respectively; the scores for samples in the Cold set would be all zeroes. The entering of dust variables to the equation was determined by the significance of correlations between the dust variables and blood lead concentration. The dust variable, which was the most correlated with the dependent variable (blood lead concentration), was entered into the equation and then the rest of variables were re-calculated to determine the significance of correlations. The entering sequence was repeated until the significance criterion could not be met. The selection of dust variables for the regression analysis followed the commonly used criteria ($p \leq 0.05$ to enter and $p \geq 0.10$ to remove) to derive the best results. If the regression model yielded any independent variable out of the seasonal subsets, it indicated that the blood lead concentration would be affected other seasonal factors than the seasonality of dust lead

levels. The analyses were performed separately for carpeted and uncarpeted houses, since not every house had both floor and carpet data available. There would be many missing values in the columns for floors or carpets in case all the data were used to perform the stepwise linear regression, and the result could be biased. To reduce the occurrences of missing data, the separate analyses for carpeted and uncarpeted houses were necessary.

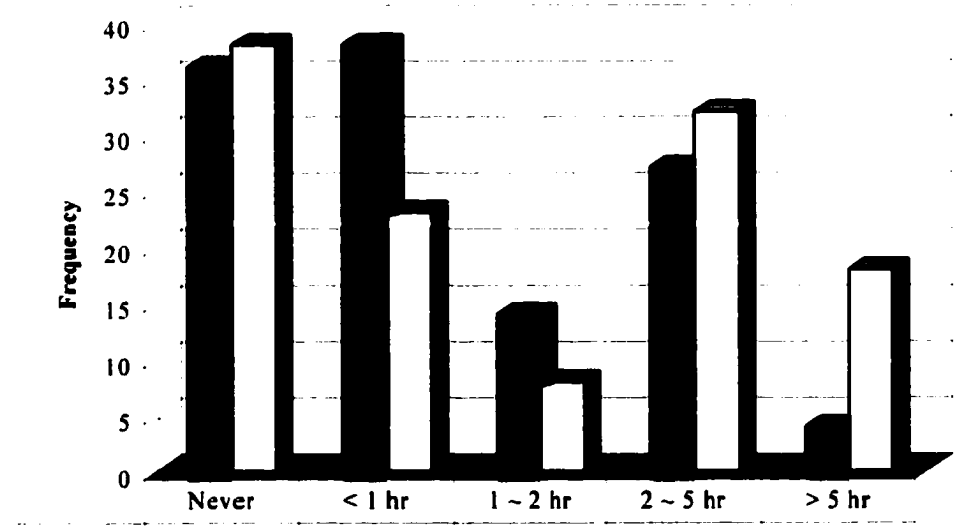

Figure 3.2 The Distribution of Children's Outdoor Playtime.

3.4 Results

The summary statistics of whole blood and dust data for the seasonality section are shown in Table 3.2. The geometric mean of blood data was 9.56 μg/dl with the peak concentration of 48.4 μg/dl. The indoor lead profiles were represented by floor, windowsill and carpet samples, while the outdoor lead concentration was shown by soil/street dust samples. The mean lead concentrations of floor, sill (wipe) and carpet (vacuum) samples were 613.0, 945.5 and 471.4 μg/g, respectively. Among the three types of dust samples, sill samples had the highest lead concentration, while carpet samples had the lowest lead concentration. This is probably because windowsills usually contain flaking paint chips or fragments to raise the mean concentration, and carpets are very likely to accumulate non-lead dust particles that may dilute the lead concentration. All these mean lead concentrations were higher than the outdoor lead cleanup standard in New Jersey (400 μg/g). The mean dust loadings for floor, sill and carpet samples were 0.39, 0.70 and 6.86 g/m^2, respectively, demonstrating that carpets were a larger reservoir of dust than floors and sills. Lead loading, a product of lead concentration and dust loading, had a geometric mean of 0.24, 0.66 and 3.23 mg/m^2 for floors, sills and carpets, respectively. The outdoor soil/street dust samples showed high mean lead concentration of 1052 μg/g, 1.7 and 2.2 times higher than those of floor and carpet samples, respectively.

Table 3.2 General Lognormal Distribution Parameters for all Blood, Floor, Sill, and Carpet Samples for the Seasonality Analysis.

Blood	n	GM	GSD
Lead Concentration	313	9.56 μg/dl	1.8
Floor (wipe)	**n**	**GM**	**GSD**
Dust Loading	413	0.39 g/m^2	3.0
Lead Loading	413	0.24 mg/m^2	3.7
Lead Concentration	413	613.0 μg/g	2.6
Sills (wipe)	**n**	**GM**	**GSD**
Dust Loading	214	0.70 g/m^2	2.7
Lead Loading	214	0.66 mg/m^2	5.1
Lead Concentration	214	945.5 μg/g	3.5
Carpet (vacuum)	**n**	**GM**	**GSD**
Dust Loading	245	6.86 g/m^2	3.6
Lead Loading	245	3.23 mg/m^2	5.4
Lead Concentration	245	471.4 μg/g	3.2
Soil/Street Dust	**n**	**GM**	**GSD**
Lead Concentration	205	1052 μg/g	2.6

GM: geometric mean. GSD: geometric standard deviation.

3.4.1 Results of Two Seasonal Groups

The distributions of blood samples in the Winter and Summer groups are shown in Figure 3.3. The mean blood concentrations were significantly different between the two groups with the values of 10.44 and 8.61 μg/dl for the Summer and Winter groups, respectively ($p = 0.004$). This represented 17.5% lower in blood lead concentration of the Winter group in houses without a cleaning intervention. Consistent with the blood data, most of the dust data on Table 3.3 showed the seasonal effects. For the floor samples, lead loadings and lead concentrations were 21.4% and 11.5% lower for the Winter group, respectively, but the differences were not statistically significant. The comparison for the sill samples showed a 17.1% lower value in the Winter group for dust loading, although the difference was not statistically significant. In contrast, the carpet samples had significantly higher dust loadings and lead loadings in the Winter group than those observed for the Summer group ($p < 0.001$ and $p = 0.002$).

3.4.2 Results for Four Seasonal Subsets

All the blood and dust data were re-organized according to the four seasonal subsets (Table 3.4). Blood lead concentrations showed a decrease in following the order: the Hot, Warm, Cool and Cold subsets. A PbB difference of 3.11 μg/dl was found between the Hot and Cold sets. Lead loadings for the floor and sill samples were the highest in the Hot subset, although they were not significantly different from the other subsets. Lead concentrations were high in the Hot subset for all three types of dust samples (floor, sill and carpet), but they were low in sills and carpets in the Warm subset.

In contrast, the carpet samples had higher levels of lead loading and dust loading in the Cool and Cold sets.

3.4.3 Correlations of Blood and Dust Data

There were 140 pairs of blood-floor dust samples, 134 pairs of blood-sill dust samples, and 95 pairs of blood-carpet dust samples available for Spearman correlation analysis. The three dust variables: lead concentration, lead loading and dust loading were compared with blood lead concentrations (Table 3.5). The highest correlations with blood lead concentration were found lead loading for floor and sill samples (r = 0.41, 0.37), and lead concentration for carpet samples (r = 0.40), illustrated in Figure 3.4, 3.5 and 3.6 for blood lead concentration versus floor lead loading, sill lead loading and carpet lead concentration, respectively. The low correlation coefficient for sill lead and blood lead may result from the significant variability possessed by the sill samples. This is consistent with Adgate *et al.* (1995), who reported high variability for sill samples in the study of exposure metrics for CLEARS. The black and white dots plotted in Figure 3.4, 3.5 and 3.6 represent data in the Winter and Summer groups, respectively. Within the two seasonal groups, blood concentration had higher correlations with floor lead loading and carpet lead concentration in the Winter group (r = 0.49, 0.46) than in the Summer group (r = 0.33, 0.39). In contrast to the floor and carpet samplings, sill lead loading showed higher correlation with blood concentration in the Summer group (r = 0.43) than in the Winter group (r = 0.29).

Table 3.3 Blood, Floor, Sills, and Carpets Data of the Summer and Winter Groups.

	Summer Group		Winter Group		
	n	GM (GSD)	n	GM (GSD)	p
Blood Concentration (μg/dl)	170	10.44 (1.8)	143	8.61 (1.9)	0.004
Floor (wipe)					
Dust Loading (g/m^2)	229	0.40 (2.8)	184	0.38 (3.2)	NS
Lead Loading (mg/m^2)	229	0.28 (3.6)	184	0.22 (3.9)	0.178
Lead Concentration (μg/g)	229	647.1 (2.5)	184	573.0 (2.7)	0.194
Sill (wipe)					
Dust Loading (g/m^2)	123	0.76 (2.7)	91	0.63 (2.7)	0.156
Lead Loading (mg/m^2)	123	0.73 (5.1)	91	0.58 (5.0)	NS
Lead Concentration (μg/g)	123	964.7 (3.3)	91	920.2 (3.9)	NS
Carpet (vacuum)					
Dust Loading (g/m^2)	127	5.22 (3.4)	118	9.21 (3.6)	<0.001
Lead Loading (mg/m^2)	127	2.35 (6.1)	118	4.56 (4.4)	0.002
Lead Concentration (μg/g)	127	450.4 (3.3)	118	495.3 (3.0)	NS

NS: not significantly different.

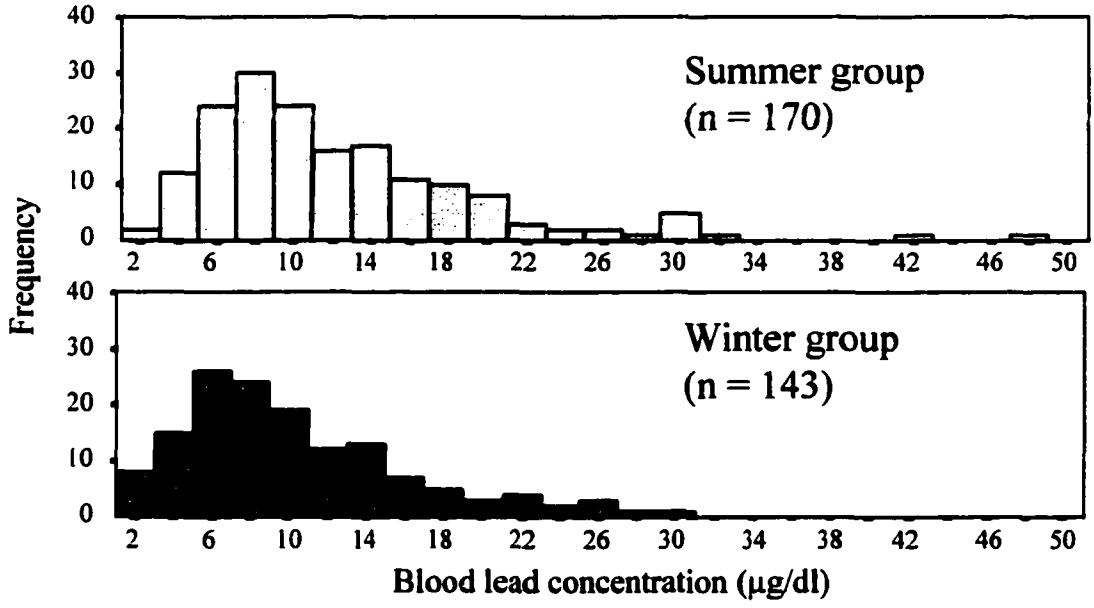

Figure 3.3 Blood Lead Distributions of the Summer and Winter Groups.

Table 3.4 Blood and Dust Data of the Subsets of the Two Seasonal Groups.

	Summer Group		Winter Group	
	Hot	Warm	Cool	Cold
Blood				
n	89	81	68	75
Lead Concentration (μg/dl)	10.77 (1.9)	10.08 (1.6)	9.5 (1.6)	7.66 (2.0)^S
Floor (wipe)				
n	82	147	108	76
Dust Loading (g/m^2)	0.40 (2.8)	0.39 (2.7)	0.38 (3.3)	0.37 (3.0)
Lead Loading (mg/m^2)	0.31 (3.6)	0.23 (3.6)	0.23 (4.0)	0.19 (3.7)^S
Lead Concentration (μg/g)	766.6 (2.5)	588.7 (2.5)^S	608.9 (2.8)	525.4 (2.5)^S
Sills (wipe)				
n	56	67	43	48
Dust Loading (g/m^2)	0.70 (2.6)	0.82 (2.7)	0.57 (2.5)	0.68 (2.9)
Lead Loading (mg/m^2)	0.84 (4.1)	0.65 (6.0)	0.48 (5.7)^S	0.68 (4.3)
Lead Concentration (μg/g)	1214.3 (3.0)	795.8 (3.4)^S	834.9 (4.1)	1004.1 (3.8)
Carpet (vacuum)				
n	75	52	56	62
Dust Loading (g/m^2)	4.43 (3.4)	6.59 (3.3)	9.56 (3.3)^S	8.91 (3.9)^S
Lead Loading (mg/m^2)	2.61 (6.2)	2.01 (5.9)	5.05 (4.7)^S	4.16 (4.2)
Lead Concentration (μg/g)	589.3 (3.4)	305.6 (2.8)^S	528.7 (3.5)	466.8 (2.6)

Data are in geometric means (GSD in parenthesis). S denotes significant difference from the Hot subset ($p = 0.05$).

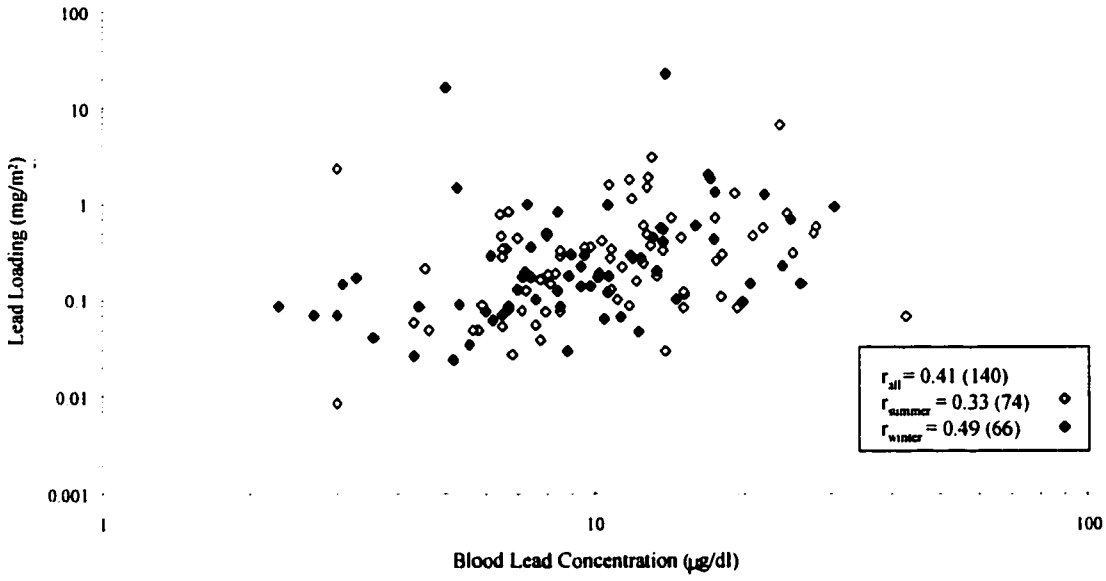

Figure 3.4 Scatterplot between Blood Concentrations and Floor Lead Loadings (r: Spearman correlation coefficient [p = 0.001]. Sample number in parenthesis).

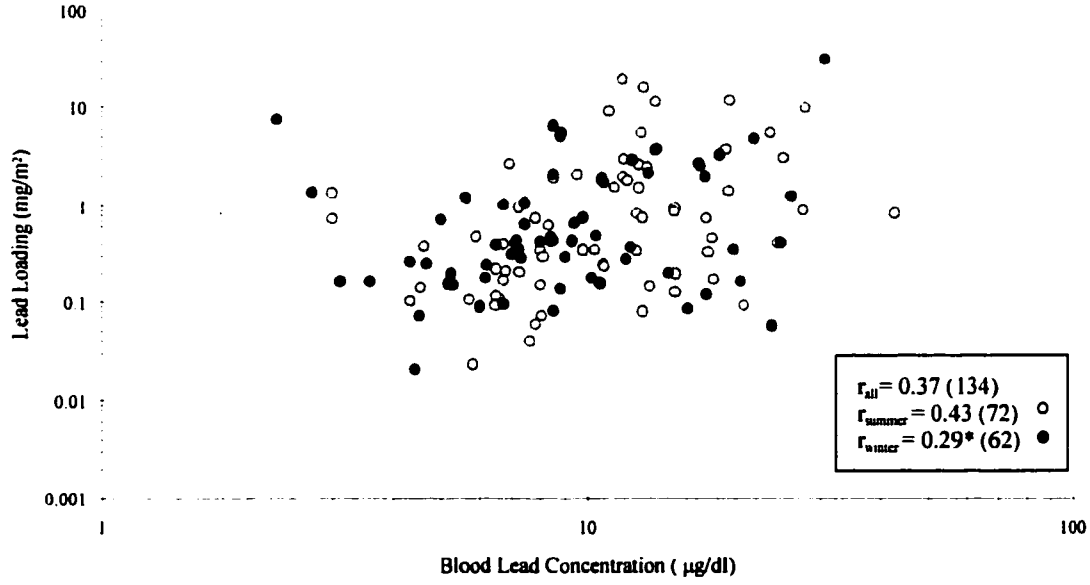

Figure 3.5 Scatterplot between Blood Concentrations and Sill Lead Loadings (r: Spearman correlation coefficient [p = 0.001, except * 0.05]. Sample number in parenthesis).

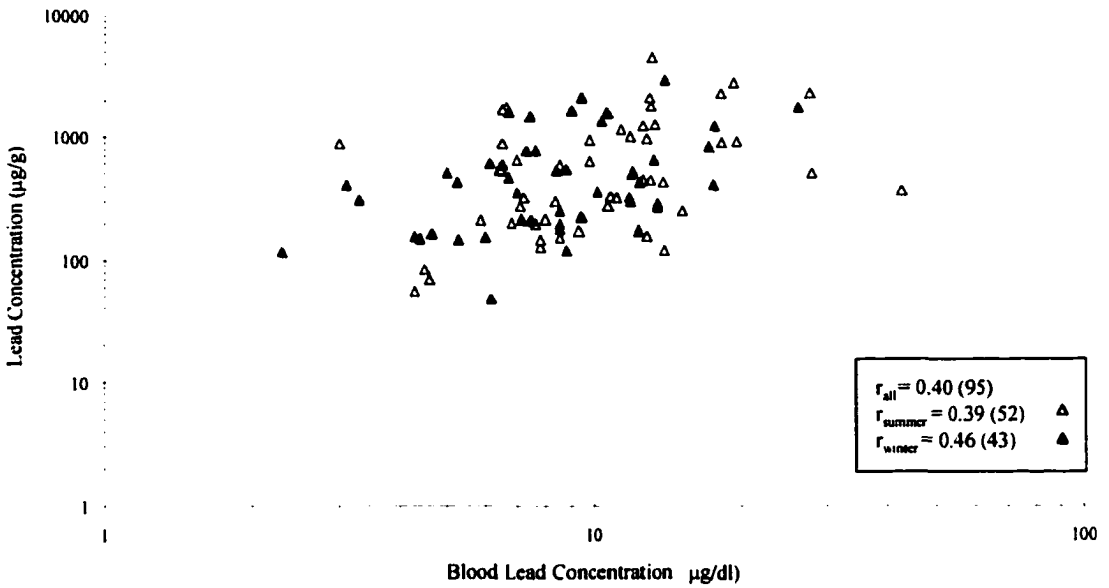

Figure 3.6 Scatterplot between Blood Concentrations and Vacuum Lead Concentrations (r: Spearman correlation coefficient [p = 0.001]. Sample number in parenthesis).

Table 3.5 Spearman Correlation Coefficients of Blood Concentration and Corresponding Dust Data (CLEARS).

	Number of Pairs	Correlation Coefficient	Probability
Floor			
Dust Loading (g/m^2)	140	0.23	0.006
Lead Loading (mg/m^2)	140	**0.41**	< 0.001
Lead Concentration (μg/g)	140	0.24	0.005
Sill			
Dust Loading (g/m^2)	134	0.26	0.003
Lead Loading (mg/m^2)	134	**0.37**	< 0.001
Lead Concentration (μg/g)	134	0.29	0.001
Carpet			
Dust Loading (g/m^2)	95	- 0.04	0.682 *
Lead Loading (mg/m^2)	95	0.22	0.033
Lead Concentration (μg/g)	95	**0.40**	< 0.001

Best correlation coefficient of each sample type in bold.
*: not significant.

Table 3.6 Coefficients of Stepwise Multiple Linear Regression.

	Unstandardized Coefficients		Standardized Coefficients	
	B	Standard Error	Beta	Significance
Carpeted Households				
Constant	0.712	0.177		< 0.001
Log_{10}(Carpet PbC)	0.272	0.062	0.517	< 0.001
Log_{10}(Sill PbL)	0.121	0.037	0.335	0.002
Log_{10}(Floor PbC)	-0.160	0.067	-0.282	0.020
Uncarpeted Households				
Constant	1.262	0.049		< 0.001
Log_{10}(Floor PbL)	0.311	0.057	0.634	< 0.001

PbL denotes Lead Loading.
PbC denotes Lead Concentration.

3.4.4 Regression Analysis of Blood and Dust Data

There were 74 pairs of blood, floor, sill and carpet data for the carpeted households and 46 pairs of blood, floor and sill data in the non-carpeted households, used for the stepwise multiple linear regression analysis. The regression model, as expected, included the three highest-correlated variables (floor lead loading, sill lead loading and carpet lead concentration) in the equations, and was completed for the carpeted households:

$$Log_{10}BloodPbC = (0.712 \pm 0.177) + (0.272 \pm 0.062)Log_{10}CarpetPbC + (0.121 \pm 0.037)Log_{10}SillPbL + (-0.160 \pm 0.067)Log_{10}FloorPbC, \quad R^2 = 0.337 \cdots (3.1)$$

and for the uncarpeted households:

$$Log_{10}BloodPbC = (1.262 \pm 0.049) + (0.311 \pm 0.057)Log_{10}FloorPbL, \quad R^2 = 0.403 \cdots (3.2)$$

where

PbC: Lead concentration.
PbL: Lead loading.

The standardized coefficients, an indication of the importance of independent variables to the dependent variable, were shown on Table 3.6 for the carpeted and uncarpeted households. The lack of any other seasonal variables in the above indicate they did not have significant influences on children's blood lead concentrations. The form of the model used is consistent with the work of Rust *et al.* (1997), who indicated that log-linear model should be the default model for developing blood lead-dust lead relationship.

3.4.5 Outdoor Activity Patterns for Two Seasonal Groups

There were 29 and 27 households with questionnaires completed during the Summer and Winter periods, respectively. Data for weekdays and weekends are separately distributed in Figure 3.7. Approximately 80% of the non-intervened families never or seldom (< 1 hour) let their children play outdoors on either weekdays or weekends during the Winter period. However, during the Summer period, only about 50% and 35% of the families limited their children playing outdoors (never and < 1 hour) on weekdays and weekend, respectively. Playing outdoors for 2 through 5 hours was common for most families in the Summer group. Therefore, children playing longer outdoors would have greater opportunities to be in contact with lead present in street dust or soil.

3.5 Discussion

The blood lead levels of the children that were not part of the CLEARS cleaning intervention were highest during our broadly defined summer session, and the Hot subset appeared to be associated with the highest blood lead levels. The finding of high blood lead concentration in the summertime for non-intervened children agrees with the results found in previous studies (Hunter, 1977; Hunter, 1978; Stark *et al.*, 1980; Rabinowitz *et al.*, 1985; Rothenberg *et al.*, 1996). In addition, the finding of associations between blood lead and dust lead was consistent with lead studies conducted over the last two decades (Charney *et al.*, 1983; Bornschein *et al.*, 1986; Thornton *et al.*, 1990; Davies *et al.*, 1991; Clark *et al.*, 1991; Cambra and Alonso, 1995; Lanphear *et al.*, 1996).

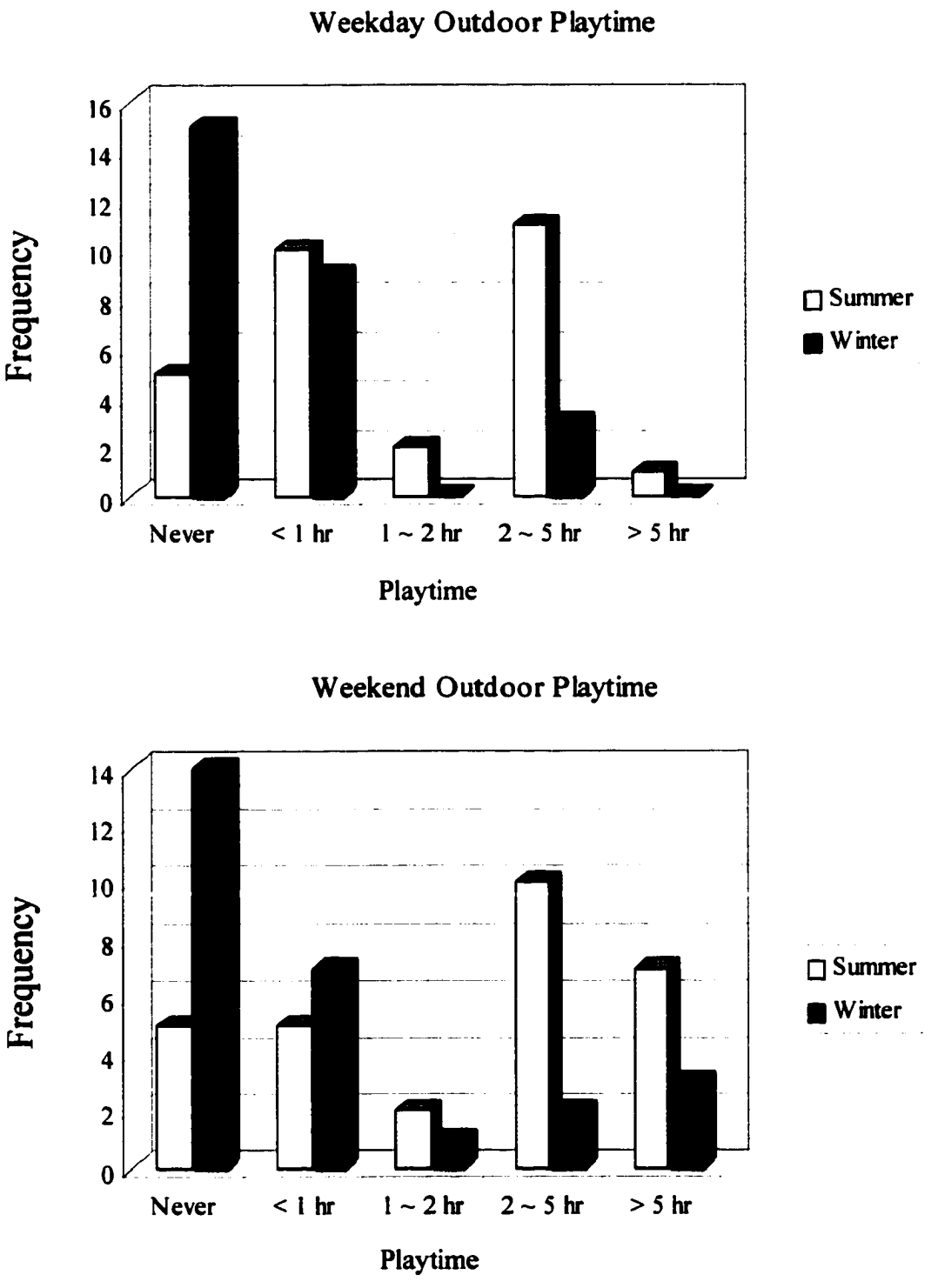

Figure 3.7 Outdoor Activity Patterns for the Summer and Winter Groups.

3.5.1 Seasonal Distributions of Dust Data

Consistent with blood lead concentrations, floor and sill samples showed high levels in the Summer group. In Adgate *et al.*'s study of chemical mass balance source apportionment for CLEARS (1998), nearly 50% of household lead dust came from street dust and soil, and 33% and 17% came from lead-based paint and air-borne lead particles, respectively. Thus, almost two-third lead in house dust would be derived from outdoor sources. Since pathways of dust entry into the home, such as human and pet activities and opening of doors and windows, are affected by the seasons, changes of indoor lead content would be anticipated between the summer and winter seasons. The high indoor dust lead levels would occur in summer, because contaminated outdoor sources would contribute more lead to indoor dust. However differences in the dust data found between the two seasonal groups were not statistically significant. One reason may be the existence of lead-based paint in the homes. Thirty-three percent of lead mass in household dust came from lead-based paint, which contributed lead particles to the home regardless of seasons. The non-seasonal contribution of lead paint might decrease the variability of seasonal distribution of household lead dust and probably narrowed the PbD difference caused by seasonal changes of the exterior lead sources. Therefore, mean comparisons of the seasonal groups hardly showed significant results.

The trend for carpet dust and lead loadings was an interesting result. Carpets or rugs are known for their capability to store dust. In the four seasonal subsets, dust loadings and lead loadings were higher in the Warm, Cool and Cold subsets than in the Hot subset. The Cool and Cold sets included periods of snow, during which people would carry in mud or soil into the house that adhered to their shoes or boots. For instance, the

Cool set included the month of March 1993, during which "the blizzard of the century" affected the eastern states of the United States. During the Cool and Cold periods higher amounts of mud or soil were brought in via shoes and then wiped off to floors or carpets. Mud or soil would be deposited on carpets and rugs and trapped and stored in there. This probably resulted in the high dust loading found for the Cool and Cold subsets. On smooth surfaces such as floors, however, the mud or soil could be carried elsewhere (e.g. outdoors or carpets in the home) by frequent human or pet activities. Subsequently, only portion of the mud would remain on the floor, since, in contrast to carpets, it is a poor reservoir for dust. This may explain why no significant increases of the dust loadings were found for floor samples during the Cool and Cold periods.

A moderately high level of dust loading was found for carpet samples in the Warm subset (April, May and September). During those months, a variety of pollens spread over New Jersey. In the months of April and May, tree pollens had the highest counts in the year, while weed pollens reached a peak in September (Bielory *et al.*, 1988). Usually most participating families did not use air-conditioners but kept windows open these three months. It is believed that the indoor and outdoor pollen levels are not significantly different when balconies (or windows) are open (D'Amato *et al.*, 1996). Thus, during the Warm period, the high fallout of pollens might significantly increase carpet dust loading, although pollens are light-weighed materials. Since the non-lead particles would be mixed with leaded house dust, the mean lead concentration for carpets could be diluted to be lowest among the four seasonal subsets. This likely dilution factor for allergen concentration was also effective on sill samples. The sill lead concentration was also found lowest in the Warm subset. However, the floor samples in the Warm

subset did not show the highest dust loading or the lowest lead concentration, because dust accumulation on floors, unlike windowsills or carpets that allowed long-time dust deposition, might vary substantially by frequent residential activities.

3.5.2 Relationships between Blood and Dust Data

3.5.2.1 Representatives of floor, sill and carpet samples

Analyses were completed for blood and dust data to determine what dust variables were best correlated with blood lead concentration. The results indicated that lead loading (mg/m^2) was well correlated with children's blood lead concentration for floor and sill samples, while lead concentration ($\mu g/g$) had the best correlation with blood lead concentration for carpet samples (Table 3.5). Lead loading (units $\mu g/ft^2$ or mg/m^2) has been widely used in previous studies to represent the dust lead levels (Charney *et al.*, 1983; Bornschein *et al.*, 1986; Davies *et al.*, 1991; Clark *et al.*, 1991; Adgate *et al.*, 1995; Lioy *et al.*, 1998), because it has been shown to be correlated well with blood lead concentration. The results for floor and sill samples (wipe) agreed with most previous studies on lead loading; however, the results for carpet samples (vacuum) showed that lead concentration was more appropriate to indicate dust lead levels than lead loading. Floors or windowsills are usually smooth and flat and do not have a large quantity of dust deposited on (geometric mean < 1 g/m^2). When children's hands contact those surfaces, they easily and almost fully load leaded dust just as the LWW wipe sampler does. Thus, the actual lead loading on the floor or windowsill would substantially influence blood lead concentration in children.

Carpets or rugs, however, trap and store a high amount of dust with furs and fibers (geometric mean: 6.86 g/m^2). In contrast to a vacuum cleaner, children's hands are not able to maintain contact with the dust present deep in the carpet or rug. Thus, the lead intake from carpets or rugs should be far lower than that predicted by the total lead loading of carpets or rugs. However, lead concentration in the carpet becomes important. Since children's routine home activities may yield a nearly constant contact with dust in the carpet, lead concentration in the carpet would be a better indicator of the dust contact and then have the influence on blood lead concentration. This result is supported by the work of Laxen *et al.* (1987), who used lead concentration to predict blood lead rather than lead loading when using a vacuum sampling method.

Knowing the dust variables that were most correlated with blood lead concentration helped examine the seasonality of lead exposure. The representative dust variables, floor lead loading, sill lead loading and carpet lead concentration, all showed the highest levels for the Hot subset (Figure 3.8). This finding was consistent with blood lead concentration, which had the highest mean value in the Hot subset. It is suggested that the seasonal distribution of PbDs may have an impact on the seasonality of lead exposure.

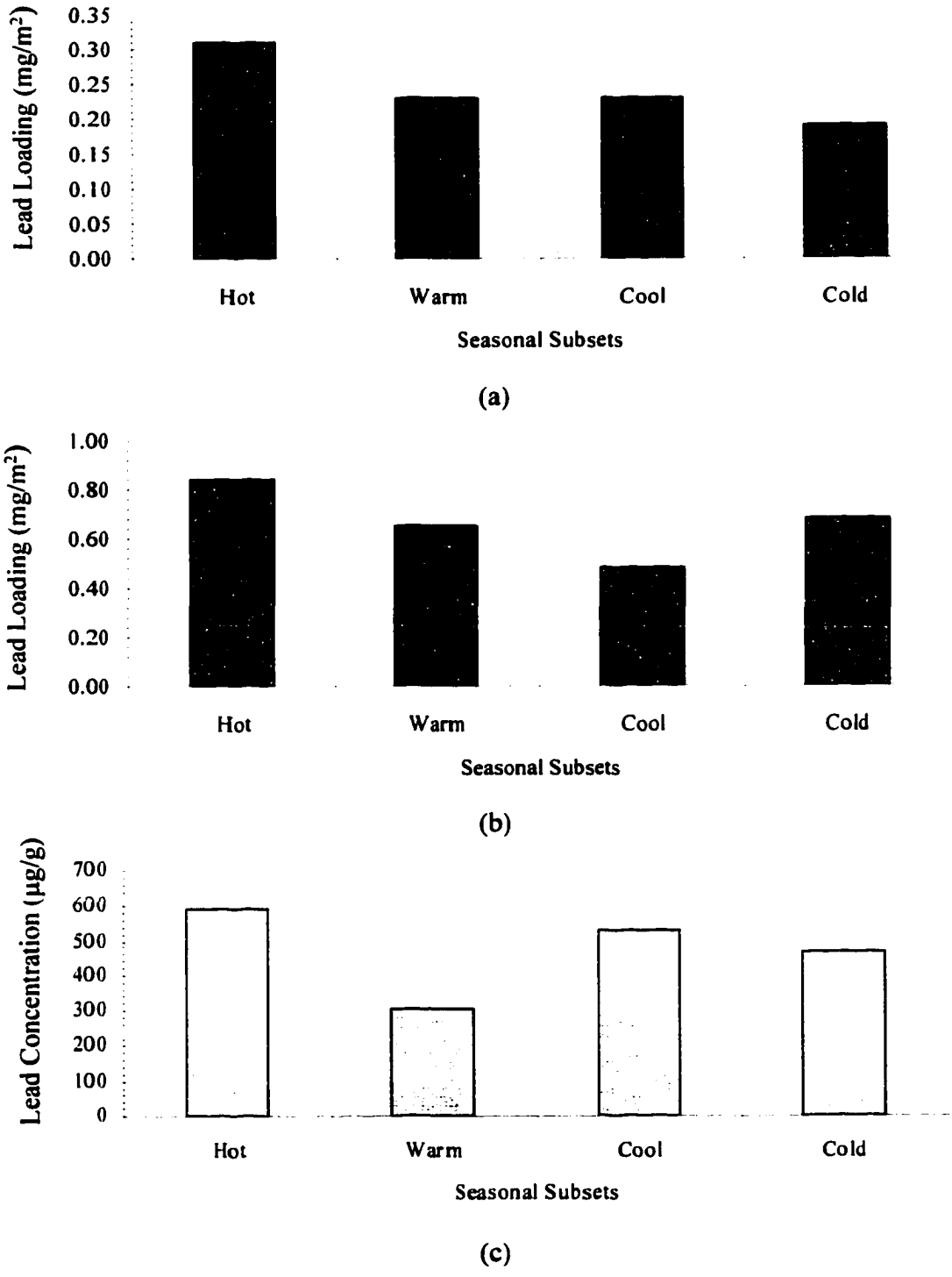

Figure 3.8 Geometric Means of Dust Lead Levels in Four Seasonal Subsets. (a): Floor Lead Loading; (b): Sill Lead Loading; (c): Vacuum Lead Concentration.

3.5.2.2 Seasonality of lead exposure from floors, sills and carpets

After the representative dust variables of floor, sill and carpet samples were identified, the correlation analysis within the Summer or Winter group was conducted to examine the associations between the dust variables and blood lead concentration (Figure 3.4-3.6). It was found that floor lead loading and carpet lead concentration had better correlations with blood lead concentration in the Winter group (r = 0.49 and 0.46, respectively) than those in the Summer group (r = 0.33 and 0.39, respectively). In contrast, sill lead loading in the Summer group had the better correlation with blood lead concentration in the two seasonal groups (r_{summer} = 0.43; r_{winter} = 0.29). The result indicates that the patterns of indoor lead exposure may differ from season to season. Children might contact windowsills more often in summer than in winter, while contacting leaded dust on floors and carpets might be the major pathway of lead exposure during the winter. Since the mean lead loading of sills was 2.75 times higher than that of floors and the mean lead concentration of sills was twice higher than that of carpets (Table 3.2), high blood lead concentration occurring during the summertime might result from more contact with high lead contaminated dust on the windowsill.

3.5.2.3 Examination of other likely seasonal factors

The stepwise regression model derived two equations (Equation 3.1 and 3.2) for the carpeted and uncarpeted households, and both found that blood lead concentration was a function of dust lead levels. It suggested that the seasonality of the lead exposure in CLEARS would result from the seasonal distribution of dust lead levels in a home, and other plausible seasonal factors (e.g. high vitamin D levels in summer) did not have any significant influence on the seasonality of blood lead levels. The results agree with the

work of Koo *et al.* (1991), who found no direct relationship between vitamin D metabolism and blood lead levels in children with low to mild lead exposure.

3.5.3 Outdoor Activity Pattern on Lead Exposure

Although preschool children spent most of time staying indoors, the few outdoor hours might have an impact on the seasonality of lead exposure because time spent outdoors was found to be associated with children's PbBs (Lanphear and Roghmann, 1997). According to the questionnaire survey, the outdoor activity patterns for the non-intervened families were significantly different in the Summer and Winter periods. During the Summer period, more than 50% of families let their children play outdoors at least 2 hours on weekdays, and even more families took their children to outdoor environments on weekends. The outdoor lead sources, street dust and soil, had an approximately 2 times higher mean lead concentration than the PbDs in indoor environments (Table 3.2). Thus, children playing outdoors were subject to receiving higher lead doses than staying indoors. During the Winter period, children did not play outdoors very often probably due to the coldness, and they would not be likely to contact street dust or soil directly. Consequently, the higher outdoor activities in summer contribute to higher lead exposure and higher blood lead concentration.

CHAPTER 4: THE INFLUENCES OF HOME FLOOR SURFACING (FLOORS OR CARPETS) ON CLEARS

4.1 Introduction

Lead laden dust distributed in residential environments is known to be transported from the interior and exterior sources. In CLEARS, the dust data in the micro-environments of houses, such as floors, carpets and windowsills, showed various ranges of lead levels (Table 2.1, 3.2). It has been known that windowsills usually show the highest lead levels in the household because there are lead-based paint chips or fragments flaking off from deteriorated windows (al-Radady *et al.*, 1993). The dust lead levels in carpets and on floors, which are a major source of lead exposure (Roberts *et al.*, 1995a), show different in dust loading, lead loading and lead concentration, probably because they possess distinct characteristics to hold dust. The fiber structure of carpets is capable of storing a large quantity of dust, while smooth floors only hold relatively small quantity of dust. In addition, dust variables associated with blood lead content in children are not the same for the two types of floor surfacing. Lead loading (mg/m^2 or $\mu g/ft^2$) has been widely used to predict blood lead concentration for sampling on floors and windowsills (Charney *et al.*, 1983; Bornschein *et al.*, 1986; Davies *et al.*, 1991; Clark *et al.*, 1991; Adgate *et al.*, 1995; Lioy *et al.*, 1998); however, lead concentration ($\mu g/g$) is considered to be the appropriate indicator of blood lead levels for vacuuming on carpets (Laxen, *et al.*, 1987). Some studies using regression models have shown blood lead associations with air (Snee, 1982), soil (Schilling and Bain, 1988), or household dust and drinking

water (Laxen, *et al.*, 1987), but little is known about the influences of various types of floor surfacing in the microenvironments of homes on childhood lead exposure.

The CLEARS demonstrated that cleaning intervention could effectively reduce PbDs in the household and subsequently lowered PbBs in children who had low to mild elevations (< 25 μg/dl) (Chapter 2; Rhoads *et al.*, 1999). In contrast to Ewers *et al.*'s findings (1994), which showed no cleaning effect on vacuuming carpets, the CLEARS did show significant declines of dust loading in carpets during the cleaning intervention; however, the effect of declines in carpet dust loading on children's PbB has yet been analyzed individually. In this chapter, the influence of home floor-surfacing types on childhood lead exposure was studied by separating the participant families into the two subgroups: carpeted and uncarpeted, and testing with statistical analyses. Prior to examining the floor-surfacing effect, the Lead Intervention of CLEARS was first re-examined in the floor-surfacing split database to verify the consistency with the results of Rhoads *et al.* (1999). Blood data of the carpeted and uncarpeted subgroups, within the Lead Intervention or Accident Prevention (control) group, were examined using Analysis of Variance (ANOVA) models to investigate the effect of floor surfacing on the cleaning intervention and lead exposure.

4.2 Background

In order to be consistent with the previous CLEARS intervention study (Rhoads *et al.*, 1998), the data selection for the re-examination of cleaning intervention was based on the database used in that report. The database included 99 children's blood lead data with both baseline (first home-visit) and final (third home-visit) blood measurements. In the

re-examination, the midterm (second home-visit) blood lead data were added for the requirement of the ANOVA. Participant houses in which carpets were present in major children's activity rooms (e.g. living rooms, playrooms or bedrooms) were allocated to the carpeted subgroup, while others were in the uncarpeted subgroup. Data with missing midterm blood values or with different floor surfacings due to a move were excluded for the study. There were 26 and 17 sets with all three home-visit blood lead data for the carpeted and uncarpeted subgroups in the Accident Prevention Group, respectively, and 21 sets for each subgroup in the Lead Intervention Group.

4.3 Methods

4.3.1 Sample Analysis

All the dust and blood sample analyses and cleaning protocol for the Lead Intervention Group were described in Chapter 2.

4.3.2 Data Analysis

The re-examination of cleaning effect on children's PbBs was completed with a three-factor nested factorial design of ANOVA model, stated as:

$$Y_{ijk} = \mu + S_i + H_{j(i)} + V_k + SV_{ik} + HV_{kj(i)}$$

where

Y represents the measured variable, blood lead concentration.
μ represents the true value.
S is the effect of floor surfacing subgroups (carpeted and uncarpeted), i = 1, 2.
H represents houses within subgroups (carpeted and uncarpeted), j = 1, 2...H_f.
V is the effect of treatment among three home visits (cleaning intervention for Lead group and prevention education for Accident group).
SV is the interaction effect of S and V.
HV is the interaction effect of H and V.

The blood lead data were log-transformed prior to the ANOVA, because they appeared to be a log-normal distribution (Figure 3.3). The ANOVA was separately performed for the Accident and Lead groups, since the treatments for the two groups among the three home visits were not the same. The unbalanced data for the carpeted and uncarpeted subgroups in the Accident group were statistically analyzed for ANOVA using the General Linear Model. The diagram of the ANOVA model for the Lead Intervention Group or Accident Prevention Group is illustrated in Figure 4.1. The S effect was tested against H, while the V effect and the SV interaction effect were both tested against HV. The null hypothesis for the S effect is stated as:

$$H_O : PbB_{carpeted} = PbB_{non-carpeted}$$
$$H_A : PbB_{carpeted} \neq PbB_{non-carpeted}$$

and for the V effect is stated as:

$$H_O : PbB_{V1} = PbB_{V2} = PbB_{V3}$$
$$H_A : \textit{PbB not equal for three home visits}$$

Repeated-measures design of AVOVA (used in Chapter 2 for comparing PbDs between visits) was applied here to investigate the influence of floor surfacing on childhood lead exposure. The ANOVA compared blood lead concentrations between

visits within the carpeted or uncarpeted group to examine if the treatment (cleaning intervention or accident prevention education) within either group was effective in reducing children's PbBs. The design of ANOVA in this chapter is stated as:

$$Y_{ijk} = \mu + H_i + V'_j + HV'_{ij}$$

where

Y represents the measured variable, blood lead concentration (log-transformed).
μ represents the true value.
H represents houses within the subgroups.
V' is the effect of treatment among home visits, but only within one floor-surfacing subgroup (carpeted or uncarpeted).
HV' is the interaction effect of H and V.

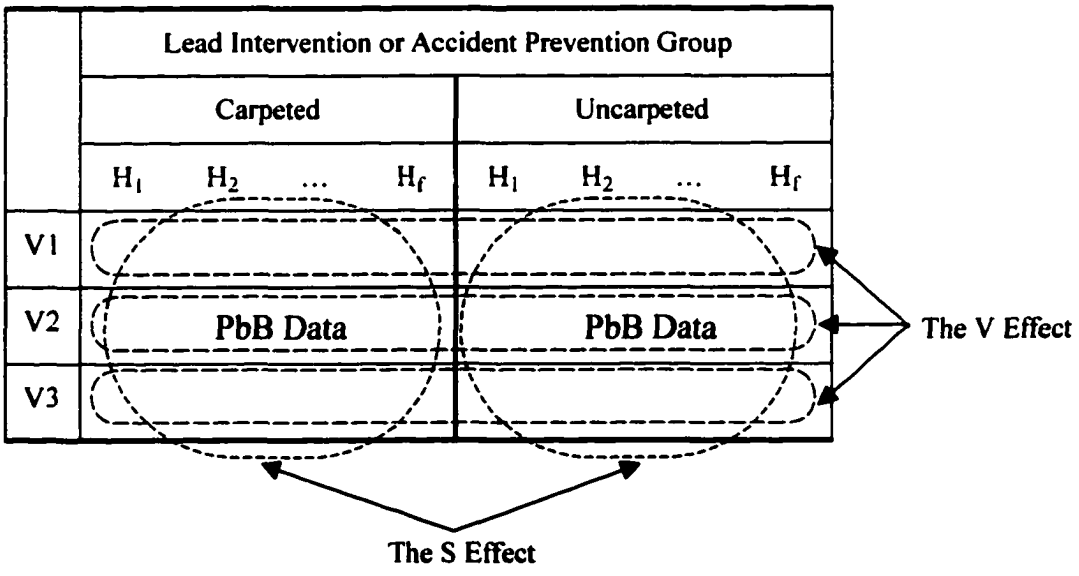

Figure 4.1 Diagram of the Nested-Factorial Deign of ANOVA for the Lead Intervention or Accident Prevention Group.

4.4 Results

4.4.1 Re-examination of Cleaning Intervention

The blood lead results for the nested-factorial design of ANOVA in the Accident and Lead groups are given in Table 4.1 and 4.2, respectively. The effect of carpeted or uncarpeted floor surfacing (denoted as S) did not show statistically significant for the Accident group ($p = 0.755$) or the Lead group ($p = 0.406$). The result indicated that the PbBs derived from the three home visits were not significantly different between the carpeted and uncarpeted subgroups for the Accident or Lead groups. The further examination for floor surfacing, considering the effect of group treatments among the three home visits, were shown in the next section of repeated-measures design of ANOVA. The effect of group treatment (denoted as V), which was the cleaning intervention for the Lead group, was statistically significant ($p = 0.006$), and a 20.6% decline was observed from the first visit to the third visit (Table 4.3a). There was no significant difference in mean blood lead concentrations between the three visits for the Accident Prevention homes, since the V effect for the controlled Accident group was not significant ($p = 0.186$). The same results were derived by using Rhoads *et al.*'s database (1999) for the ANOVA model with only the baseline and final PbBs (Table 4.3b). Therefore, the cleaning intervention was effective in reducing children's lead exposure.

The interaction between the S and V effects was neither statistically significant for the Lead group ($p = 0.153$), nor for the Accident group ($p = 0.163$). The result indicated that the effect of cleaning intervention among the three visits (V) on blood lead concentration was not significantly affected by the types of floor surfacing (S) in the

Lead Intervention or Accident Prevention homes. The geometric mean blood lead concentrations are illustrated in Figure 4.2 and 4.3 for the Lead and Accident groups, respectively. Since the trends in the net PbB change (Visit 3 – Visit 1) for the carpeted and uncarpeted subgroups did not appear apparently opposite in either the Lead (Figure 4.2) or Accident group (Figure 4.3), the interaction effect (SV) were not statistically significant for either group.

4.4.2 Detailed Examination of Floor Surfacing

The re-examination of cleaning intervention verified that children's PbBs were effectively reduced for the Lead Intervention homes during the CLEARS. The split data for the Lead group showed that PbBs in the carpeted and uncarpeted subgroups were both lowered by the implementation of cleaning intervention, but only the decline for the uncarpeted subgroup was statistically significant ($p = 0.007$) (Table 4.3a). The result indicated that children living in the uncarpeted homes could have their PbBs 28.7% lower after receiving the cleaning intervention. Those who lived in the carpeted homes, however, did not have their PbBs lowered significantly, although the cleaning intervention was effective in reducing PbDs in the carpet (Chapter 2). Based on the above examination, the effectiveness of the cleaning intervention observed for CLEARS was attributed to the cleaning work in the uncarpeted houses. Consequently, the cleaning effect was more pronounced in the uncarpeted houses than in the carpeted houses for the Lead Intervention Group.

The carpeted or uncarpeted homes in the Accident group did not show significant differences in PbBs between the three home visits (Table 4.3a). The result indicated that,

without cleaning intervention, children's blood lead concentrations remained at the same high levels regardless of living in the carpeted or uncarpeted houses.

Table 4.1 ANOVA for the Accident Prevention Group.

	df	SS	MS	F	Probability	EMS
S_i	1	0.02	0.02	0.10	0.755	$3\sigma^2_H + C_1\phi_S$
$H_{j(i)}$	41	7.76	0.19			$3\sigma^2_H$
V_k	2	0.03	0.02	0.88	0.421	$\sigma^2_{HV} + C_2\phi_V$
SV_{ik}	2	0.06	0.03	1.86	0.163	$\sigma^2_{HV} + C_3\phi_{SV}$
$HV_{kj(i)}$	82	1.37	0.02			σ^2_{HV}
Total	128	9.24				

df: Degree of Freedom; SS: Sum of Squares; MS: Mean Square; EMS: Expected Mean Square;
C_n: Constant for unbalanced general linear model.

Table 4.2 ANOVA for the Lead Intervention Group.

	df	SS	MS	F	Probability	EMS
S_i	1	0.09	0.09	0.70	0.406	$3\sigma^2_H + 63\phi_S$
$H_{j(i)}$	40	5.09	0.13			$3\sigma^2_H$
V_k	2	0.21	0.11	5.55	0.006	$\sigma^2_{HV} + 42\phi_V$
SV_{ik}	2	0.07	0.04	1.92	0.153	$\sigma^2_{HV} + 21\phi_{SV}$
$HV_{kj(i)}$	80	1.54	0.02			σ^2_{HV}
Total	125	7.00				

df: Degree of Freedom; SS: Sum of Squares; MS: Mean Square; EMS: Expected Mean Square.

Table 4.3a Mean Blood Lead Concentrations (unit: μg/dl) in the ANOVA with 3 visits.

Accident Prevention								
	n	Visit 1		Visit 2		Visit 3		p
		GM	GSD	GM	GSD	GM	GSD	
Total	34	9.94	2.0	11.17	1.8	10.02	1.7	0.186[a]
Carpeted	26	9.29	1.9	10.12	1.7	10.05	1.8	0.567[b]
Uncarpeted	17	10.98	2.0	10.97	2.0	9.28	2.1	0.102[b]
Lead Intervention								
	n	Visit 1		Visit 2		Visit 3		p
		GM	GSD	GM	GSD	GM	GSD	
Total	42	10.99	1.7	10.05	1.6	8.73	1.8	0.006[a]
Carpeted	21	10.81	1.7	11.22	1.5	9.56	1.8	0.231[b]
Uncarpeted	21	11.18	1.8	9.01	1.7	7.97	1.8	0.007[b]

GM denotes geometric mean; GSD denotes geometric standard deviation.
a: p value derived from nested- factorial design; b: p value derived from repeated-measures design.

Table 4.3b Mean Blood Lead Concentrations (unit: μg/dl) in the ANOVA with 2 visits.

Accident Prevention						
	n	Baseline		Final		p
		GM	GSD	GM	GSD	
Total	53	9.91	1.8	9.74	1.9	0.619[a]
Carpeted	33	9.45	1.8	9.81	1.8	0.685[b]
Uncarpeted	20	10.71	1.9	9.62	2.0	0.232[b]
Lead Intervention						
	n	Baseline		Final		p
		GM	GSD	GM	GSD	
Total	46	11.06	1.7	8.95	1.7	0.006[a]
Carpeted	23	10.79	1.6	9.51	1.7	0.205[b]
Uncarpeted	23	11.34	1.8	8.43	1.8	0.013[b]

GM denotes geometric mean; GSD denotes geometric standard deviation.
a: p value derived from nested- factorial design; b: p value derived from repeated-measures design.

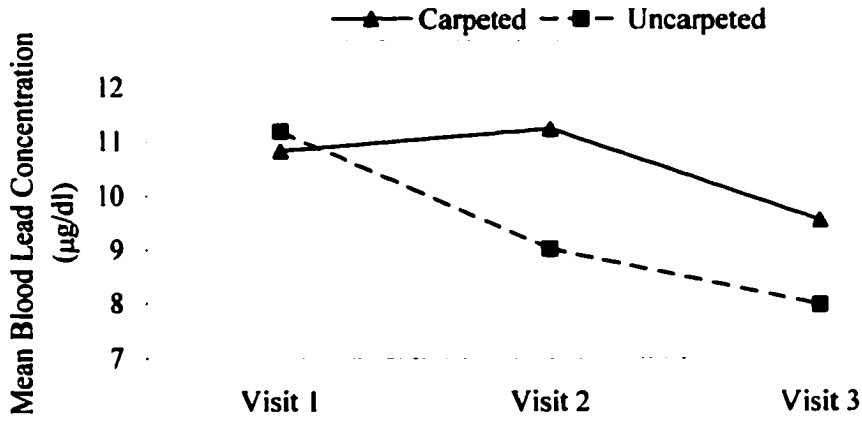

Figure 4.2 Geometric Mean Blood Lead Concentrations for Three Home Visits in the Carpeted and Uncarpeted Subgroups of the Lead Intervention Group.

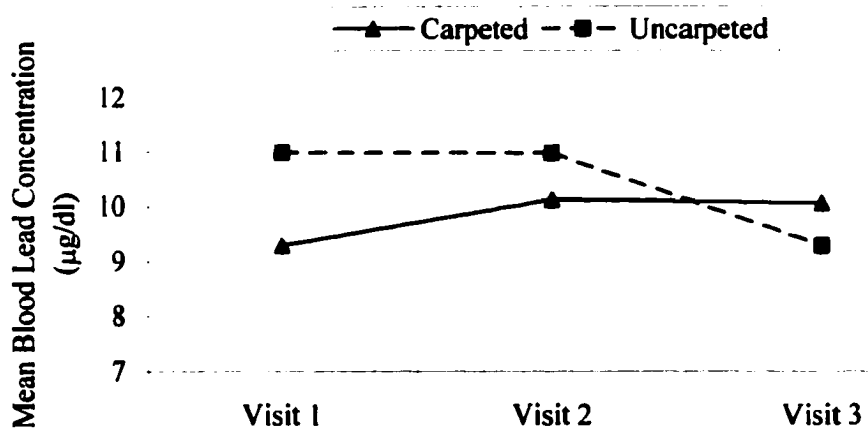

Figure 4.3 Geometric Mean Blood Lead Concentrations for Three Home Visits in the Carpeted and Uncarpeted Subgroups of the Accident Prevention Group.

4.5 Discussion

The re-examination of cleaning intervention with the addition of second-visit blood data was consistent with the result of Rhoads *et al.* (1999), who used arithmetic statistics to analyze the CLEARS data. Although the statistical analyses used in the work of Rhoads *et al.* (1999) and in this chapter were not the same, both the results demonstrated the effectiveness in reducing children's PbBs for the Lead Intervention Group, but no significant differences in PbBs for the Accident Prevention Group. The detailed examination for the home floor surfacing found that the effect of cleaning intervention in reducing lead exposure were significant on children living in the uncarpeted houses, but insignificant on those living in the carpeted houses. Therefore, the types of floor surfacing in the residential homes had an influence on the cleaning intervention and children's lead exposure.

To explore the likely reasons that the cleaning intervention yielded different outcomes for the carpeted and uncarpeted home environments, the relationships between children's PbBs and household PbDs in the two floor-surfacing types of houses would be essential. In the uncarpeted homes, children's blood lead concentrations were found to be a function of floor lead loading only (Equation 3.2). In Chapter 2, the wipe samples (floors and sills) showed a 35% decline in lead loading for the third home visits in the Lead Intervention homes. The decline of floor lead loading, derived from the implementation of cleaning intervention, could result in children's PbB reduction in the uncarpeted houses. Therefore, the cleaning intervention was effective in the uncarpeted

households to reduce floor lead loading and, consequently, children's blood lead concentrations.

In the carpeted subgroup, blood lead concentration was mainly associated with carpet lead concentration and sill lead loading (Equation 3.1). Although carpet dust loading and lead loading were effectively reduced by applying the HEPA filter vacuum method, carpet lead concentration failed to show a statistically significant decline during the cleaning intervention (Table 2.5). However, sill lead loading, combined with floor lead loading, showed a significant decline in the Lead Intervention homes. Since the standardized coefficients indicated that carpet lead concentration (β = 0.517) was the more important component than sill lead loading (β = 0.335) in Equation 3.1 (Table 3.6), the effect of cleaning intervention on sill lead loading was compromised by the lack of effect on carpet lead concentration. Therefore, children who lived in the carpeted homes did not obtain as much benefit from the cleaning intervention.

The statistically insignificant intervention effect in the carpeted households may also be due to the characteristics of carpets. Carpets are known as a dust sink that contributes to long-term dust lead exposure in the household. The cleaning intervention reduced dust and lead loadings, but did not substantially change lead concentration in the carpet. Even though the cleaning intervention was implemented on carpets, there was the geometric mean dust loading of 2.90 g/m^2 remaining in the carpet (Table 2.2). Thus, the source of lead exposure to children was still rich in the carpeted house, and children living in such home environments remained being exposed to lead. The results agreed with Hilts *et al.*'s work (1995), which demonstrated a significant decline of mean carpet

lead loading with using a HEPA vacuuming method but no significant difference observed in children's blood lead levels.

CHAPTER 5: COMPARISONS OF TWO URBAN LEAD STUDIES

5.1 Introduction

Two lead studies with different objectives were conducted in the urban areas of New Jersey in the 1990s. The CLEARS, which was conducted in Jersey City, NJ, examined the lead exposure of children who had low to moderate blood lead levels (< 25 μg/dl), and tested a combined cleaning and educational intervention to minimize the lead exposure. The Treatment of Lead-exposed Children (TLC) Trial, which was sponsored by the National Institute of Environmental Health Sciences (NIEHS), located one of the sites in Newark, NJ. The TLC Trial was designed to investigate the effects of lead chelation therapy on developmental status in pre-school children with baseline blood lead concentrations between 20 and 44 μg/dl. Dust sampling was implemented in the residential environments of the two studies to measure the dust lead levels in the homes. Since the two studies targeted on the different ranges of children's blood lead levels, the collected blood lead and dust lead data for the two projects were compared to examine relationships between blood lead and dust lead for the two blood lead levels of childhood lead exposure.

The LWW wipe sampler used in the TLC Trial was modified from the one used in CLEARS. The modified LWW sampler provided more sampling surface area and a better mechanism to hold a filter in place. In this chapter, the comparisons of the two LWW wipe samplings were conducted first to determine a relationship between results derived from the original and modified samplers, and then the comparison of the two urban childhood lead exposures were conducted with the known dust sampling relationship.

Since the subjects in the TLC Trial had moderately high lead levels, the influence of iron status in the participant children might be of concern. Iron deficiency and elevated lead levels are both causes of high levels of erythrocyte protoporphyrin (EP) (ATSDR, 1993). The Second National Health and Nutrition Examination Survey (NHANES II), 1976-1980, found that iron status (measured as ferritin serum) in the blood was inversely associated with blood lead levels that were equal to or over 30 μg/dl (Yip *et al.*, 1984; Mahaffey and Annest, 1986). However, other studies with the different results showed no correlation between lead and iron in the blood (Hershko *et al.*, 1984; Markowitz *et al.*, 1996), or an inverse correlation between blood lead levels and dietary iron intake instead (Hammad *et al.*, 1996). The TLC data of serum ferritin, blood lead and dust lead were examined using partial correlation analysis to determine the effect of iron status in the blood on the relationship between blood lead and dust lead.

5.2 Background

The details of CLEARS were described in Chapter 2. The TLC Trial, starting from September of 1994, was a national multi-center trial of lead chelation therapy. It was designed to compare the effect of lead chelation with the drug succimer (2,3-*meso*-dimercaptosuccinic acid) and placebo therapy in lead-exposed children aged 12 to 32 months with blood lead concentrations between 20 and 44 μg/dl (protocol of TLC Trial, 1994). Besides the age and blood lead range, the children who were considered eligible in the TLC Trial had to meet the other criteria, such as staying within the area during the study, no prior lead chelation therapy, and no known diseases. Upon receipt of informed consent from a parent or legal guardian, eligible children were randomized to chelation

therapy with succimer or placebo (control). Children enrolled in the succimer group received one to three rounds of chelation therapy. Blood lead levels were measured two weeks after the completion of each round of chelation. Residential lead clean-up and nutritional supplementation with multivitamins and minerals were provided to all children in both the succimer and placebo groups. Enrolled children are followed for at least 3 years with periodic assessment of the developmental status, including measurement of IQ, and changes in height, weight and head circumference.

Sampling for lead content was conducted before and after the cleaning intervention to provide the pre- and post clean-up dust lead levels in the residential environments. The cleaning intervention in the trial was implemented to reduce children's exposure to lead attributable to lead-based paint or lead-containing house dust, since the dust lead exposure might affect the detection of lead chelation therapy. Sampling locations were chosen by the trained TLC personnel in the rooms where children were likely to spend the most time. Windowsills and the adjacent floors in the playroom or bedroom, and kitchen floors were the usual sampling sites in the residences. The HUD (House and Urban Development) dust wipe sampler and the LWW modified wipe sampler were used side by side on each smooth-surface sampling site. A vacuuming method was used to sample dust in carpets or rug; however, less than 10% of sampling locations in the trial were carpeted. Therefore, the HUD and LWW dust wipe samplers were the primary sampling methods in the TLC Trial, and the comparison of the two urban lead studies will focus on the dust wipe measurements in the two urban areas of New Jersey.

In order to examine the compatibility of the two LWW wipe samplers, a side-by-side LWW wipe sampling was performed in laboratory and in the field of TLC Trial. With the determination of relation between the two LWW samplings, the dust lead data derived for CLEARS and the TLC Trial were able for the comparison of two urban lead studies.

5.3 Methods

5.3.1 The LWW Dust Wipe Samplers

The original LWW wipe sampler, which was used in CLEARS, was described and shown in Chapter 2 (Figure 2.1). The modified LWW wipe sampler was designed to increase the sampling surface areas and enhance the strength of holding filter media to the sampling block. Each sample pack, wrapped with aluminum foil, contained 3 rectangular pieces of filter media (Nucleopore #810111 50 × 55 mm PE Drain Disc), and it was weighed pre-sampling in an environment controlled chamber. Before sampling, a rectangle of Acquell Polyurethane ¼ inch thick foam (3 ½ × 2 ½ inches) was first placed into a rectangular plastic stamp pad of the same size by hands with a pair of non-powdered vinyl gloves on. The stamp pad with the foam was wetted by deionized water and then was ready to moisturize the sampling filter media. The sampling block assembly was formed by putting the filter under the small block and then pushing the block with the filter through the top opening of the frame block (Figure 5.1). When sampling, the filter clipped on the sampling block assembly was wetted by pressing it on the wet foam in the plastic stamp pad, and the assembly was moved back and forth five times within a 150 cm^2 template on the sampling surface. The second and third filters were repeated

following the same procedure. After sampling, the filters were wrapped with aluminum foil and sent back to the environment-controlled chamber for air dry at least 3 days before the post-sampling weighing.

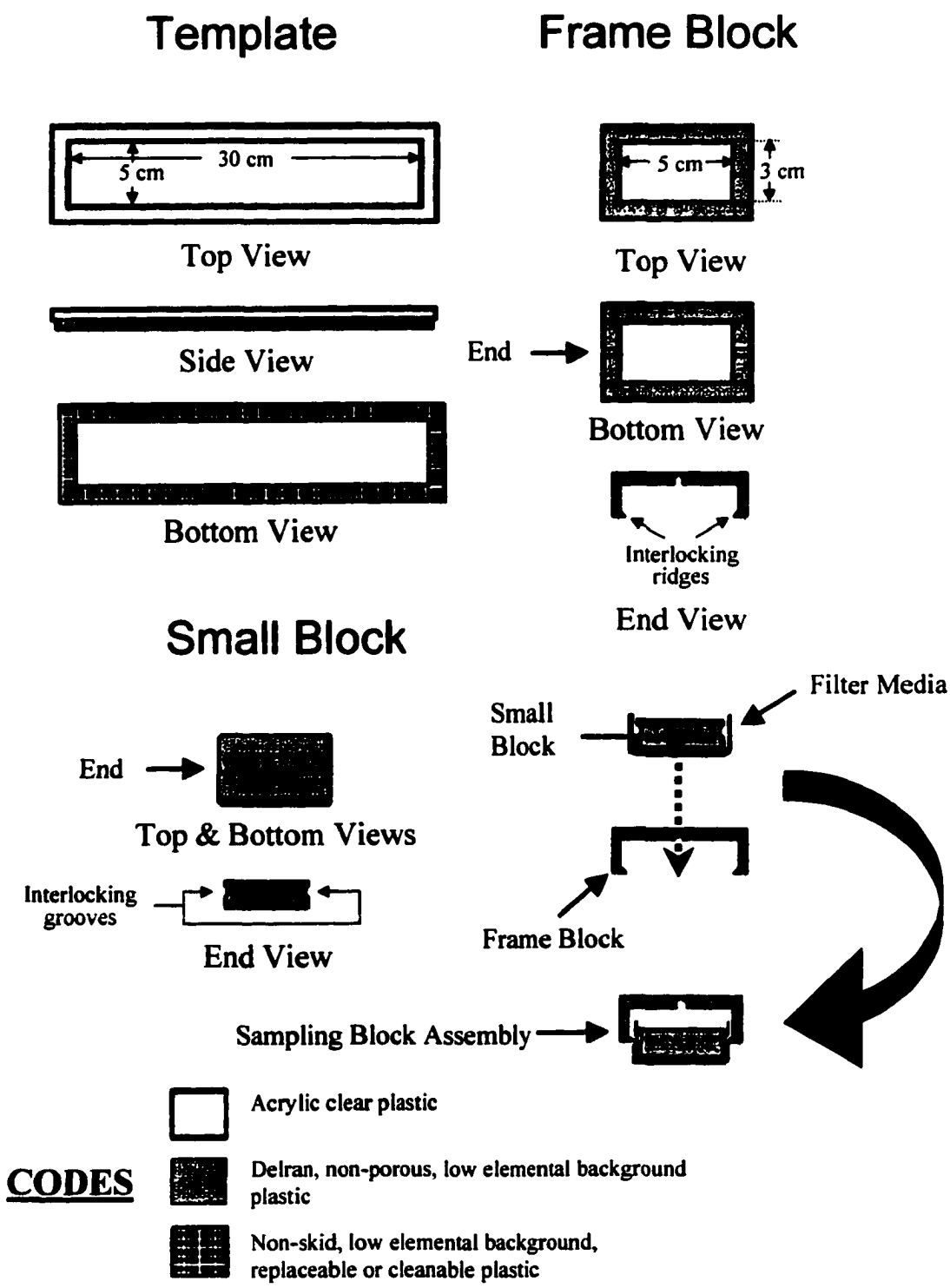

Figure 5.1 The Modified LWW Wipe Sampler.

5.3.2 Comparison of Two LWW Samplers

The original and modified LWW samplers were compared in the field and laboratory. In the field study, side-by-side wipe samples were collected with the two LWW samplers in the TLC participant houses in Newark, NJ. At least one pair of side-by-side wipe samples was taken for windowsills and floors at each residential house. There were 39 pairs of floor wipe samples and 33 pairs of sill wipe samples taken from 31 houses available for the side-by-side comparison.

In the laboratory study, a settled dust chamber was used to re-suspend and settle dust evenly over flat surfaces (Edwards, 1999). The dust used in the experiment was collected from a vacuum bag in a household in New Brunswick, NJ, and it was sieved using a 250 μm sieve prior to use. The settled dust chamber (2 × 2 × 5 feet) was a rectangular box with a square wooden top and enclosing cardboard walls (Figure 5.2). Four 3 × 12 inch slides of the same material (glass, wood or vinyl) were placed on the turntable at the bottom of the chamber for each experiment. The turntable then rotated at a rate of 11 revolutions per minute. Dust suspension was conducted by passing compressed air (30 psi) for one minute through the dust that fed into an aluminum chamber containing a fluidized bed of glass beads. The air stream from the fluidized bed was divided into four identically shaped copper tubes that then entered the top of the settled dust chamber. To have even dust deposition on the turntable, at least 60-minute dust re-suspension was necessary. Side-by-side sampling using the two LWW samplers was conducted after the dust re-suspension.

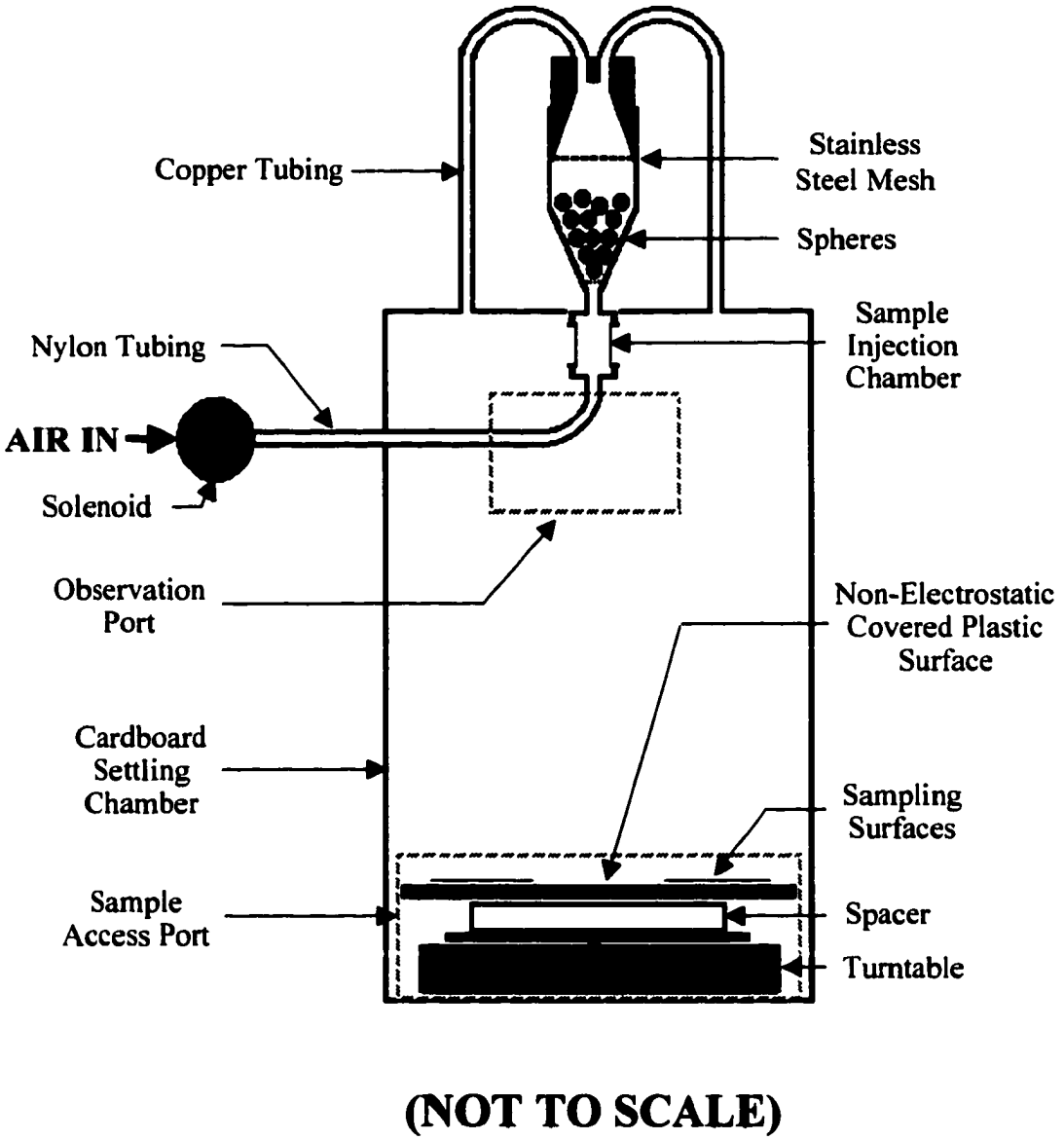

Figure 5.2 Settled Dust Chamber (Edwards, 1999).

Sample analyses for the two types of LWW samples were conducted with the same procedures for the acid digestion and ICP-MS analysis described in Chapter 2. The three dust variables, lead concentration, lead loading and dust loading, were derived for each wipe sample. All the dust data were log-transformed prior to statistical analyses because of the log-normal distributions. In the field study, paired-samples t-tests were used to compare the geometric mean lead concentrations, lead loadings, and dust loadings derived from the original and modified LWW wipe samplers, and Spearman correlation analyses were performed to examine correlations between the two LWW wipe samplers. In the laboratory study, only dust loading would be tested for paired-samples t-test and Spearman correlation analysis, since the use of a source of leaded dust did not produce the variability in lead concentration or lead loading for the statistical analyses.

5.3.3 Comparisons of Two Urban Childhood Lead Exposures

In order to compare childhood lead exposures in the two urban areas, only blood and dust lead data not involved with any potential intervention (e.g. cleaning) were eligible for use. For CLEARS, the database in the Accident Prevention Group was used in the comparisons (same data analyzed for seasonality study in Chapter 3). In the TLC Trial, data collected before a cleaning intervention occurred were available for the comparisons. The blood lead analysis for the TLC Trial was as same as described in Chapter 3 for CLEARS. The blood and dust lead data for the two urban lead studies were log-normally transformed and paired into blood lead-dust lead corresponding formats for correlation and regression analyses. The descriptive statistics for the two urban lead studies were analyzed first to compare the blood lead and dust lead distributions between the two cities of New Jersey. Spearman correlation analyses were conducted to examine

the associations between PbDs and PbBs for CLEARS and the TLC Trial. Stepwise multiple linear regression analysis was used for further examination of the two urban lead exposure studies.

5.3.4 Ferritin Effect on TLC Blood Lead and Dust Lead

Ferritin (serum iron) analysis of blood samples was also performed by the CDC in Atlanta, GA using the Bio-Rad Laboratories "Quantimmune Ferritin IRMA" kit which was a single-incubation two-site ^{125}I-immunoradiometric assay (IRMA) (Addison *et al.*, 1972; Miles, 1977). Since blood lead might be inversely associated with ferritin (Yip *et al.*, 1984; Mahaffey and Annest, 1986) and meanwhile varied with dust lead, partial correlation analysis, which derived a new correlation coefficient between two variables when the other related variable was held constant, was used to investigate the likely ferritin effect on blood lead and dust lead. Prior to the partial correlation analysis, Spearman correlation analysis was first conducted to derive the bivariate correlations between dust lead, blood lead and ferritin levels. New correlation coefficients were calculated with ferritin in the blood controlled in the partial correlation analysis, and were compared with the bivariate correlation analysis to examine the effect of iron status on the PbB-PbD relationships for the TLC Trial.

5.4 Results

5.4.1 Results for Comparisons of the Two LWW Samplers

Seventy-two pairs of side-by-side LWW samples were obtained in the field study (Table 5.1). Paired-samples t-tests showed no significant differences between the original and modified LWW samplings in lead concentration ($p = 0.48$), lead loading ($p = 0.46$),

and dust loading (p = 0.18). The side-by-side wipe sampling yielded a significant correlation between the two LWW samplers for each dust variable in the field study. Lead concentration and lead loading showed strong correlations between the two LWW samplers ($r > 0.80$), but dust loading only yielded a fair correlation ($r = 0.44$) (Figure 5.3-5.5). The results, showing no significant differences in the mean comparisons and significant correlations, indicated that the original and modified LWW samplers were functionally equal in dust wipe sampling.

The fair correlation in dust loading for the field study might be of concern when comparing the two LWW samplers, although dust loading was the least term to be used in lead exposure studies. Some likely outliers of samples, which were probably collected on extremely rough surfaces, were found for the lower correlation in dust loading (Figure 5.5). In the laboratory study using a dust chamber, 17 pairs of side-by-side samples were obtained, and dust loading showed a significant and high correlation ($r = 0.86$) and no significant difference in the means derived from the two LWW samplers (p = 0.19) (Table 5.1). The laboratory result indicated that the performances of the original and modified LWW samplers on dust loading should be of no difference when sampling on regular surfaces. Therefore, the different LWW samplers used in CLEARS and TLC Trial did not produce any bias for the comparisons of the two lead exposure studies.

Table 5.1 Comparisons of the Original and Modified LWW Samplings.

Dust Variable	Original		Modified		p (t-test)	r*
	GM	GSD	GM	GSD		
Field Study (n = 72)						
Lead Concentration (μg/g)	1270	4.5	1345	4.5	0.48	0.89
Lead Loading (mg/m^2)	0.73	6.3	0.66	7.2	0.46	0.85
Dust Loading (g/m^2)	0.57	2.2	0.49	2.6	0.18	0.44
Laboratory Study (n = 17)						
Dust Loading (g/m^2)	0.42	1.9	0.47	1.8	0.19	0.86

*: Significance levels of correlations < 0.001.

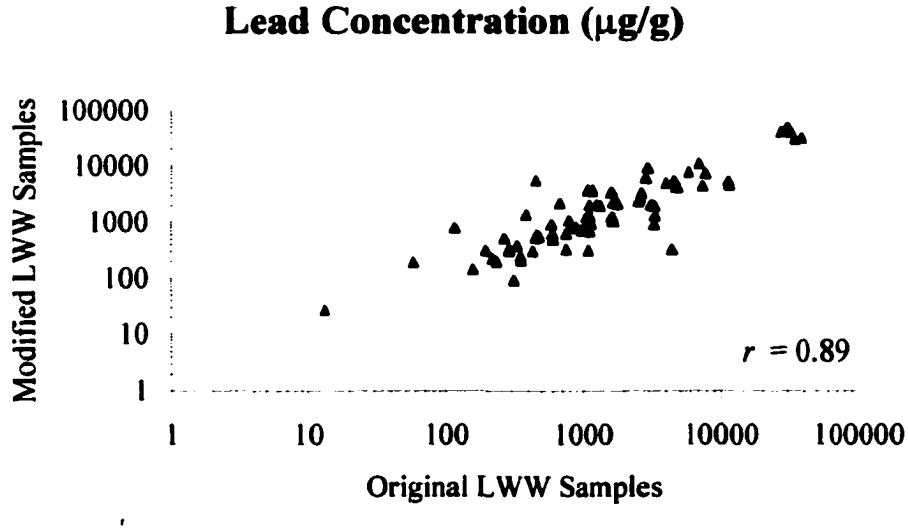

Figure 5.3 Correlation of Lead Concentrations between the Two LWW Samples.

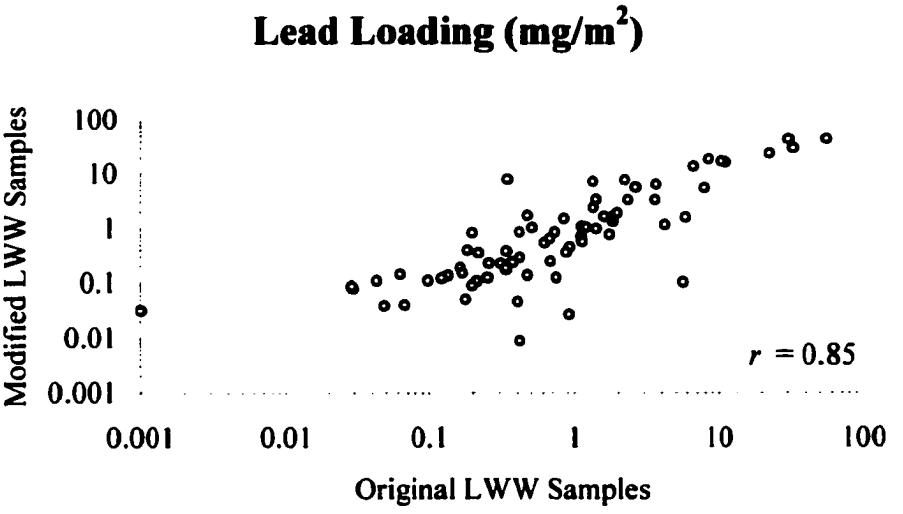

Figure 5.4 Correlation of Lead Loadings between the Two LWW Samples.

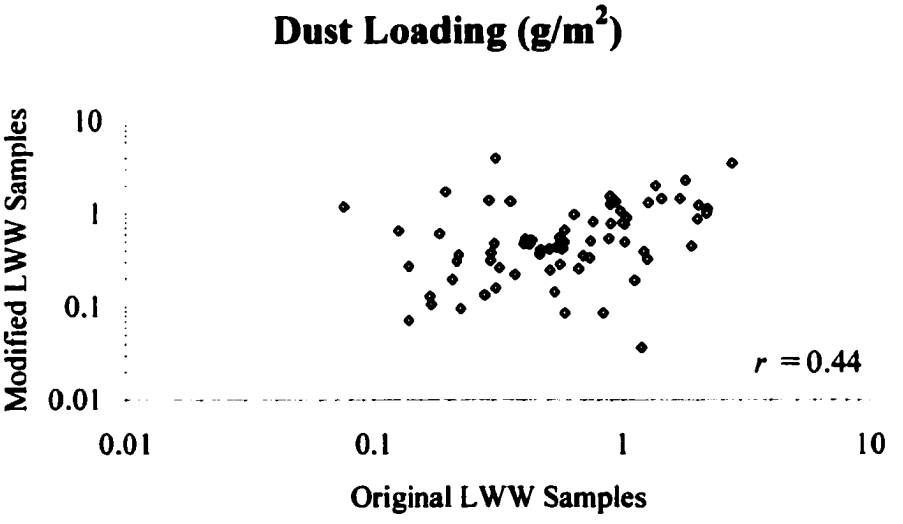

Figure 5.5 Correlation of Dust Loadings between the Two LWW Samples.

Table 5.2 General Lognormal Distribution Parameters for Blood, Floor and Sill Samples for CLEARS and TLC Comparisons.

	CLEARS (Jersey City)			TLC (Newark)		
	n	GM	GSD	n	GM	GSD
Blood						
Lead Concentration (μg/dl)	313	9.56	1.8	274	27.01	1.2
Floor						
Dust Loading (g/m^2)	413	0.39	3.0	491	0.60	2.7
Lead Loading (mg/m^2)	413	0.24	3.7	491	0.49	4.8
Lead Concentration (μg/g)	413	613.0	2.6	491	830.4	3.6
Sill						
Dust Loading (g/m^2)	245	0.70	2.7	292	1.14	2.6
Lead Loading (mg/m^2)	245	0.66	5.1	292	2.55	7.9
Lead Concentration (μg/g)	245	945.5	3.5	292	2230.8	6.2

GM and GSD denote geometric mean and geometric standard deviation, respectively.

Table 5.3 Spearman Correlation Coefficients of Blood Lead Concentration and Corresponding Dust Lead Data in the TLC Trial.

	Number of Pairs	Correlation Coefficient	Probability
Floor			
Dust Loading (g/m^2)	204	0.06	0.432
Lead Loading (mg/m^2)	204	0.14	0.050 *
Lead Concentration (μg/g)	204	0.16	0.027 *
Sill			
Dust Loading (g/m^2)	195	0.05	0.532
Lead Loading (mg/m^2)	195	0.08	0.260
Lead Concentration (μg/g)	195	0.07	0.364

*: significant.

5.4.2 Results for Comparisons of the Two Urban Lead Exposures

5.4.2.1 Descriptive statistics

The summary of descriptive statistics for CLEARS and the TLC Trial is shown in Table 5.2. The TLC Trial showed the higher blood lead and dust lead levels of the two lead studies. The mean blood lead concentration in the TLC Trial was 2.8 times higher than that in CLEARS, while the mean lead loadings for floor and sill samples were 2 times and 3.9 times higher in the TLC Trial, respectively. The lower geometric standard deviation (GSD) for the TLC Trial (1.2 μg/dl) was due to the narrower acceptable blood lead range (20-44 μg/dl). In contrast, the GSDs for floor and sill lead loadings in the TLC Trial were higher than those in CLEARS.

5.4.2.2 Correlation analysis

Spearman correlation analysis showed that floor lead loading and sill lead loading were associated with blood lead concentration for CLEARS (r = 0.41 and 0.37, respectively) (Table 3.5). However, in the TLC Trial, floor lead loading and sill lead loading were found little correlated with blood lead concentration (r = 0.14 and 0.08, respectively) (Table 5.3). The scatterplots of floor lead loading and sill lead loading versus blood lead concentration for the TLC Trial were shown in Figure 5.6 and 5.7, respectively, with the CLEARS regression lines as a reference. The differences in correlation analysis for CLEARS and the TLC Trial were probably due to the blood data selection. The TLC blood lead concentrations was confined since the blood data were pre-selected within the specific range (20-44 μg/dl), but the corresponding residential dust lead appeared a wide-ranged distribution. For example, low PbDs, which appeared as outliers, might be obtained from samples taken in the houses that were just cleaned

prior to dust sampling. Thus, the low PbDs, corresponding to the high range of PbBs, could lower the significance of correlation between PbBs and PbDs. In CLEARS, children were eligible to participate according to the criteria (described in Selection 2.2) but not to any pre-selected blood lead range. Therefore, without the pre-selected blood range the CLEARS data yielded better results for correlation analysis than did the TLC data. Since these two lead exposure studies had the different blood lead ranges, a combination of CLEARS and TLC data might provide a better opportunity to examine the relationship between blood lead and dust lead in the range of potentially low to moderately high lead exposure. This part will be examined in Section 5.4.4.

5.4.3 Ferritin Effect on TLC PbB-PbD Relationship

The correlation between ferritin and blood lead was not significant (r = 0.02, p = 0.760) in the TLC Trial, and ferritin in the blood was not correlated with floor and sill dust lead data (Table 5.5). It seemed to indicate that ferritin was not important to the study; however, partial correlation analysis showed some improvement on the correlation between blood lead and dust lead as ferritin was held constant. Correlation coefficients for floor lead loading and lead concentration were enhanced from 0.14 and 0.16 to 0.22 and 0.21, respectively (Table 5.3 and 5.6). Correlations for sill dust lead data were also improved, although the improvements were not statistically significant. The result indicated that PbBs in children would have had a better correlation with PbDs in the home for the TLC Trial if ferritin (serum iron) had been constant. Consequently, ferritin, at high levels of lead poisoning in the TLC Trial, had a diminishing effect on the PbB-PbD relationship.

5.4.4 Stepwise Multiple Linear Regression of Combined Data

The stepwise multiple linear regression for CLEARS in the uncarpeted houses was performed in the previous seasonality study as shown in Equation 3.2. The blood concentration was only a function of floor lead loading in the CLEARS uncarpeted homes. The regression model was not individually conducted for the TLC Trial, because of the low correlations between PbBs in children and PbDs in the home. More than 50% data of the TLC floor lead loading was distributed within the CLEARS 95% confidence interval (CI) lines (Figure 5.6), and nearly all data of the TLC sill lead loading was located within the CI lines (Figure 5.7). An attempt of regression analysis was made for the combined CLEARS and TLC data to examine the PbB-PbD relationship assuming that the two studies followed the same exposure pattern. The result of regression analysis for the two-study combination was completed as:

$$Log_{10}BloodPbC = (1.343 \pm 0.018) + (0.098 \pm 0.022)Log_{10}FloorPbL + (0.059 \pm 0.016)Log_{10}SillPbL, \quad R^2 = 0.200 \cdots (5.1)$$

Besides floor lead loading, which only appeared in Equation 3.2, sill lead loading was added to the equation for the two-study combination. The standardized coefficients, 0.282 and 0.229 for floor lead loading and sill lead loading, respectively (Table 5.4), showed that floor lead loading was the most important component in relation to blood lead concentration within the combined lead exposures. However, the poor R^2 value (0.200) in Equation 5.1, compared to that in Equation 3.2 for CLEARS (0.403), indicated that children's PbBs were slightly determined by residential PbDs for the combination of the TLC Trial and CLEARS.

Table 5.4 Coefficients of Stepwise Multiple Linear Regression for CLEARS and the Combination of CLEARS and the TLC Trial.

	Unstandardized Coefficients		Standardized Coefficients	
	B	Standard Error	Beta	Significance
CLEARS (Equation 3.2)				
Constant	1.262	0.049		< 0.001
Log_{10}(Floor PbL)	0.311	0.057	0.634	< 0.001
CLEARS and TLC				
Constant	1.343	0.018		
Log_{10}(Floor PbL)	0.098	0.022	0.282	< 0.001
Log_{10}(Sill PbL)	0.059	0.016	0.229	< 0.001

PbL denotes Lead Loading.
PbC denotes Lead Concentration.

Table 5.5 Spearman Correlation Coefficients of Blood Ferritin Concentration and Corresponding Dust Lead Data in the TLC Trial.

	Number of Pairs	Correlation Coefficient	Probability
Floor			
Dust Loading (g/m^2)	194	0.17	0.021
Lead Loading (mg/m^2)	194	0.10	0.172
Lead Concentration (μg/g)	194	0.01	0.907
Sill			
Dust Loading (g/m^2)	185	0.05	0.500
Lead Loading (mg/m^2)	185	0.02	0.812
Lead Concentration (μg/g)	185	0.01	0.850
Blood			
Lead Concentration (μg/dl)	197	0.02	0.760

Table 5.6 Partial Correlation Coefficients of Blood Lead Concentration and Corresponding Dust Lead Data in the TLC Trial as Ferritin Was Controlled.

	Number of Pairs[a]	Correlation Coefficient	Probability
Floor			
Dust Loading (g/m^2)	191	0.09	0.226
Lead Loading (mg/m^2)	191	0.22	0.002 *
Lead Concentration ($\mu g/g$)	191	0.21	0.003 *
Sill			
Dust Loading (g/m^2)	182	0.03	0.671
Lead Loading (mg/m^2)	182	0.13	0.072
Lead Concentration ($\mu g/g$)	182	0.14	0.063

*: significant. a: fewer cases due to missing ferritin values.

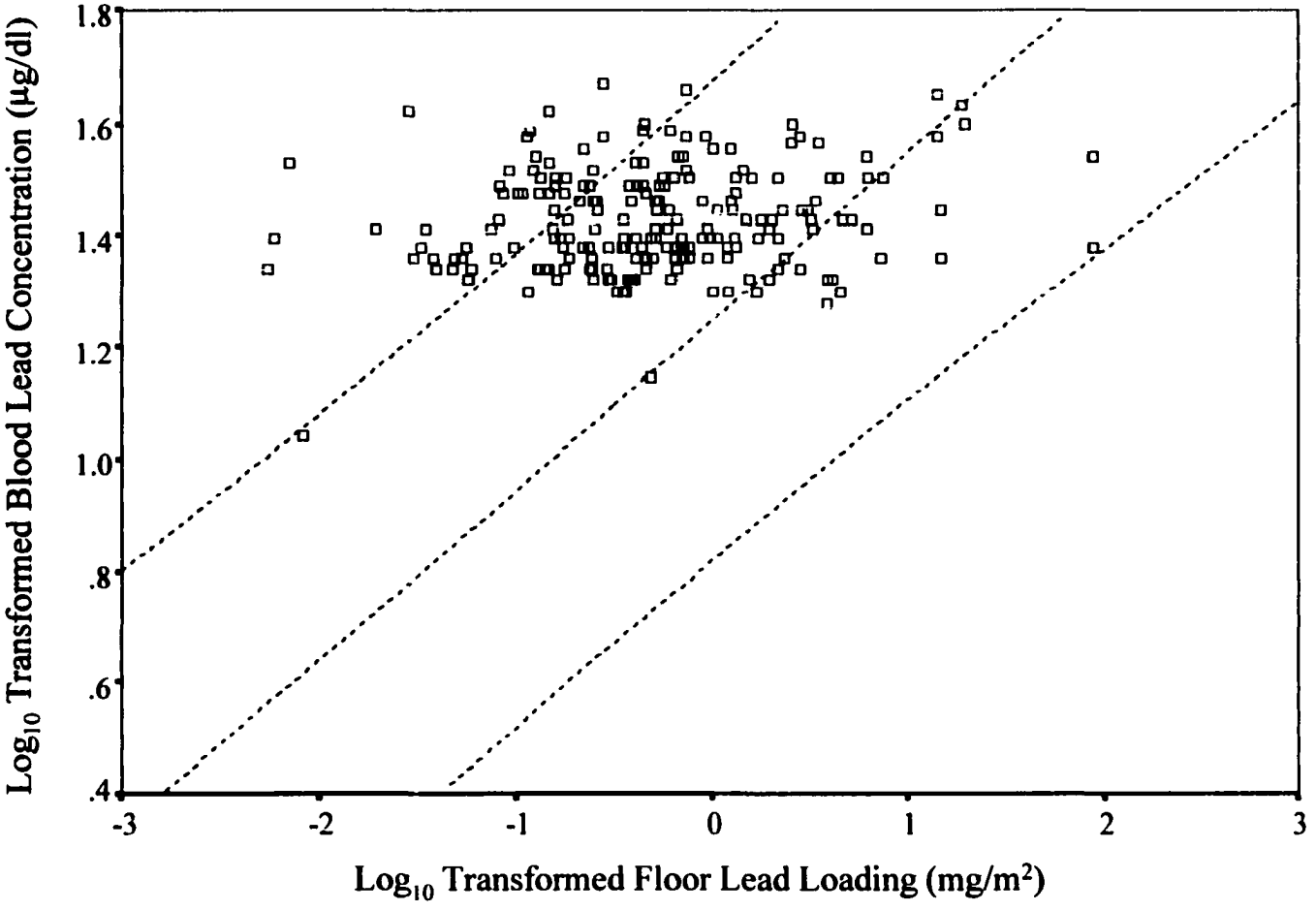

Figure 5.6 Scatterplot of TLC Floor Lead Loading versus Blood Lead Concentration (CLEARS regression lines at 95% confidence intervals).

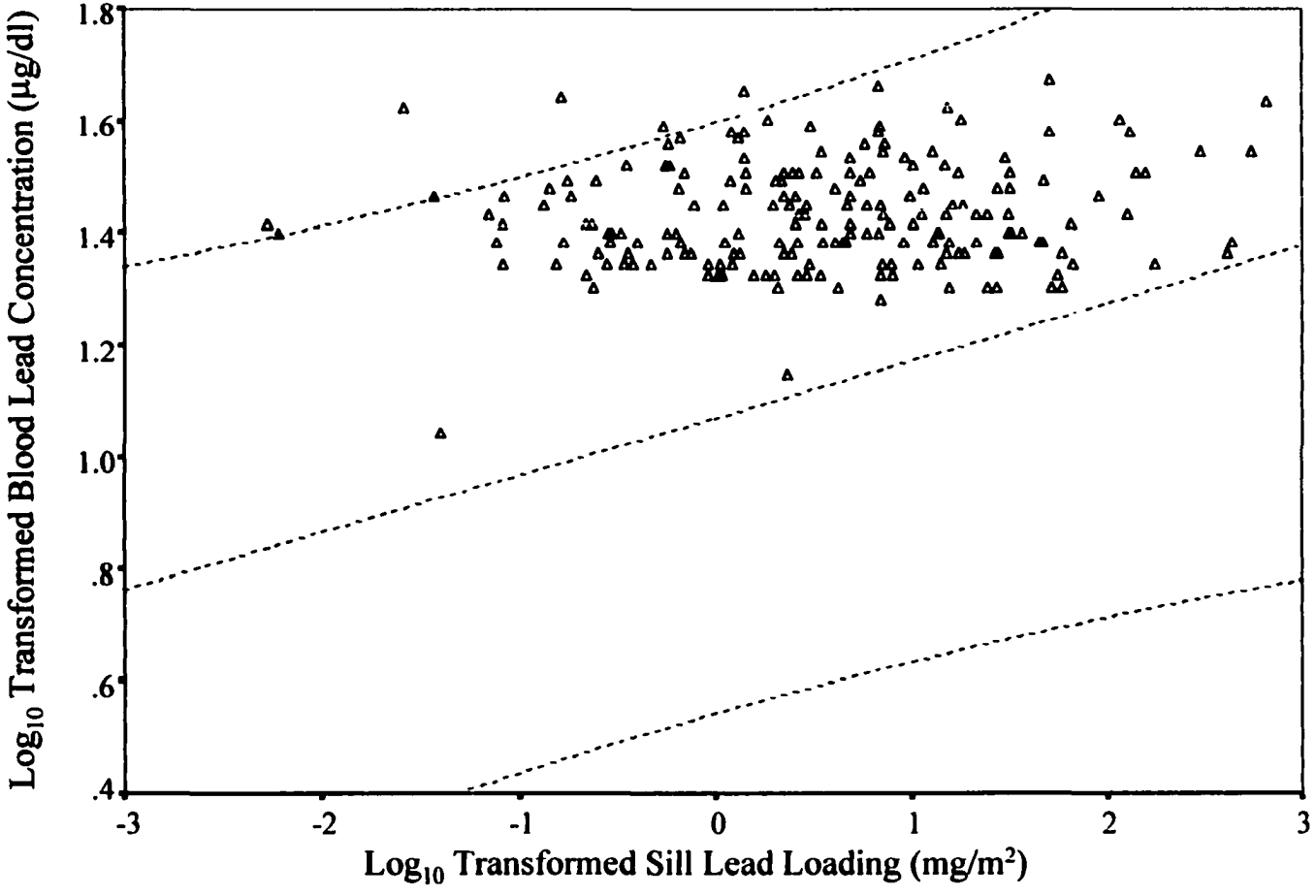

Figure 5.7 Scatterplot of TLC Sill Lead Loading versus Blood Lead Concentration (CLEARS regression lines at 95% confidence intervals).

5.5 Discussion

5.5.1 Comparisons of the Two LWW Samplings

The side-by-side LWW comparisons demonstrated that no significant differences in lead concentration, lead loading or dust loading between the original and modified samplers were observed (Table 5.1). However, the low correlation for dust loading in the field study was somewhat questionable, although dust loading showed a good correlation in the laboratory study and it was irrelevant to predicting blood lead concentration. Some likely outliers far from the correlation trend line were found in the dust loading chart, and they lowered the correlation between the two wipe samplings (Figure 5.5). The outliers commonly had large differences in dust loading between the two wipe samplings, and the differences might result from the functioning failure of either the original sampler or the modified sampler. During the field sampling, the non-skid rubber pad that was stuck to the sampling block of the original LWW sampler occurred to be peeled off by friction in some occasions when sampling on a rough surface. In those occasions, the original sampler collected much less leaded dust than did the modified sampler. Therefore, the outliers for the correlation in dust loading appeared above the trend line (Figure 5.5).

The modified LWW sampler with enhanced filter-holding strength would function properly when sampling on a rough surface. However, when it was used on a smooth but irregular surface in the field, it was unable to collect all the dust within the template since the rigid sampling block did not have a full contact onto the sampling surface. In contrast, the original LWW sampler with filter media mounted on no-skid rubber pad could have a full contact onto the irregular surface, and collected all the dust on the surface. In this occasion, the original sampler obtained more leaded dust than the

modified sampler did, and the outliers were located below the correlation trend line (Figure 5.5). Consequently, since rough surfaces were more frequently met than irregular surfaces in the field sampling, the modified LWW sampler should be a better tool for lead exposure measurement and assessment.

5.5.2 Comparisons of the Two Urban Lead Exposures

The CLEARS covered low to mild levels of lead poisoning in children (< 25 μg/dl), while the TLC Trial focused on moderately high range of blood lead concentrations (20-44 μg/dl). The CLEARS showed that PbBs in children were correlated with PbDs in the residences (Table 3.5). The TLC Trial, with a confined range of data selection, did not show significant correlations between PbBs and PbDs (Table 5.3). Although the PbB-PbD correlations in the TLC Trial were improved after the adjustment of ferritin effect on blood lead concentration, they were not as significant as those observed in CLEARS (Table 5.6). The result indicated that lead exposure in the TLC Trial might be more complicated than that in CLEARS.

The poor correlation between PbB and PbD for the TLC data (Table 5.3) and the lowered R^2 value (0.200) for the regression model of combined CLEARS and TLC data (Equation 5.1) implied that there might be some other factors or sources of lead present in the TLC Trial. For the low and mild lead poisoning as CLEARS (< 25 μg/dl), high significance of the PbB-PbD relationship indicated that household lead dust was the major source of childhood lead exposure. Thus, changes in dust lead levels, such as household clean-ups (Chapter 2) and seasonal variation (Chapter 3), resulted in significant impacts on blood lead concentration. For the high lead poisoning (20-44

μg/dl), however, the above phenomena might not be observed because of the low PbB-PbD correlation. The ferritin effect, which increased the variability of blood lead and decreased the significance of correlation between blood lead and dust lead, only improved the PbB-PbD correlation slightly. There must have been some other factors that might be influential in the process of lead exposure. A study focusing on hygiene- and food-related behaviors of children indicated that children who ate food dropped on the ground or ate sticky/greasy foods (e.g. hamburgers, doughnuts, or jelly sandwiches) were associated with elevated blood lead levels, while those who took vitamins and yogurt were associated with low blood lead levels (Freeman *et al.*, 1997). In addition, high lead-containing toys would be an acute source of childhood lead exposure. Therefore, when studying on a high lead-poisoning exposure, such as the TLC trial, any possible factors besides dust lead (source) and blood lead (outcome) have to be examined cautiously.

Although dust lead might not be the major source in the TLC Trial, it could been observed, by comparing the two regression models, that patterns of dust lead exposure for the TLC Trial and CLEARS were different. The regression model showed that blood lead concentration was only related to floor lead loading in CLEARS (Equation 3.2), but it was a function of floor lead loading and sill lead loading in the combined data of the TLC Trial and CLEARS (Equation 5.1). It was not hard to find that the presence of sill lead loading for the combined data resulted from the addition of the high TLC blood lead and dust lead data. Lead dust on floors was the major lead source to children in the uncarpeted houses, since floors in the residential environments were easily accessible. In the low to mild blood lead levels in CLEARS, children were likely to receive lead exposure most from the floor. In the levels of low to moderately high lead poisoning

(combined TLC Trial and CLEARS), however, lead dust on the windowsill became a significant source of lead exposure. Because of the accessibility of floors and windowsills in the houses, floor lead loading was still more important than sill lead loading in relation to blood lead concentration during the lead exposure. The fact was also shown by the high standardized coefficient (β) for floor lead loading from the regression model. Consequently, the result indicated that high lead-poisoned children in the TLC Trial not only were exposed to lead-laden dust on the floor and the windowsill but also were affected by other factors (e.g. hygiene- and food-related behaviors) to fluctuate their lead exposure in the homes.

CHAPTER 6: CONCLUSIONS AND PUBLIC HEALTH IMPLICATIONS

6.1 Summary of Research Results

The research presented in this thesis examined the relationship between children's blood lead concentrations and their residential dust lead levels in multiple ways, including cleaning intervention implementation, seasonal variation, and floor-surfacing types in the home. The thesis also examined the PbB-PbD relationships for two lead exposures with different levels of lead poisoning. The research results described in Chapter 2-5 can be summarized as follows:

- The CLEARS cleaning intervention effectively reduced dust loading and lead loading in carpets or rugs and on surfaces, such as floors and windowsills. No changes in lead loading or dust loading were found in the control group (Accident Prevention Group).
- The seasonality of children's blood lead levels (highest in summer) was associated with the same seasonal pattern of dust lead levels and the outdoor activity pattern.
- Blood lead concentration was found a function of lead loading of floor wipe samples in the uncarpeted homes, while in the carpeted homes, blood lead concentration was significantly related to lead concentration of carpet vacuum samples and lead loading of sill wipe samples.
- Different types of floor surfacing (carpeted or floor tiles paved) resulted in different outcomes in children's blood lead concentrations after the cleaning intervention. The blood lead levels of children living in the uncarpeted houses were lowered when the

dust lead levels in the houses decreased by the cleaning intervention. However, the significant PbB declines in children living in the carpeted houses were smaller, even though the dust and lead loadings were effectively reduced by the cleaning intervention.

- The side-by-side comparisons of dust wipe sampling methods using the original and modified LWW samplers demonstrated no differences in lead concentration, lead loading or dust loading.
- Dust lead levels were associated with blood lead levels in children for the low or mild lead exposure (< 25 μg/dl), but no significant correlation was found between PbBs in children and PbDs in the home for the high levels of lead poisoning (20-44 μg/dl).

6.2 Conclusions

The summarized research results in this thesis have supported the relationship between blood lead levels in children and dust lead levels in the residential environments. Dust lead control, which is considered to reduce sources of lead exposure, can be implemented by applying frequent cleaning work. The cleaning intervention in CLEARS has effectively reduced dust lead levels in the residences (Chapter 2) and geometric mean blood lead concentration in preschool children (Rhoads *et al.*, 1999). It seemed that 0.12 mg/m^2 was the background value for lead loading on floors since the cleaning intervention could not reduce the PbD any further below that value. The effect of cleaning intervention on children's blood lead concentrations, however, varied with the types of home floor surfacing. (Chapter 4). The geometric mean blood lead concentration in children living in the uncarpeted Lead Intervention homes was significantly reduced

28.7% to be below 8 μg/dl (Table 4.3a). However, in the carpeted homes, the decline in geometric mean blood lead concentration was only 11.6% and not statistically significant. This result indicated that, even though the cleaning intervention effectively reduced dust lead levels in the carpet, carpets in the home remained a source of lead exposure for children.

The high blood lead concentration in preschool children, the high dust lead levels in the homes, and the outdoor high-lead source exposure pattern were observed during the summertime. The indoor dust lead levels of floor lead loading, sill lead loading and carpet lead concentration showed the highest levels in the hottest months (June, July and August) in New Jersey, and were strongly correlated with blood lead concentration. No other seasonal factors than household dust lead levels were found to have a significant relation to children's blood lead concentrations. In addition, the outdoor activity patterns indicated that children spent more hours staying or playing outdoors in summer than in winter. It implied that children who had longer playing time outdoors were more likely to contact high lead-content dust sources. The seasonality of different sources and patterns appeared to reflect the seasonality of childhood lead exposure.

At low to mild levels of lead poisoning, children's blood lead concentrations were determined as a function of floor lead loading for the uncarpeted houses (Equation 3.2), and were related to carpet lead concentration and sill lead loading for the carpeted houses (Equation 3.1). Given the PbB-PbD relationships, it is not hard to understand the different results of cleaning intervention for carpeted and uncarpeted homes, since the intervention was effective in reducing floor lead loading in the uncarpeted homes but not carpet lead concentration in the carpeted homes (Chapter 2). At high levels of lead poisoning in the

uncarpeted homes, lead loading on windowsills, besides lead loading on floors, became significant in relation to blood lead concentration (Equation 5.1). The comparison between the two levels of lead poisoning indicated that higher blood lead concentration in children might, at least in part, result from more contact with lead dust on the windowsills in the homes.

Unlike CLEARS, the TLC Trial did not have a significant correlation between PbBs and PbDs. This indicated that other factors, such as hygiene- and food-related behaviors of children and nutritious status (e.g. iron and calcium), became an influence on childhood lead exposure. More work on factors other than dust lead and blood lead for the TLC Trial is necessary to complete this study of lead exposure.

6.3 Implications of Public Health Policy

The goal of childhood lead exposure study is to understand the sources of lead in the household and to prevent children from lead poisoning. The relationship between dust lead levels in the residences and blood lead concentrations in children is very important, because it provides the information to control lead exposure occurring in the home. In CLEARS, the cleaning intervention was provided to the Lead Intervention homes every two weeks, and it was testified to be effective in reducing dust lead levels of the residential environments. However, it seemed that the cleaning intervention was sufficient for floors but not for carpets, since the PbB decline in the carpeted Lead Intervention homes was not statistically significant. Carpets or rugs, which were a huge lead dust reservoir, might still contain much dust after the implementation of cleaning intervention. To reduce lead exposure in the carpeted houses, the fastest way is to replace

old carpets or rugs with new ones or floor tiles instead to avoid high lead accumulation in the home. Alternatively, taking shoes off prior to entering homes can avoid track-in lead dust and soil (Roberts *et al.*, 1991b), and vacuuming more frequently than once per two weeks may reduce dust lead levels even lower. Since carpet lead concentration is related to blood lead concentration, attempts to lower lead concentration in the carpet may also help reduce lead exposure. The geometric mean carpet lead concentration in CLEARS (502 μg/g) was above the outdoor lead cleanup standard in New Jersey (400 μg/g) (Table 2.1). Children's blood lead concentration should be significantly lowered, if lead concentration in the carpet can drop below the 400 μg/g limit.

Windowsills are usually a microenvironment that stores the highest lead-contaminated dust in the home. At the high levels of lead poisoning in the TLC Trial, sill lead loading became significant in relation to blood lead concentration. Windowsills are a potentially high lead source, because residents easily ignore the importance of cleaning on the windowsill. Lead-based paint chips or particles should be carefully removed from the windowsill to keep children from acute lead poisoning.

Children's high blood lead concentrations during the summertime are of concern. Not only were dust lead levels in the home the highest, but also children had more chances to contact outdoor high leaded street dust/soil when playing longer outdoors. To prevent children from high lead poisoning in summer, frequent and thorough cleaning work is necessary to remain low dust lead levels in the household. In addition, children's hygiene- and food-related behaviors should be taken care of, because improper behaviors may worsen lead poisoning but vitamins and minerals (e.g. calcium and iron) intake may reduce lead absorption occurring inside children's bodies.

CHAPTER 7: FUTURE RESEARCH RECOMMENDATIONS

Three future research goals may be needed to complete the lead exposure study:

1. The XRF values of houses indicate the potential lead sources in the household. The XRF levels in the homes may influence the effect of cleaning intervention. Besides, to examine the relationships between the XRF levels and dust lead levels may be of interest.

2. High variability was observed for the PbB-PbD relationships in the levels of high lead poisoning. Ferritin levels were found a slight influence on blood lead concentration. Other nutrition status, such as intakes of calcium and vitamins, may be also influential to children's blood lead levels. It may help examine and reduce childhood lead exposure in high lead contaminated houses.

3. Cleaning on carpets was not effective in reducing children's blood lead concentration in CLEARS. To find a carpet cleaning method that can be effective to lower children's blood lead concentration may be of interest.

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APPENDICES

Appendix 1. Protocol of the Childhood Lead Exposure Assessment and Reduction Study

PROTOCOL

Children's Lead Exposure and Reduction Study

BACKGROUND AND SPECIFIC AIMS

In recent years there has been increasing evidence that lead may be the most important environmental toxin affecting the health and development of children in the United States. It is clear that specific metabolic processes are affected at lead concentrations that are found in the blood of many young children,[1] and a number of good studies have suggested that youngsters with levels as low as 10-25 ug/dl may suffer neurologic and cognitive deficits. These studies are particularly damning, because they provide direct prima facie evidence that ambient lead, at levels that are commonly found in our society, is directly contributing to the destruction of human potential, and, consequently, to the cycle of poor educational outcome, unemployment, and welfare support that is much too frequent in American inner cities.

While the ultimate solution to this problem is the removal of lead from residential environments, this will not be possible in the near or intermediate term. There remain tens of millions of housing units with lead painted surfaces, many of which also have high lead levels in their water supply, in household dust and/or in the surrounding soil.[1] There is little prospect that funds can be found to eliminate these ubiquitous lead sources.

Since it is inevitable that children will continue to live in lead contaminated housing, the object of this proposal is to refine our understanding of the sources of lead to which these children are exposed, to search for ways of identifying infants at increased risk, and to test potential interventions that could minimize their exposure to lead. While contaminated paint has historically been the major source of intake for children with lead levels above 40 ug/dl, control of intake from additional sources of exposure will be required to bring lead levels down to currently proposed target levels--i.e. 10 ug/dl. The relative significance of the routes of exposure to lead will categorized, and used to define the types of intervention used to mitigate the exposure.

The project has the following specific aims:

1. Quantitate lead content in paint, in water, and in household dust of children's homes as well as in nearby soil.

2. Estimate each child's exposure derived from contact with lead from different media and routes of exposure.

3. Identify biological and other markers measurable prenatally and in the first nine months of life that are best able to predict blood lead at age two years. As part of this effort we expect to develop a lead sampling kit that the client can use in her own home to collect dust in a standard fashion suitable for testing for lead content and screening for individuals with high exposure.

4. Test a vigorous intervention-exposure reduction program in a randomized trial to examine its capacity to minimize the increase in blood lead that usually occurs in young inner city children. The approach will combine a lead reduction educational program with biweekly help in dust control.

BACKGROUND

The toxicity of lead has been recognized for many centuries. However, it is only in recent decades that the mechanisms of this toxicity have begun to be understood and that substantial evidence has accumulated that blood levels well below those associated with acute symptoms and anemia may nevertheless be harmful.

In one of the best known of these studies, Needleman[2] looked at first and second grade children in two Boston suburbs and found a 4.5 point difference on the full scale Wechsler IQ test between the lowest lead exposed group (dentine lead level <6 ppm) and the highest group (dentine lead level >24 ppm). In an 11 year follow-up these authors[3] re-examined 132 of the 158 children originally examined. The subjects who were retested tended to have slightly lower dentine lead levels, and were from families with higher educational attainment and greater socioeconomic status. For the young adults with dentine lead levels > 20 ppm, as compared with those whose dentine lead levels were < 10 ppm, the unadjusted odds ratio for having a reading disability, defined by a score two grades below that expected for the highest grade completed, was 3.9 (95% C.I. 1.5 to 10.5). Adjustments for covariates increased the odds ratio to 5.8 (95% C.I. 1.7 to 19.7). Higher dentine lead levels were also associated with lower class rank, increased absenteeism, and lower scores on vocabulary and grammatical-reasoning tests.

A number of other investigators have reported results that also attest to the damaging effect of modest levels of lead exposure. Yule examined 166 children between the ages of 6-12 years living near a lead works in outer London.[4] In a summary of analysis of covariance with social class controlled, Yule found a 7.5 point difference on the full scale IQ test between the low lead group(blood lead 7-10 ug/dl) and high lead group(blood lead 17-32 ug/dl).

Hansen carried out a cross-sectional study of first graders in 1982-1983.[5] Of the 1,291 children who donated a useable tooth, 162 were given selected psychometric tests. The low exposure group had dentine lead levels < 5 ug/g (mean = 3.25 ug/g) and the high exposure group had dentine lead levels >18.7 ug/g (mean = 26.8 ug/g). Using the matched-sample t-test the high-lead children scored lower on the WISC Verbal and Full scale IQ than the low-lead children, the differences being 8.6 ($p<0.001$) and 5.9 ($p<0.01$) points respectively. There was no significant difference between the high and low exposure groups on the Performance IQ. Impaired function associated with lead exposure was found on the Bender Visual Motor Gestalt Test ($p<0.001$) and on the behavioral ratings test ($p<0.01$). The authors state that the results remained statistically significant even after controlling for socio-economic and other confounding variables.

Blood lead levels of the magnitude found in the above studies are common in American children. Fully half of African-American inner city children were found to have blood lead in excess of 20 ug/dl in 1976-80,[6] and although levels are believed to have fallen since then, 8% of children screened in Newark in 1988 still had levels above 25 ug/dl combined with elevated EP.[7] A very substantial fraction of American children are believed to develop blood lead levels above 10 ug/dl which has now been promulgated by CDC as the upper limit of the acceptable range.

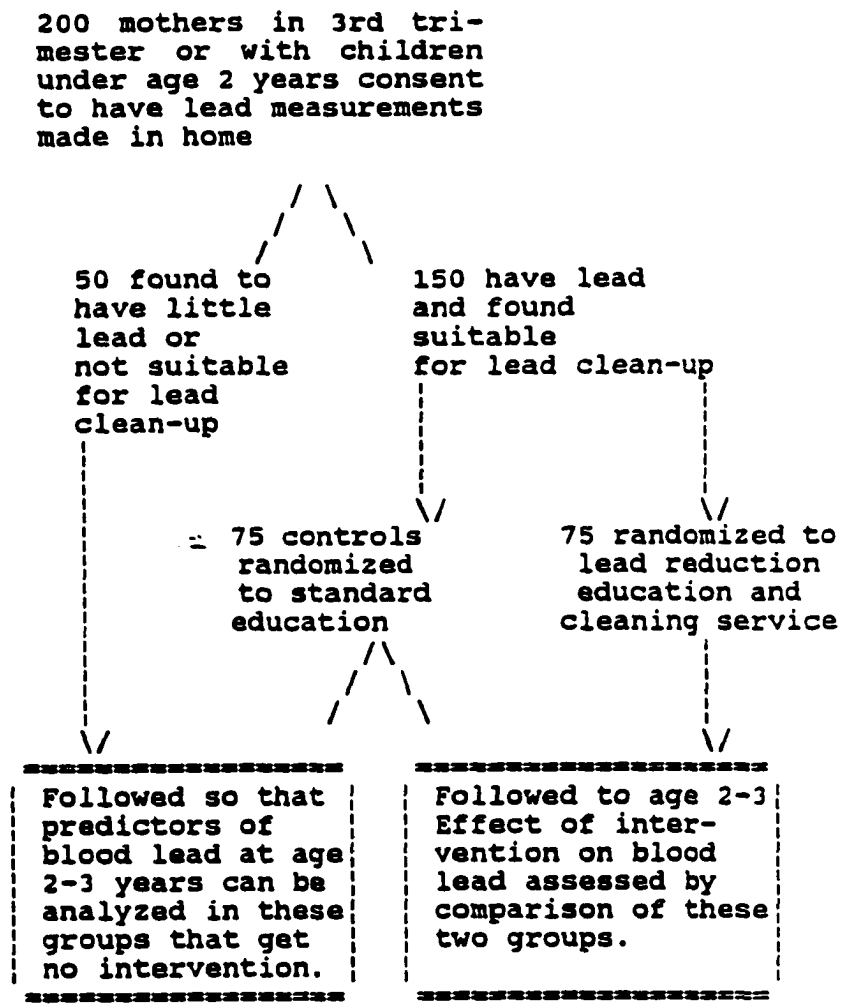
While these studies define the problem, the question that confronts public health and environmental scientists is what can be done to prevent it. Lead contamination from past and present use of leaded gasoline, from deteriorating paint, from water tanks and pipes, and from contamination of the food chain, is ubiquitous and leads to especially severe multi-route exposure problems in the inner cities. Since it will take decades to abate sources which are found in an individual's home or environment, there is a pressing need to develop practical strategies that can be used in the near term to minimize the exposure of young children.

Charney et al have shown in a randomized trial that careful household cleaning can reduce lead levels by 6 ug/dl in older children with significant lead poisoning (mean blood lead about 40 ug/dl) over a period of one year.[8] This reduction was achieved despite the body burdens that these children already carried. We believe it would be useful to examine this approach to see if intervention-exposure reduction strategies can be used to prevent high risk children from building up excessive lead levels in the first place. As noted below, a very modest reduction of mean blood lead would have a large impact on the number of children developing levels in the toxic range above 10 ug/dl.

METHODS

We will study a cohort of young inner city children from the late prenatal period up to the age of 2-3 years in order to assess the roles of different sources of lead exposure and to test a multi-faceted approach to minimizing exposure and absorption of this important toxin. Women will be recruited from a prenatal clinic or because their infant or toddler is known to be at increased risk of excessive lead exposure. Lead exposures in their homes will be carefully measured, participants will be assigned randomly to intervention and control groups, and outcome will be assessed both in terms of the extent to which lead dust is diminished in the home and in terms of blood lead after 12-18 months of intervention. Analysis will focus on identifying the most important predictors of blood lead at age 18-36 months and on the efficacy of the intervention in reducing the lead levels attained at these ages. The overall study outline is shown on the next page.

Figure 1



Recruitment

Women will be recruited in Jersey City, where, in 1980, 73% of children between the ages of 6 months and 2 years were living in housing that was built before 1950.[1] Two principal sources of subjects will be used:

1. Prenatal clinic registrants believed to be living in private housing built before 1960 will be recruited up to the end of 1992. These women will be identified by direct approach in the clinic, through posters and brochures advertising the study, and by referrals and word of mouth. Preference will be given to those with a prior child known to have screened positive for lead (Class II or higher as determined from the lead screening program records).

2. Children under the age of two years believed to be at increased risk of lead poisoning from home exposures. These children will be referred because of:

a) blood lead levels above 10 ug/dl (but below levels currently being abated or medically treated)

and b) other evidence of risk based on a known contaminated home or an older sibling who has had elevated lead levels. Home lead contamination is based on an average XRF reading of 2.0 mg/cm^2 or greater on at least one interior surface or a dust lead of greater than 1500 ppm obtained from a composite wipe sample.

A home interview will be scheduled with all potential participants. The nature of the project will be explained including the plan to assign participants with suitable homes by chance to one of the two groups. Consent is obtained and an initial interview is completed including questions about any elevated lead levels in older siblings, and occupational and other exposure to lead for the subject or her family (Appendix I). A baseline assessment of lead contamination and of accident hazards in the home is carried out (see below).

Subjects giving consent, completing the home assessment, and providing a baseline blood lead will all be followed. Most of these

subjects will be randomized. However, participants will be excluded from randomization a) if it appears likely at the time of initial interview that they will move, b) if the child will not mainly be cared for at home during the study period, c) if they indicate that they are using street drugs, d) if they will not consent to randomization, e) if they are unwilling to provide a blood sample for a blood lead determination, f) if there is no evidence of lead in the home by the above criteria, or g) if the cleaning protocol would be too difficult to implement because of the very poor condition of the home or because of security concerns. Those subjects participating in the baseline home evaluation, but who are not randomized will be given educational materials and offered blood lead screening.

Baseline Home Environment Assessment

At the initial home visit a member of the technical staff of the Exposure Measurement and Assessment Division (EMAD) will complete a standardized qualitative assessment of the state of the home. The floor plan of the home is sketched and the dimensions of all rooms recorded. Lead content of major types of painted surfaces in the kitchen, the child's bedroom and one other room where the child is likely to play are estimated by portable XRF. The EMAD staff member will collect micro-environmental samples of dust as follows: a) A wipe sample is collected from the floor of each room that is not covered by carpeting. The location of this sample is chosen to represent the area where the child is most likely (or is known) to play. b) A wipe sample is taken from one window sill, usually in the living room. c) A rug vacuum sample is collected from each room where there is a carpet. A maximum of two vacuum samples may be collected from one room if there are two different types of carpet represented there. d) If all XRF readings are below 2.0 ug/dl, an additional composite wipe sample is taken from areas that will afford a substantial mass of dust. (The purpose of this extra sample is to provide an adequate amount of material to allow an expedited flame AA analysis so that a judgment can be made as to whether the home is lead contaminated despite the negative XRF readings.) e) A water sample will be collected from the kitchen tap.

In addition to these items related to lead exposure, the home assessment will include an inventory of accident hazards including unguarded stairs and windows, absence of smoke alarm, unguarded cleaning materials and other poisons, hot water temperature, and electrical hazards.

Assignment to Interventions

Study participants meeting the criteria for randomization will be randomly assigned to two sub-groups: one to receive an intervention comprised of intensive lead exposure education and household cleaning services to reduce the potential for exposure, and the other (to serve as a control) to receive comparable educational sessions devoted mainly to accident prevention. For the study group assignment process, sealed, opaque envelopes will be prepared ahead of time using a randomized block design with variable blocks sized 2, 4, or 6. At the end of each block one-half of the subjects will have been assigned to the control group and one-half to the intervention group, but within a block the order of assignment will be random. Pregnant women and infants (up to six months)are randomized from the front end of the box of envelopes while babies over six months and toddlers are randomized from the back end-- in effect achieving stratified randomization to assure that each type of subject will be approximately equally divided between the two treatment groups. Only 20 pregnant women are expected to be recruited because of the much longer follow-up that they require to reach a suitable blood lead end point in a toddler.

Lead Reduction Education for the Intervention-Exposure Reduction Group

The overall goal of the health education program is to increase the subjects' awareness of the lead and accident issues and to present the necessary technical information in a non-threatening way. It is important to promote their sense that they can improve their environment and reduce these environmental risks for their children. Wherever possible active learning approaches will be used in order to maximize the amount of material that is retained.

The educational program for women randomized to the lead reduction group will emphasize several ways in which mother can minimize the exposure of her infant to lead. Areas covered will include a) letting the water run for 2 minutes before using it to make up baby's juice or formula; b) keeping the house clean, especially those areas where the infant will be crawling and playing; c) advice about wet mopping/wiping with high phosphate detergents for cleaning; d) keeping baby's hands clean and minimizing opportunities for the baby to put dust contaminated objects in the mouth; and e) encouraging the use of iron supplementation, where appropriate, to reduce lead absorption. We anticipate that most of the young children will have iron supplementation in their formula.

The health education protocol will be organized in five sessions. The timing of these sessions and the order of presentation differs somewhat between the subjects enrolled before six months of age and those enrolled later:

	Enrolled Before 6 Mo.	Enrolled after 6 Mo.
Session I	At baseline home visit	At baseline home visit
Session IP*	2 wks after baseline Focuses on formula preparation and letting water run 2 min	
Session II	Age 3 months Focuses on dust lead & ways of reducing exposure	2 wks after baseline More on dust lead plus letting water run
Session III	Age 6 months Review	3.5 months post baseline Review
Session IV	Age 9 months Review	6.5 months post baseline Review
Session V	Age 18-24 months Post-test	11-13 months post baseline- Post-test

*This extra session is provided to pregnant mothers and mothers of children under six months.

Mother will be given a variety of aids to help her implement what she learns about the lead issue - stickers to put above the kitchen and bathroom faucets to remind her to let the water run; a planning booklet about where baby will play and a cleaning schedule to use; a supply of high phosphate detergent in a childproof container; a supply of appropriately packaged and labeled iron supplements; and other items.

The educational sessions will be scheduled to last about 45 minutes and will take place as much as possible in the program office, preferably with groups of 3-4 mothers (all randomized to the same group). As noted above the content of the first few sessions will differ somewhat between subjects recruited while still pregnant and those recruited with exposed infants/toddlers. It is anticipated that some re-inforcement of lead reduction education will occur through the biweekly contacts with the cleaning staff.

The pretest and post-test will assess the client's concept of what lead is, her perceived ideas about lead and accidents, and whether she believes she has any control over these issues.

Incentives will be used not only as a reward system to increase cooperation, but also as effective tools in fostering a relationship between the study and the client. They are chosen to encourage the client to take control and participate in reducing the risks of lead poisoning and accidents for her family. Increased self esteem and coping skills are seen as important adjuvants to the more specific educational messages. Incentives chosen include a pacifier to diminish hand-to-mouth activity, hand scrubbies to increase participation in hand washing, and cleaning supplies to encourage participation in cleaning of the home.

More detail about the materials used in the educational sessions is given in a separate Health Education Protocol.

Accident Prevention Education for the Control Group

Women in the control group will receive a baseline packet of information about lead which is at least as detailed as that provided by their usual source of pediatric care, and in addition will receive limited additional education about lead in conjunction with the accident education program. Emphasis will be placed on the importance of obtaining follow-up lead screening which will be provided by the study. The accident prevention part of these sessions will be based on materials developed by the American Academy of Pediatrics and/or other well developed accident prevention packages and will include a supply of ipecac and information about their local poison control center.

Lead Dust Control Services

The women randomized to the intervention group will receive lead dust control service every two weeks over a 12-18 month period which will begin when the child reaches six months of age or, for older children, as soon after randomization as possible. This activity will be continued for twelve months or until the child reaches two years of age, whichever occurs later. Home dust control is carried out by a crew of two persons, who are trained in practical ways to reduce lead contamination in the home. The dust reduction staff will discuss with mother where the child is playing so that special attention can be given to these areas. Special attention will also be given to areas, if any, which have been identified as having a particularly high lead loading. Floors and smooth surfaces will be cleaned with a high phosphate detergent (Spic and Span), while rugs and carpets will be cleaned with a HEPA vacuum. Carpets that are identified as lead contaminated will be replaced whenever possible. Effort will be made to involve the family in these clean-up efforts and to give them a sense that they can take control of this important area of their lives. If modest areas of loose paint are noted in accessible areas, family members will be encouraged to repair them with simple wet-scraping and repainting.

Follow-up Blood Lead Determinations

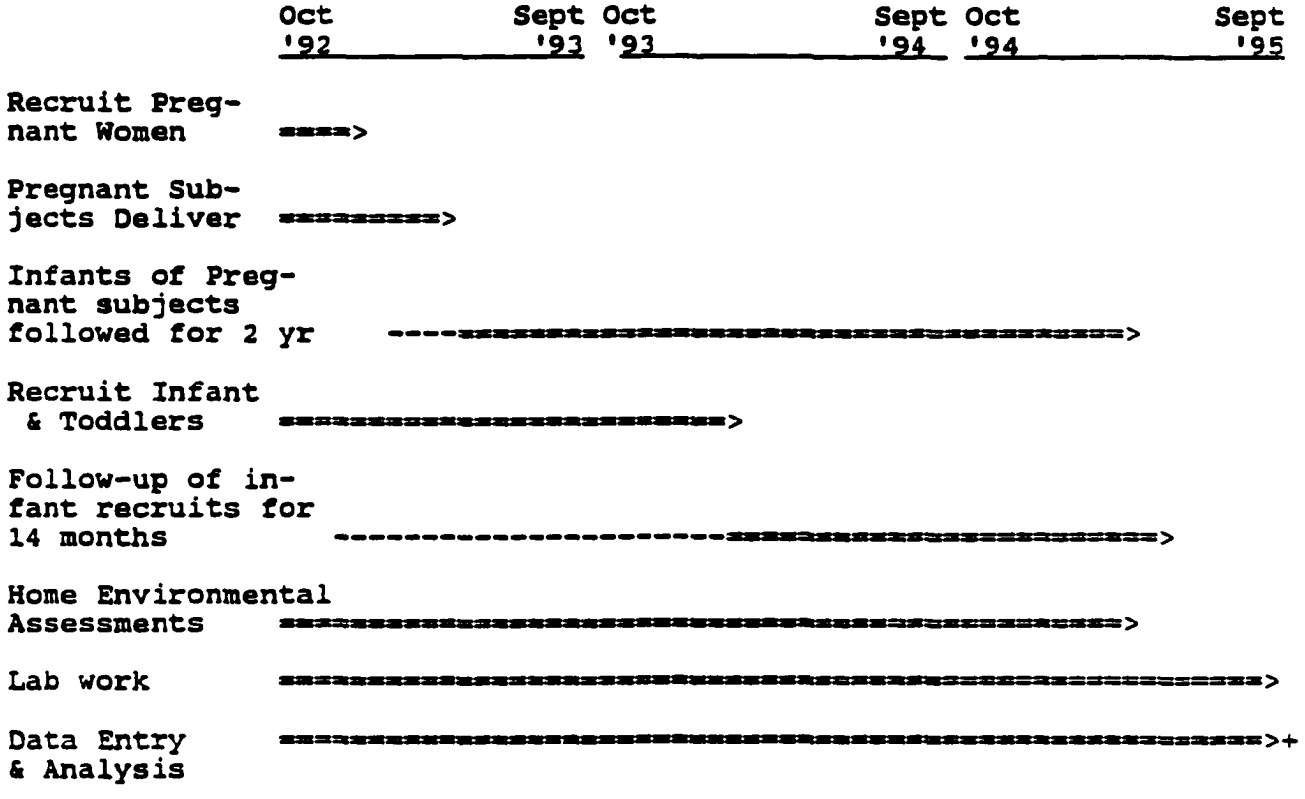
It is anticipated that the children enrolled while in-utero would normally have blood drawn from a finger tip at nine months and at eighteen months of age as part of their routine care in the clinic. When possible, arrangements are made to obtain venous blood at these times to monitor the blood lead levels of the children. An additional blood lead will be drawn at two years. These follow-up blood leads will be obtained for both the randomized children and also for those whose homes were deemed unsuitable for randomization. Children enrolled after birth will have a blood lead drawn at enrollment and two blood leads drawn at least one week apart at the conclusion of their participation in the study (in the interval between 11 and 13 months after enrollment) or between 18 and 24 months of age, whichever comes later. Many of these children will have interim blood leads every three months in accordance with CDC recommendations for children with levels over 10 ug/dl.

Follow-up Home Lead Exposure Sampling

For children enrolled from birth the micro-environmental measurements in each of the study homes in the randomized part of the study will be repeated once at nine months and once at 18 months in close conjunction with the time of blood lead determination. Assessments of lead exposure in dust will be repeated using the same protocols that were used in the baseline assessments. In the homes randomized to the lead dust control service, these assessments will be scheduled as closely as possible to be half way between two cleanings.

For cases enrolled after age 1 year a single follow-up assessment will be completed between 11 and 12 months after the initiation of household dust reduction. Other assessment dust lead measurements will be carried out in the interim as needed to evaluate the efficacy of cleaning methods.

Time Line for the Study



---------indicates follow-up that is proceeding simultaneously with recruitment

It is anticipated that about 20 pregnant women will be recruited by early 1993 and will deliver by April of 1993. These children will need to be followed until they are two years of age, so that their follow-up will be compete by April of 1995. The bulk of the study subjects will be recruited as infants and toddlers with mild elevations of blood lead. These children will be recruited over a 18 month period from October 1992 through March 1994 at a rate of about 8 per month. We anticipate that it will take about 14 months to get these children assigned to their protocols, maintain them on protocol for a minimum of one year and collect the final home assessment and blood lead. Thus, these final assessments are scheduled to be completed in March of 1995 (see below)

Estimates of work load by calendar time

Biweekly dust control visits to homes randomized to the lead intervention will begin in October, 1992. The following projected numbers of homes to be visited focus on subjects recruited as infants and toddlers. Extra cleaning work load for homes of pregnant women is shown only in the last column

Calendar for Recruitment and Cleaning of Homes Randomized to Lead Group

	No. Homes Recruited Lead Group	No. Homes Continuing	No. Homes Completed	No.Visits in Month @2.2/home
1992				
October	2	0	0	4
November	4	2	0	13
December	4	6	0	22
1993				
January	4	10	0	31
February	4	14	0	40
March	4	18	0	48
April	4	22	0	57
May	4	26	0	66+2*
June	4	30	0	75+4
July	4	34	0	84+6
August	4	38	0	93+9
September	4	42	0	101+11
October	4	46	2	106+11
November	4	48	4	106+11
December	4	48	4	106+11
1994				
January	4	48	4	106+11
February	4	48	4	106+11
March	4	48	4	106+11
April	0	44	4	97+11
May	0	40	4	88+11
June	0	36	4	79+11
July	0	32	4	51+11
August	0	28	4	40+11
September	0	24	4	29+11
October	0	20	4	18+11
November	0	16	4	7+9
December	0	12	4	0+6
1995				
January	0	8	4	0+4
February	0	4	4	0+2
March	0	0	0	0

Laboratory Determinations

An average of 5 dust wipe samples, 1.5 vacuum samples and one water sample are expected to be generated from each baseline and from each follow-up home assessment. A soil sample will be collected at the follow-up assessments and will be analyzed at the Environmental Protection Agency. Detailed descriptions of the collection and analysis of these specimens is contained in the Quality Assurance document.

Statistical Power

We assume that the control children will develop a mean blood lead of about 10 ug/dl with a standard deviation of about 6 ug/dl. This would imply that 97% of them would have values under 22 ug/dl, which reasonably reflects current levels reported in inner city children. Assuming that we successfully followed 50 children in the intervention group and 50 children in the control group we would have 90% power to detect a reduction in average blood lead of 2.5 ug/dl (one-sided alpha = 0.05).

Data Analysis

Primary Endpoint:

The primary endpoint for the major analyses will be a biological marker of exposure: blood lead at the conclusion of the study. In most children we will be able to use the average of the two values obtained during this period. If only a single value is available (because of lost specimens, poor cooperation, etc) it will be used by itself for that child. If there are differences between the randomized groups in age at enrollment, adjustments will be made for the actual age(s) at which the blood leads are collected. As noted below the separate values will also be analyzed.

Baseline predictors of lead levels:

We will examine several multivariate models to test their ability to predict blood lead levels at the conclusion of the study. This analysis will be restricted to the homes that are not included in the lead intervention group. One model will be comprised of data that can be obtained from the mother and the from the medical records at baseline: age and parity, presence or absence of an older sib who screened positive for lead, and similar information. Another will add the child's first blood lead (obtained at entry or at age nine months) and a composite dust lead score that is obtained from the material mother collects and returns for analysis. A third will add summary statistics reflecting all

environmental lead exposure data that are collected by study staff at baseline.

The strategy behind this approach is to see how much the prediction is improved by adding increasingly specific information that is not generally available. If it turns out that a few pieces of specific information substantially improve the prediction of which children are at risk, that would enable environmental exposure reduction efforts to be better focused on specific children.

These analyses can either be done using multiple regression with blood lead as the dependent variable, or the blood leads could be dichotomized at 10 ug/dl and put in a multiple logistic model. A backward step-wise approach will be used to eliminate variables that do not contribute to the various models except that where a readily accessible variable is co-linear with one that is hard to obtain, the former will be preferentially retained.

These analyses will allow us to identify variables that are useful for identifying children at high risk of undue lead absorption. They will also allow us to formulate a specific screening strategy and to examine its specificity, sensitivity and predictive value in these data. If such a strategy looks promising, it could provide the impetus for validation in an independent data set.

The clinical trial:

Every clinical trial should have a primary analysis specified ahead of time that is used to estimate the power of the study during the planning phase and that can be carried out at the end without the criticism that it is only one of many significance tests that are computed. The primary analysis for this trial will examine whether blood lead at the conclusion of the intervention period is lower in the experimental group than in the control group. For this analysis subjects will be retained in the groups to which they are originally randomized without regard to their level of compliance with the recommendations for lead reduction. This is a standard, conservative approach that ensures that the comparability of the groups created by randomization is retained. This primary analysis will be carried out with and without adjustment for differences in household dust lead at baseline.

Important additional analyses will be done to see if the intervention is associated with reduced levels of ambient lead in household dust and whether the levels in dust correlate well with blood levels in the children.

Lead source analyses:

A variety of other analyses will be undertaken. In particular the relation of blood lead to lead in dust, tap water, and soil will be examined. The relationship between the amount of lead in the interior painted surfaces of the house (as measured by portable XRF) and the amount in the dust will also be of interest.

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Appendix 2. Protocol of the Treatment of Lead-exposed Children Trial

1. PURPOSE AND RATIONALE

1.1. Introduction

The adverse effects of exposure to high levels of lead have been known for hundreds of years. Only recently, however, have the effects of relatively low level exposures to lead on development, blood pressure levels, and other health endpoints been recognized. Epidemiologic studies[1,2] have, for example, reported deficits of three to seven intelligence quotient (IQ) points per 10 micrograms per deciliter (μg/dL) increase in average blood lead concentration in cognitive test scores of exposed children tested at ages four to eleven. Primate and human neurodevelopmental research has provided evidence that attention, learning, short-term memory, and executive function may be the selectively deficient domains of cognition that underlie these IQ differences.[3] The Clean Air Science Advisory Committee of the Environmental Protection Agency[4] has recommended 10 μg/dL as the maximum safe blood lead concentration for an individual child. The U.S. Centers for Disease Control and Prevention[5] has also recommended 10 μg/dL as the blood lead level of concern; values above this level trigger a series of actions including monitoring of exposed children, steps to prevent further exposure, and assessment of the utility of treatment.

Children living in inner cities in the United States, along with those living in older homes with leaded paint, are at highest risk of exposure to lead. The U.S. Agency for Toxic Substances and Disease Registry[6] estimates from 1984 census data that over 12 million children are at risk from leaded paint alone. Unfortunately, little is currently known about the developmental effects of treatment of children with elevated blood lead concentrations. Lead chelation with a variety of agents is known to reduce blood lead concentrations acutely, but the concentration may rebound to as much as 70% of its baseline value within weeks to months after treatment, often requiring repeated courses of treatment. Strategies for treating children with elevated blood lead concentrations and for assessing the developmental effects of those treatments are urgently needed. The Treatment of Lead-Exposed Children (TLC) Trial has been designed to assess the effects of lead chelation with succimer in children aged 12 to 32 months at the beginning of treatment as measured by developmental status three years after the initiation of treatment.

1.2. Study Objectives

1.2.1. Primary Objective

To compare the effects of lead chelation with the drug succimer and placebo therapy on developmental status, as measured by full-scale deviation IQ score measured using the Wechsler Preschool and Primary Scales of Intelligence – Revised (WPPSI-R), three years after initiation of treatment of children initially aged 12 to 32 months with baseline blood lead concentrations between 20 and 44 μg/dL. Residential lead clean-up and nutritional supplementation with multivitamins and minerals will be provided to all study children, irrespective of treatment group.

1.2.2. Secondary Objectives

To evaluate the effect of chelation on other measures of developmental status, including the verbal and performance scales of the WPPSI-R, the Child Development Inventory, Conners' Parent Rating Scale, the Woodcock-Johnson Memory for Names, the Stanford-Binet Bead Memory, Kaufman's Magic Window, Diamond's Modified Stroop Task, and the Tower of Hanoi.

To compare the effects of lead chelation and placebo therapy on change in height, weight, and head circumference during the three-year period of treatment and follow-up.

To compare the effects of lead chelation and placebo therapy on change in systolic and diastolic blood pressure levels during the three-year period of treatment and follow-up.

2. OVERVIEW OF THE TLC TRIAL

2.1. Study Design

The TLC Trial is designed to compare the effect of lead chelation with succimer to placebo therapy in boys and girls who are between 12 and 32 months of age and have blood lead concentrations (PbB) from 20 to 44 μg/dL at enrollment in the trial. Children who are referred to TLC-affiliated Clinical Centers with elevated blood lead concentrations will be enrolled in a screening and home evaluation program that includes a minimum of two clinic visits and one home visit. During the screening period, the blood lead levels of referred children will be remeasured by the TLC's central laboratory at the Centers for Disease Control and Prevention (CDC), other eligibility criteria will be checked, and their homes will be visited to determine whether they are amenable to environmental clean-up. Children whose blood lead is confirmed to be in the range of 20 to 44 μg/dL by the CDC laboratory and whose home environments meet TLC criteria will be eligible for enrollment in the randomized trial. Upon receipt of informed consent from a parent or legal guardian, eligible children will be randomized to chelation therapy with succimer or placebo. The trial will be conducted as a double-blind, placebo-controlled trial and will enroll both boys and girls equally as mandated by the NIH Revitalization Act. TLC participants will be enrolled without regard to race, but it is expected that the majority will be of African-American descent. Except for the Newark site, where many of the study participants will be Hispanic, enrollment of linguistic minorities will not be possible due to small or non-existent populations at each clinic and due to language capabilities of TLC staff.

Children enrolled in the succimer group will receive one to three rounds of chelation therapy as described subsequently. Blood lead levels will be measured two weeks after the completion of each round of chelation and reported to the Data Coordinating Center. If a child has been randomized to the succimer group and this blood lead measurement is greater than or equal to 15 μg/dL, the Clinical Center will be directed to schedule an additional round of succimer treatment. At most three rounds of treatment will be given. To preserve the double blind, the Data Coordinating Center will direct the Clinical Centers to schedule an equal number of rounds of retreatment in the placebo group. Clinical Centers will not have access to blood lead measurements during the treatment period except under special circumstances as described below. The two treatment groups will receive identical vitamin and mineral supplementation and a common lead dust management program which may be supplemented by various Clinical Centers within limitations of budget. Enrolled children will be followed for at least three years, with periodic assessment of their developmental status. The test of the trial's primary hypothesis will be based on developmental status as measured by the Wechsler Preschool and Primary Scale of Intelligence three years after enrollment. A number of additional measures of developmental status will also be considered, particularly measures of learning, short-term memory, attention, and executive function.

2.2. Administration

The TLC Trial is sponsored by the National Institute of Environmental Health Sciences (NIEHS) with support from the Office of Research on Minority Health of the National Institutes of Health (ORMH, NIH). The Trial will be conducted at four Clinical Centers: the Children's Hospital of Philadelphia (Philadelphia PA); the Kennedy Krieger Institute, in association with the Johns Hopkins University and the University of Maryland (Baltimore MD); the University of Cincinnati (Cincinnati OH) in conjunction with Columbus Children's Hospital (Columbus OH); and the University of Medicine and Dentistry of New Jersey (Newark NJ). These sites were selected on the basis of technical merit and cost from an open, nationwide competition. They serve inner city communities that are primarily African-American

and reflect well the national distribution of lead poisoning. The Harvard School of Public Health (Boston MA) will serve as the Data Coordinating Center, the Centers for Disease Control and Prevention (CDC, Atlanta GA), through its Nutritional Biochemistry Branch, will serve under an Intra-agency Agreement as the Central Laboratory for the Trial, and the Public Health Service Supply Service Center (Perry Point MD) will serve under an Intra-agency Agreement as the Drug Distribution Center.

Central policy for the Trial will be set by a Steering Committee composed of one representative from each of the above-mentioned organizations and the Project Officer (from NIEHS) who will serve *ex officio*, making a total of seven members. Each regular representative will have one vote. The NIEHS Project Officer will vote to resolve ties. The Committee will elect its own Chair. The Steering Committee will be ultimately responsible for the Trial protocol and manual of operations. It will review and approve all requests to undertake ancillary studies that involve TLC subjects or TLC data as well as all proposals for publications and presentations based on TLC subjects or TLC data. The power to control the budget of the Trial and of the individual contracts rests with NIEHS under the usual federal laws and regulations.

NIEHS has appointed a Data and Safety Monitoring Committee which will be advisory to the Institute. The Committee is composed of the following seven members:

Stephen Gehlbach, Amherst, MA (Chair)
Carol Angle, Omaha, NE
John Faison, Philadelphia, PA
Bernadette Gray-Little, Chapel Hill, NC
Sherman James, Ann Arbor, MI
Lemuel Moyé, Houston, TX
Herbert Needleman, Pittsburgh, PA

Membership was determined by the NIEHS and was limited to people without appointments at the Universities involved in implementing the Trial. Meetings of the Data and Safety Monitoring Committee will be arranged by the Data Coordinating Center. The Project Officer, the Principal Investigator from the Data Coordinating Center, and the Chair of the Steering Committee will commonly attend all or parts of these meetings, but the Data and Safety Monitoring Committee shall have the prerogative of working in executive session without these other individuals. The Data and Safety Monitoring Committee will review and approve the Trial protocol and will monitor the accumulating data and progress of the Trial at least annually. It is anticipated that ordinary recommendations from the Data and Safety Monitoring Committee will be made to the Project Officer, but unusually important findings or opinions of the Committee can be forwarded, at the Committee's discretion, to the Director of NIEHS or to other officials.

A Planning Committee composed of the Steering Committee members and other professional personnel at the various sites will meet as necessary and will be responsible, with assistance from the Data Coordinating Center staff, for writing the Trial protocol and for developing a manual of operations for the Trial. The planning committee will assist with arrangements for the comparable and coordinated implementation of the protocol at the various sites. Meetings of the entire or of partial membership of the Planning Committee may be called by the Steering Committee or by the Project Officer in consultation with the Principal Investigator from the Data Coordinating Center and the Chair of the Steering Committee. The Chair of the Steering Committee will also chair the Planning Committee. The protocol and manual of operations developed by the planning committee will be subject to amendment and approval by the Steering Committee and to approval by the Data and Safety Monitoring Committee.

The work of the Planning Committee will be facilitated by subcommittees with expertise in the several areas related to the Trial. These subcommittees may be established, altered, or abolished as

necessary by the Planning Committee. Their membership and responsibilities are subject to review by the Steering Committee. Subcommittees established at the outset of the Trial are: Clinical Issues, Psychometrics, Environmental Issues, Screening and Eligibility, Treatment and Toxicity Monitoring, Community Relations, and Drug Management.

See Appendix 1 for a list of TLC Centers and for committee and subcommittee membership.

2.3. Study Population

The planned sample size for the TLC Study is 1,332. Each of four Clinical Centers will enroll 333 children. The racial and ethnic composition of the study sample is expected to reflect the composition of the clinic population at each Clinical Center. However, linguistic minorities will be excluded in all centers except Newark, where Hispanic children make up a sizable portion of the population and will be included.

Table 1 provides estimates in percentages of the racial and ethnic makeup of each Clinical Center's population and of the overall Study population.

Table 1: Racial and Ethnic Makeup of Study Population by Clinical Center and Overall

Clinical Center	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic origin	Hispanic	White, not of Hispanic origin	Other or unknown	Total
Baltimore, MD	0%	< 1%	87%	< 1%	11%	1%	100%
Cincinnati & Columbus OH	0%	< 2%	79%	< 1%	19%	0%	100%
Newark, NJ	0%	0%	71%	23%	5%	1%	100%
Philadelphia, PA	0%	5%	85%	2%	8%	0%	100%
OVERALL	0%	< 2%	81%	6%	11%	0%	100%

Table 2 provides estimates in percentages of the racial and ethnic makeup of the proposed Study sample, given the planned exclusion of linguistic minorities.

Table 2: Racial and Ethnic Makeup of Proposed Study Sample by Clinical Center and Overall

Clinical Center	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic origin	Hispanic	White, not of Hispanic origin	Other or unknown	Total
Baltimore, MD	0%	0%	89%	0%	11%	0%	100%
Cincinnati & Columbus, OH	0%	0%	81%	0%	19%	0%	100%
Newark, NJ	0%	0%	72%	23%	5%	0%	100%

Philadelphia, PA	0%	0%	91%	0%	9%	0%	100%
OVERALL	0%	0%	83%	6%	11%	0%	100%

Overall, we estimate that 80 to 85% of TLC subjects will be African-American. Due to physical location and language capabilities at the Clinical Centers, only one Center (Newark, NJ) will have substantial Hispanic representation, at approximately 23% of the Center's population. The Hispanic population is small at the remaining Centers and none of these Centers has the linguistic capability to perform the proposed psychometric testing in Spanish. Asian, Pacific Islander, Alaskan Native and American Indian representation in the TLC population is small at all Clinical Centers and none of the Centers has the linguistic capability to deal with the wide range of languages possible in these racial groups. In addition, the psychometric instruments proposed as outcome measures in this Trial are not available in the appropriate languages and normed for the appropriate cultures. However, since the issue is one of language, not ethnic background, children from these racial groups will be recruited as TLC participants unless the family's primary language is not English.

2.4. Compliance with the NIH Revitalization Act of 1993

The TLC Trial must comply with the NIH Revitalization Act of 1993, which requires that any NIH-funded clinical research include women and minorities as research subjects. In addition, in any trials in which women and minorities are included as subjects, the trial must be designed in a way that will allow for valid sub-group analyses. NIH has completed a set of proposed guidelines for the implementation of the act and these guidelines were published in the Federal Register on March 28, 1994.

The study population will reflect the population known to be at greatest risk due to lead exposure, i.e., low income, urban, African-American children. Consequently, the TLC Trial is primarily a study of a minority population. There is currently no evidence suggesting that there are or are not differences in the effects of lead on cognitive development or of the efficacy of succimer by racial or ethnic group.

The TLC Trial will recruit boys and girls equally as Trial subjects. Research on gender differences in the effects of lead on cognitive development has yielded mixed results.[7] With the expected balanced enrollment by gender, we will be able to perform valid analysis on differences by gender.

We are committed to meeting the spirit as well as the letter of the law with respect to the inclusion of women and minorities in the TLC Trial. A number of leadership positions in the Trial administrative structure are held by women, including the Principal Investigator of the Philadelphia Center and the Chair of the Treatment and Toxicity Subcommittee. Membership on the various TLC committees is well-balanced by gender. With respect to minority representation, the administrative structure of the TLC Trial does not reflect the population to be recruited. However, we are aware of the need for sensitivity to this issue. The proportion of minority membership on the Data and Safety Monitoring Committee is greater than 50%. One of the criteria applied in selecting Clinical Centers was the level of experience of the site in working with inner city communities that are primarily African-American, reflecting the national distribution of lead poisoning. We intend to employ minorities whenever possible in this project, especially as case managers, psychometricians, and other key positions involving interaction with the community. For Spanish-speaking families in the Newark Center, all Informed Consent forms will be translated into Spanish and at least one of the

psychometricians will be bilingual to ensure that all neurobehavioral assessments are performed in the preferred language of the children. The Newark Center will also have bilingual members of the environmental assessment team and there will be a translator available for the study as needed.

Every effort will be made to provide courteous and culturally sensitive service to participating TLC families. The training of TLC personnel will cover issues surrounding the need for cultural sensitivity in working with patients, their families, and the larger community. The TLC staff will attempt to provide assistance to the family that goes beyond the confines of the TLC protocol, for example, assistance in obtaining benefits such as WIC and food stamps. In addition, the removal of barriers to participation, such as lack of transportation, is crucial to recruitment and retention. Accordingly, TLC will cover the costs of transportation to and from all study visits. Trial-related treatments will be provided free of charge, including drug or placebo, multivitamin and mineral supplements, blood lead tests, developmental assessments, and assessment and clean-up of homes. In addition, the subjects and their families will be given small gifts to establish a sense of camaraderie between TLC families and staff. Such gifts might include small toys for the children and food coupons, diaper coupons, cleaning supplies, and door mats for the families. Participating Centers have found these kinds of gifts to be very welcome to their Clinic families. Such an incentive strategy benefits not only the subjects and their families but is also crucial for a successful Trial, in that incentives tend to encourage long-term followup.

Each Clinical Center will develop and implement a plan to educate key individuals and groups in its constituent community about the TLC Trial. The details of these efforts will vary among the Centers, but their general theme will be to inform key individuals about the need and rationale for the trial, about the opportunities that it creates to provide better care to local children with lead poisoning, and about more general issues regarding lead in the environment. Such education will serve to prevent misunderstanding about the randomized, placebo-controlled design of the TLC trial and may assist with recruitment. This educational effort will be carried out primarily through meetings with selected groups and individuals in the respective communities. Limited use of mass media is a possibility. Centers may establish Community Advisory Committees to guide these educational efforts.

3. ELIGIBILITY

3.1. Pre-randomization Visit 1 (V1)

3.1.1. Inclusion Criteria

a. Projected age at randomization (in approximately five weeks) of 12 to 32 months.
b. Elevated blood lead level per local laboratory.
c. English-speaking family or, in Newark, English or Spanish-speaking family.
d. Willingness of parent or legal guardian to participate as evidenced by first informed consent.

3.1.2. Exclusion Criteria

a. Exclusions based on pre-existing medical conditions by parental report and/or physical examination:
   (1) Pre-existing significant developmental deficit or disease or syndrome known to be associated with mental retardation, neuromuscular disorder, or sensory deficit, including, but not limited to, PKU, Down Syndrome, and Fetal Alcohol Syndrome.
   (2) Birth weight under 3 pounds by best available information.
   (3) Psychiatric or psychological disorder which would prohibit adequate evaluation, including, but not limited to, autism and reactive attachment disorder.
   (4) Known renal or hepatic disease.
   (5) Known chronic anemia which is not due to iron deficiency; including, but not limited to, sickle cell disease and thalassemia major.

(6) Cyanotic congenital heart disease.
(7) Known HIV positive.
(8) Allergy to sulfa or mercaptans as evidenced by hives or anaphylactic reaction.
(9) Prior chelation therapy for lead poisoning.
(10) Body surface area greater than 0.713 m^2.

b. Any child living in the same household with another child in the treatment phase of the TLC protocol. Housemates may be sequentially entered after six months.

c. Children currently enrolled in any other research drug protocols, other research protocols using psychometric assessments, or other research protocols conflicting with this protocol.

d. Exclusions based on residential history:
(1) The child's current address is outside the defined catchment area of the Center.
(2) The family has definite plans to move from the catchment area of the Center within the foreseeable future.
(3) Family plans for child to be away for three months or more during the first six months of participation.
(4) Child's current residence is too dangerous for TLC personnel to visit.

e. Exclusions based on abnormalities in laboratory values obtained at pre-randomization clinic visit 1 (V1):
(1) PbB < 20 μg/dL or PbB > 44 μg/dL.
(2) Iron status
(a) Hemoglobin level less than 9 g/dL from any cause.
(b) Hemoglobin level greater than or equal to 9 g/dL and less than 10 g/dL combined with an increased red cell distribution width. Such children will be prescribed three months of therapeutic iron and will return for repeat testing in one month. If the hemoglobin is greater than or equal to 10 g/dL at repeat testing, the child will be enrolled.
(3) Liver function studies
(a) Alkaline phosphatase greater than twice the upper limit of normal for the local laboratory.
(b) AST greater than twice the upper limit of normal for the local laboratory.
(c) ALT greater than twice the upper limit of normal for the local laboratory.
(d) Absolute neutrophil count below 800/mm^3.
(e) Platelet count below 150,000/mm^3.
Children with abnormalities in alkaline phosphatase, AST, ALT absolute neutrophil count, or platelet count will be scheduled for repeat testing of the abnormal laboratory value(s) in two to three weeks. Any further TLC activities will be deferred until the results of this repeat testing are known. If the results are normal, the child will be enrolled.
(4) Other laboratory values
(a) Serum creatinine greater than 1.0 mg/dL.
(b) Proteinuria greater than 2+ on dipstick.
(c) Glucosuria on dipstick.
Children whose serum creatinine is greater than 1.0 mg/dL or with glucosuria or proteinuria will be referred for further work-up of their condition and may be reconsidered for study eligibility if these abnormalities resolve. In such cases, repeat testing of the abnormal laboratory values will be required before any further TLC activities are carried out.

3.2. Pre-randomization Visit 2 (V2)

3.2.1. Inclusion Criteria

a. Projected age at randomization (in one week) of 12 to 32 months.
b. Venous blood lead level from CDC of 20 - 44 μg/dL.

c. Willingness of parent or legal guardian to participate as evidenced by second informed consent.

3.2.2. Exclusion Criteria

a. Inability of family or child to comply with the TLC protocol:
   (1) Children missing 50% or more of scheduled visits without extenuating circumstances during the pre-randomization period.
   (2) Children at the extremes of multivitamin compliance during the pre-randomization period, i.e., inability to give medication to TLC subject or dispensation of medication to other than TLC subject.
   (3) Children or families who, in the best judgment of the clinician, are unable to comply successfully with trial requirements.

b. Exclusions on the basis of the home visual assessment:
   (1) Child's current residence is too lead-hazardous to be adequately cleaned and child cannot be relocated in lead-safe housing. The child may be enrolled later if these conditions change.
   (2) Child's current residence is too dangerous for TLC personnel to visit.
   (3) The child spends significant amounts of time in two or more residences and the TLC Home Assessor is unable to assure that the child's total residential environment will be sufficiently clean to begin chelation therapy.

c. Body surface area less than 0.357 or greater than 0.713 m^2.

4. CLINICAL INTERVENTION

4.1. Pharmacology of Succimer

Succimer (2,3-meso-dimercaptosuccinic acid) is an orally active dithiol compound that is a relatively specific chelating agent for heavy metals, especially lead, arsenic and mercury. The drug undergoes limited absorption in the gastrointestinal tract and then is rapidly metabolized to mixed disulfides which are eliminated in the urine. Blood levels decline slowly with an apparent elimination half-life of about 48 hours in adults.

Succimer has several advantages over other available lead chelating agents. Urinary excretion of essential elements (Ca, Fe, Zn, Cu) is only minimally increased after succimer, in contrast to extensive metalluresis following $CaNa_2EDTA$. Plumburesis appears to be greater following administration of succimer compared to conventional doses of other lead chelating agents. Oral administration of succimer allows for outpatient therapy which is impractical with the parenterally administered $CaNa_2EDTA$. Finally, clinical experience to date has shown succimer to be well-tolerated with minimal toxicity during single or repeated courses of therapy.

To date, reversible adverse effects of succimer include hypersensitivity (incidence about 1-2%) and asymptomatic serum transaminase elevation. Neutropenia and asymptomatic, reversible alkaline phosphatase elevation occasionally have been reported. Other than drug hypersensitivity, these effects have not required discontinuation of succimer therapy.

Disadvantages of succimer relate to the drug's characteristics and pharmacologic information gaps. The "rotten-egg" odor and bad taste may affect compliance as well as produce occasional gastrointestinal upset in children taking the drug. Whether succimer enhances lead absorption is unknown, but it is an important consideration when a child taking the drug continues to reside where lead paint hazards are unabated. Data from animal studies suggest that succimer may produce a redistribution of internal lead stores.

Data from McNeil Laboratories on the stability of succimer in various liquids is presented in Table 3.

Table 3. Stability of Succimer in Liquid After 15 Minutes

Liquid	% Retention of original activity
Cranberry juice	96%
Apple juice	85%
Coca Cola	78%
7-Up	75%
Kool-Aid	66%

Food is a difficult matrix for analysis and background interference precluded analysis of chocolate-containing foods. However, McNeil chemists estimate that about 80% of active drug remained 15 minutes after it was mixed with applesauce. It is not believed that succimer bioavailability will be affected by the protein content of any food with which the drug might be mixed.

The optimal dosing regimen and duration of therapy with succimer have yet to be determined.

4.2. Treatment Regimen

The treatment dosing in this trial will be based on body surface area (BSA). BSA will be calculated using the following formula, developed by Du Bois and Du Bois.[8]

$$\text{BSA in mm}^2 = (\text{WEIGHT}^{0.425} \times \text{HEIGHT}^{0.725} \times 71.84) / 10{,}000$$

Children randomized to succimer will receive approximately 1050 mg/m^2 of succimer in three divided doses per day for seven days, followed by 700 mg/m^2 in two divided doses per day for 19 days for a total course of therapy of 26 days. Table 4 provides the exact succimer dose by body surface area.

Table 4. Succimer Dose by Body Surface Area

BSA CLASS	BSA RANGE (m^2)	DAYS 1 - 7		DAYS 8 - 26	
		DAILY DOSE in mg (# caps/dose)	DOSE DELIVERED (mg/m^2/day)	DAILY DOSE in mg (# caps/dose)	DOSE DELIVERED (mg/m^2/day)
A	0.357 - 0.428	400 (1-1-2)	1120 - 935	300 (1-2)	840 - 702
B	0.429 - 0.499	500 (2-1-2)	1167 - 1002	300 (1-2)	700 - 602
C	0.500 - 0.523	500 (2-1-2)	1000 - 956	400 (2-2)	800 - 765
D	0.524 - 0.618	600 (2-2-2)	1145 - 971	400 (2-2)	764 - 647

E	0.619 - 0.642	700 (2-2-3)	1131- 1091	400 (2-2)	646 - 624
F	0.643 - 0.713	700 (2-2-3)	1089 - 981	500 (2-3)	778 - 701

Children whose body surface area is less than 0.357 or greater than 0.713 will be excluded from the study. Children randomized to placebo will follow a similar BSA-specific regimen. During treatment, children will be seen on days 7, 28, and 42. At each visit, blood will be drawn to measure PbB, complete blood count (CBC), differential, platelet count, AST, ALT, and alkaline phosphatase.

Children whose PbB at day 42 is greater than 15 μg/dL will be retreated beginning on day 49. Each child on succimer requiring retreatment will be paired with a placebo child who will follow the same protocol as the retreated child. A maximum of three courses of drug therapy will be administered for up to six months in the treatment phase for children receiving three courses of drug. The protocol for retreatment will be the same as for the initial course of treatment.

In this trial, succimer will be administered using fruit juice or soda. Non-carbonated fruit-flavored beverages will be avoided. If a child refuses to take drug in one of these liquids, the drug will be mixed with approximately one teaspoonful of applesauce, jelly, or vanilla pudding for administration.

4.3. Toxicity Monitoring

If the PbB increases to 45 μg/dL or greater during the treatment period, the Data Coordinating Center will notify the Clinic to bring the subject in for a repeat blood test within three days. The repeat PbB will be processed by the central laboratory on an urgent basis. If the repeat PbB value from CDC remains above 44 μg/dL, the study treatment will be interrupted, and the child will be treated according to the Clinical Center's standards of care for children with lead levels above 44 μg/dL. This will include reassessment of the child's environment for potential lead exposure and coordination with the local health department for formal lead assessment as per local requirements. Blinding of treatment assignment will be maintained.

In the unlikely event that the PbB increases to 60 μg/dL or greater during the treatment period, the Data Coordinating Center will notify the Clinic immediately, and study treatment will be stopped immediately. The child will be treated according to the Clinical Center's standards of care for children with lead levels 60 μg/dL or greater. This will include a reassessment of the child's environment for continuing sources of lead exposure. Repeat blood testing by the CDC laboratory will not be required for treatment; however, a second blood sample will be obtained and sent to the CDC for evaluation. Blinding of treatment assignment will be maintained.

If a child's PbB increases to more than 15 μg/dL above her or his baseline (V2) PbB value within six months of randomization, a repeat PbB will be performed as soon as possible. Confirmation of the increase in PbB will trigger environmental reassessment and, where appropriate, further cleanup. Blinding of treatment assignment will be maintained.

Possible toxicities of succimer include elevation of liver function tests and decline in neutrophil counts. Elevations in liver function tests occur in about 5% of children. To maintain blinding, liver function levels will be blinded for both parents and clinic personnel until six months after randomization. Each Clinical Center will identify a physician not having direct subject or guardian contact who will review laboratory results during the period of blinding. The reviewing physician will notify the clinician if transaminase exceeds two times the upper limit of normal, alkaline phosphatase exceeds five times the upper limit of normal, the absolute neutrophil count decreases to less than 800/mm^3, the platelet count decreases to less than 150,000/mm^3, or the values change in a way which

the reviewing physician considers to be of concern. If a value is abnormal, the reviewing physician will order repeat testing. If a second abnormal value is obtained, the reviewing physician may recommend discontinuation of study drug. Blinding of treatment assignment will be maintained.

Suspected or known adverse drug reactions will be reported promptly to the manufacturer, to the Food and Drug Administration, and to the local human subjects committee.

4.4. Informed Consent

For all TLC participants, the consent of a parent or legal guardian will be required. The language of the informed consent documents will be that of the parent or legal guardian and will be geared to a 6th grade school educational level. Informed consent will be sought on two occasions. Stage I informed consent will cover the pre-enrollment period and will be obtained at pre-randomization clinic visit 1 (V1). Stage II informed consent will cover enrollment in the randomized protocol and will be obtained either during the visit immediately prior to the initiation of treatment (V2) or the visit at which treatment will be initiated (T0). See Appendix 2 for informed consent forms from each of the Clinical Centers.

4.5. Randomization

After Stage II informed consent has been obtained, subjects will be randomized in a 1:1 ratio to either the succimer or placebo treatment group. Treatment assignments will be determined by a permuted blocks randomization scheme with stratification by city (Baltimore, MD, Newark, NJ, Philadelphia, PA, Cincinnati, OH, and Columbus, OH), class of body surface area as defined in Table 4 above, and most recent CDC blood lead level (20 - 24 μg/dL and 25 - 44 μg/dL). Once a treatment assignment has been made, a child will be considered to be enrolled in the randomized trial for its duration, regardless of followup status. Children who are taken off the treatment protocol prematurely will continue to be followed according to the TLC schedule. Children will be followed according to study protocol irrespective of their level of compliance with study treatment, and all available outcome data will be included in the analyses according to the principle of "intent to treat" analysis.

4.6. Maintenance of Double-blind

Treatment will be blinded to the fullest extent possible. Both parents and clinic personnel will be blinded to the child's PbB levels during treatment until six months after randomization.

Succimer emits a strong odor of sulfur, while the placebo for succimer emits a smell of alcohol. Therefore, it will not be possible to provide a fully comparable placebo. However, to provide a more sulfur-like smell to the placebo, a vented cylindrical plastic canister, 0.5 inches in diameter and 0.6 inches in length, will be filled with 100 mg. of succimer and added to all bottles of study drug (not just those containing succimer). The addition of the canister will change the odor of the placebo to one which is qualitatively similar to, but not as intense as, that of the active drug. Further, every effort will be made to avoid the need for any clinic personnel to open any subject's medication bottle or otherwise deal directly with the study drug. The subjects taking succimer may themselves give off a strong odor; therefore, it may not be possible to blind clinic personnel entirely. For example, parents or caregivers may comment on the smell. Clinic personnel responsible for psychometric assessment, however, will not have contact with subjects or their caregivers during the treatment period.

As discussed above, local laboratory results will be reviewed by a physician who does not have direct subject or guardian contact during the treatment period. If a value is abnormal, the physician will order repeat testing. If a second abnormal value is obtained, the physician may recommend discontinuation of study drug. Blinding of treatment assignment will be maintained.

4.7. Compliance Assessment

Because succimer emits a strong odor, the use of pill counts to assess compliance at each Clinic visit will unblind TLC personnel. Several other strategies will be used to quantify compliance with study drug. The parent or caregiver of all subjects will receive a specially designed medication diary. The diary will use pictorial directions in addition to text in English or Spanish. The caregiver will make an entry into the diary when each dose is administered. In addition, they will be instructed to bring the diary and the medication bottle to each treatment visit. At each treatment visit, a member of the clinic staff will review the medication diary and talk with the caregiver about their success in complying with treatment instructions. At the end of each round of treatment, the bottle will be returned to the Drug Distrubution Center for pill counting and destruction of left-over study drug. The results of study drug pill counts will be forwarded to the Data Coordinating Center.

Pill counts, while the standard measure of compliance currently in use in most drug trials, have been shown both to overestimate compliance[9, 10] and to be unreliable.[11] Medication diaries are helpful only when used in conjunction with an objective measure of compliance. Accurate compliance monitoring will help distinguish between the two known reasons for inadequate response to succimer therapy, i.e., continued environmental exposure to lead versus noncompliance with therapy. In the Ohio Center, the Medication Event Monitoring System (MEMS) will be used to provide a more accurate measure of compliance than can be provided by pill counts or medication diaries. The standard MEMS bottle cap contains a special electronic chip which records date and time whenever the bottle is opened. The data gathered in the Ohio Center using the MEMS caps will be used to assess the accuracy of pill counts and medication diaries as measures of compliance.

A relatively new and untested version of the MEMS caps is their "smart cap", which records the number of hours between bottle openings, as well as the date and time of each opening. The "smart" cap can also be programmed to beep when a dose is scheduled to be taken and to display the number of bottle openings that have occurred during each 24-hour interval. In addition to providing an accurate measure of compliance, this new "smart" MEMS cap is hypothesized to assist parents with compliance. The Ohio Center will test the hypothesis that the newer cap enhances compliance by using "smart" caps for half the children and the standard "track" cap for the remainder of the children.

5. DEVELOPMENTAL ASSESSMENT

5.1. Introduction

Longitudinal studies of the neurobehavioral sequelae of asymptomatic lead toxicity have consistently reported deficits in IQ in lead-exposed children.[12] Thus, the primary hypothesis to be tested in the TLC Trial is that treatment with succimer will lead to improved developmental outcome as evidenced by improved scores on standardized intelligence testing. IQ of study participants will be measured by the Bayley Scales of Infant Development-II (BSID2) at baseline and at the six-month followup visit, by the BSID2 or the Wechsler Preschool and Primary Scales of Intelligence-Revised (WPPSI-R) (depending on the child's age) at the 18-month followup visit, and by the WPPSI-R at the 36-month followup visit.

Using IQ as the sole outcome measure in a study whose population is projected to be 85% African-American would be unacceptable. Controversy has surrounded the assessment of intellectual ability for over a century. Legitimate concerns were raised in the 1960s and 1970s concerning the appropriateness of existing psychological tests for the assessment of minorities, particularly African-Americans.[13] These concerns were focused on potential racial or ethnic bias in standardized measures of intellectual attainment and academic achievement. This has been one of the most emotionally and politically charged controversies in the psychological sciences.[14, 15] Until the last few decades, the instruments used to measure intellectual ability were not subjected to quantitative or qualitative

analyses aimed at evaluating racial, ethnic, or gender bias. The more recent psychometric instruments available from the major test publishers are less likely to suffer from these problems.

The assessment of intelligence using norm-referenced tests alone does not provide a complete description of developmental status. The underlying basis for poor intellectual performance (e.g., deficits in attention, organization, impulse control, ability to follow directions, or quality of motor activity) may not be captured by standardized tests of intellectual attainment. Primate and human neurodevelopmental research has provided evidence that the attention, learning, short-term memory, and executive function are the selectively deficient domains of cognition that may underlie IQ differences.[2, 3] Behavioral problems have been found to be associated with lead exposure in some observational studies.[16, 17, 18] In addition, deficits in the fine motor skills important for school work (e.g., the ability to use pencils, crayons, or scissors) have been associated with low to moderate exposure to lead.[19]

Several other measures of developmental status will be obtained. The Child Development Inventory (CDI) and Conners' Parent Rating Scale (CPRS) utilize parental reports as the principal source of data. Some studies have suggested that the diagnostic utility of standardized tests of cognitive and motor development is improved through the use of maternal reports.[20] Parents are also an important source of information about the child's behavior outside the clinical setting. The CDI will be administered to parents at all psychometric visits (baseline, six-, 18-, and 36-month followup visits) and the CPRS will be administered to parents at the 36-month followup visit. In addition, all children will be assessed at the 36-month followup visit with instruments sensitive to attention, learning, short term memory, and executive function. All children will be tested using Woodcock-Johnson Memory for Names, Stanford-Binet Bead Memory, Kaufman Assessment Battery for Children (K-ABC) Magic Window, and Diamond's Modified Stroop Task. The Tower of Hanoi will be administered to children who are 60 months of age or older at the 36-month followup visit.

Parental IQ will be obtained at the 12-month followup visit using the Wechsler Adult Intelligence Scale – Revised, Short Form. Maternal IQ is preferred; however, paternal or guardian IQ will be obtained if the biological mother is unavailable for testing.

The schedule for psychometric testing is summarized in Table 5.

Table 5. Schedule of Psychometric Testing

Instrument	Baseline	6 mos. post randomization	12 mos. post randomization	18 mos. post randomization	36 mos post randomization
Bayley Scales of Infant Development-II (BSID2)	✓	✓		✓	
Wechsler Preschool and Primary Scales of Intelligence-Revised (WPPSI-R)				✓	✓
Child Development Inventory (CDI)	✓	✓		✓	✓
Conners' Parent Rating Scale (CPRS)					✓
Woodcock-Johnson Memory for Names					✓
Stanford-Binet Bead Memory					✓
K-ABC Magic Window					✓
Diamond's Modified Stroop Task					✓

Tower of Hanoi***					✓
Wechsler Adult Intelligence Scale – Revised, Short Form (WAISR-SF) (parental IQ)			✓		

** For subjects up to and including 42 months of age at this visit
*** For subjects over 42 months of age at this visit
**** For subjects 60 months of age or older at this visit

5.2. Bayley Scales of Infant Development-II (BSID2)

The BSID2[21] is a revision and restandardization of the well-known Bayley Scales of Infant Development.[22] It is suitable for infants and young children from one to 42 months of age. The Bayley Scales of Infant Development are the most widely used and precisely constructed of all published infant intelligence tests.

The BSID2 yields a Mental Development Index (MDI) and Psychomotor Development Index (PDI) which are similar to a deviation IQ score with a mean of 100 and a standard deviation of 15. The MDI is designed to evaluate the development of sensory and perceptual acuities and discriminations, acquisition of object constancy, memory, learning, problem solving, vocalization, beginning of complex language, and mathematical concept formation. The PDI is designed to evaluate the development of postural control, coordination of the large muscles, postural imitation, and stereognosis.

The BSID2 includes a Behavior Rating Scale with which the examiner rates the infant's affective, attentional, and motivational behaviors. It consists of thirty separate 5-point items which assess qualitative aspects of the subject's attentional, emotional, and motor behaviors. Previous studies suggest that the regulation of attentional, motor, and emotional behaviors may be perturbed in children with blood PbB concentrations in excess of 20 μg/dL.

The BSID2 takes from 45 to 75 minutes to administer.

5.3. Wechsler Preschool and Primary Scales of Intelligence - Revised (WPPSI-R)

The WPPSI-R[23] is a revision of the original Wechsler Preschool and Primary Scale of Intelligence[24] and is suitable for children aged 35 to 87 months. The WPPSI and WPPSI-R possess the best psychometric properties of all published tests of preschool intelligence. Among all preschool IQ tests, the WPPSI-R has been used the most to establish the construct and criterion-based validity of other measures of preschool intellectual attainment.

The WPPSI-R consists of a collection of 12 subtests organized into two scales, a Verbal Scale and a Performance Scale. The Verbal Scales use language-based items while the Performance Scale test uses visual-motor items that are somewhat less dependent on language. The WPPSI-R yields scale scores for the 12 subtests as well as Verbal, Performance, and Full-Scale deviation IQs which have a mean of 100 and a standard deviation of 15.

The WPPSI-R takes from 60 to 75 minutes to administer.

5.4. Wechsler Adult Intelligence Scale - Revised, Short Form (WAISR-SF)

Parental intelligence is one of the most powerful predictors of child IQ. An assessment of parental IQ is included in this clinical trial to serve as a potent covariate as well as a check on the randomization.

Parental IQ will be assessed using the two-subtest short form of the Wechsler Adult Intelligence Scale - Revised[24]. Maternal IQ will be obtained whenever possible. When the maternal IQ cannot be obtained, the clinic will attempt to obtain the paternal IQ or the IQ of the child's primary caregiver. The two-subtest short-form includes the vocabulary and block design subscales. The scoring tables of Silverstein[25] will be used. The WAISR-SF will yield a full scale deviation IQ. This particular short form of the full WAIS-R has a higher correlation with full scale IQ based upon the total Wechsler battery than any other subtest dyad (corrected r = 0.90).

The WAISR-SF takes from 20 to 30 minutes to administer.

5.5. Child Development Inventory (CDI)

The CDI[26] is a revised version of the Minnesota Child Development Inventory (MCDI) and is administered to the parent or caregiver. The 270 items on the CDI are grouped to form several scales. TLC psychometricians will administer only those items which contribute to the scoring of the General Development Scale (GDS). The GDS has a correlation of 0.89 with age in the normative sample. Validity studies using the original MCDI showed that the General Development Scale correlated significantly with various outcome measures, including the Mental and Psychomotor Indices from the Bayley Scales of Infant Development and the General Cognitive Index from the McCarthy Scales of Children's Abilities.[27, 28, 29, 30]

The CDI scales were derived rationally, not through factor analysis, and were normed with reference to a sample of 568 children from South St. Paul, Minnesota, a primarily white, working class community. An earlier version of the CDI was shown to have good concurrent validity when applied to a population of minority, high-risk children.[31] The CDI is designed to require an eighth-grade reading level for parents to complete it independently. The mean years of parental education for the normative group was approximately 13 years. Interviewers will be available to guide and assist parents in filling out the CDI form. It is anticipated that there will be a significant number of TLC parents and caregivers who will need help filling out the form.

The GDS of the CDI takes approximately 20 minutes to administer.

5.6. Conners' Parent Rating Scale (CPRS)

The Conners' Parent Rating Scale[32] is a 48-item rating scale administered to the parent or caregiver and used to characterize patterns of child behavior. The items yield standard scores on five scales: Conduct Problem; Learning Problem; Psychosomatic; Impulsive-Hyperactive; and Anxiety. The scales were derived in factor analyses using normative data from 578 children aged 3 to 17 years. The CPRS has been used extensively in research, and considerable validation data are presented in the test manual[32].

The CPRS also includes a Hyperactivity Index, which is composed of the ten items most sensitive to drug (i.e., stimulant) effects. The Hyperactivity Index was developed to provide a practical, empirical assessment of the extent to which children display behaviors that are usually considered indicative of hyperactivity.

The CPRS takes approximately 10 minutes to administer.

5.7. Neurodevelopmental Battery

A small battery of supplemental neurodevelopmental measures will be administered on the final followup visit. At that time, all subjects will be between 48 and 66 months old. Cognitive areas assessed by the battery include attention, memory, learning, and executive function. Deficits in these cognitive areas have been associated with lead toxicity in various studies. The following tests will be included in the battery: Woodcock-Johnson Memory for Names, Stanford-Binet Bead Memory, Kaufman Assessment Battery for Children (K-ABC) Magic Window, Diamonds' Modified Stroop Task, and Tower of Hanoi (for children 60 months of age or older). For children under 60 months the battery will take approximately 45 to 60 minutes with an additional 25 to 30 minutes for children older than 60 months.

5.7.1. Woodcock-Johnson Memory for Names

This test is a subtest of the Woodcock-Johnson Psycho-educational Battery – Revised.[33] The Woodcock-Johnson is used widely in the diagnosis of learning disabilities and instructional planning. This particular subtest measures how well a child is able to learn to associate unfamiliar, nonsense names with drawings of imaginary alien space creatures. It assesses the efficiency of verbal and visual processing as well as memory.

The Woodcock-Johnson Memory for Names takes approximately 10 minutes to administer.

5.7.2. Stanford-Binet Bead Memory

This test is a subtest of the Stanford-Binet-V Intelligence Test.[34] It measures visual short term memory for colors, shapes (ellipsoids, cones, and saucers), and sizes. The examinee is exposed to either the tester's example construction (base and stick on which beads are assembled) or a photographed construction for five seconds. The subject must then accurately reproduce the model or picture. Children with deficits in visual-spatial abilities or who are impulsive and/or easily distracted will experience difficulties with this task.

The Stanford-Binet Bead Memory test takes approximately 10 minutes to administer.

5.7.3. Kaufman Assessment Battery for Children (K-ABC) Magic Window

The K-ABC Magic Window[35] measures the child's ability to identify and name an object whose picture is rotated behind a narrow slit, so that the picture is only partly exposed at any point in time. The subtest consists of 15 readily recognizable items such as a car, girl, apple, hat, watch, and table.

The cognitive domains of this task are attention and temporal-spatial abilities. Children who are generally impulsive, easily distracted, or unable to respond under conditions of uncertainty will have difficulty with this test. For the preschooler, Magic Window involves a fairly complex integration of spatial information presented temporally, thereby assessing cerebral hemispheric integration. It is a relatively unbiased test, providing reliable results regardless of race, gender, or overall level of intelligence.[36]

The K-ABC Magic Window test takes approximately five minutes to administer.

5.7.4. Diamond's Modified Stroop Task

Diamond's Modified Stroop Task[37] is a simplified version of the Stroop color-word task.[38] In this version, the interviewer uses a deck of cards with two kinds of cards. Half of the cards show a bright sun against a white background; the other half show a moon and stars against a black

background. The child is instructed to say "night" when shown the white card with sun and to say "day" when shown the black card with moon. The task requires inhibitory control of a natural tendency to give a different verbal response than requested. In addition, unlike the original Stroop task, the modified version also requires working memory. The task has been used with children between the ages of 3½ and 7 years, with normative data available for each six-month interval in this age range.

Diamond's Modified Stroop Task takes approximately 15 minutes to administer.

5.7.5. Tower of Hanoi

The Tower of Hanoi puzzle[39] series is a test which has been used in clinical research to measure executive function, i.e, the ability to plan and execute a series of related actions. In the Tower of Hanoi, subjects are required to assemble rings of differing sizes and colors arranged on a peg to make a tower which duplicates the examiner's disk configuration. Factor analytic studies have shown that this task loads most highly on a cognitive planning factor when used with children. Efficient performance also requires the ability to inhibit irrelevant responses.

The examiner provides subjects with an age-appropriate explanation of the task objectives and rules. For young children, the abstractness of the task is reduced by a cover story describing the test as a game concerning a family of monkeys jumping among trees (pegs) in a forest. Practice trials are administered to be certain the child is aware of the demands of the game. The scoring system yields a "planning efficiency score" which ranges from 0 to 6.

This test will be administered to children 60 months and older only. A reliability coefficient of 0.74 has been established for test-retest.[40]

The Tower of Hanoi takes approximately 25 minutes to administer.

5.8. Quality Control Procedures

The supervising TLC psychologist at each Clinical Center will train the psychometricians at that Center in all psychometric instruments. In particular, each psychometrician will obtain pilot experience in the assessment of children between the ages of 12 and 72 months using the instruments selected for the trial. On a pilot basis, each trainee will administer the BSID2 to two or three children and the CDI to their parent at ages 12, 18, 24, and 30 months. Training on the WPPSI-R, CPRS, Woodcock-Johnson Memory for Names, Stanford-Binet Bead Memory, K-ABC Magic Window, and Diamond's Modified Stroop Task will focus on the assessment of preschool children between three and five years of age. Training on the Tower of Hanoi will be performed on children five years of age or older. Pilot children will be sampled from a population similar to that expected to be recruited into the trial at that Center.

Intertester reliability in scoring will be well established prior to formal data collection through the use of video-tape or other means of observation. The performance of psychometricians will be periodically evaluated throughout the study with the use of reliability studies.

Each Center will provide a clean, quiet, and comfortable room large enough to administer all components of the psychometric examinations. To assure optimum performance and standardization among the Centers, children will be scheduled for psychometric examinations during daytime hours, avoiding the child's usual nap time. Care will be taken to ensure that the child is not tired, ill, hungry, or taking any medications which may affect performance when the exam takes place. Children who are ill will be rescheduled for psychometric evaluation.

TLC psychometricians will be required to score each test twice to prevent error resulting from the misreading of raw to scale-score conversion tables. Supervising psychologists will review each test prior to data coding on TLC forms and submission to the Data Coordinating Center.

6. ENVIRONMENTAL ASSESSMENT AND CONTROL

6.1. Introduction

The environmental intervention in this trial is designed to reduce substantially the subject's exposure to lead attributable to lead-based paint in poor condition and/or to lead-contaminated house-dust. This reduction in exposure is particularly important during the treatment phase, a period of up to six months, and during the period of greatest hand-to-mouth activity for each child, up to approximately 36 months of age. A secondary goal is to reduce exposure to lead for the duration of the trial, a period of up to three years from enrollment. In order to be able to detect any long-term impact of succimer, it is necessary that at least the primary goals be accomplished. Optimally, a child with lead toxicity should be relocated to lead-safe housing; however, this is usually not possible. Lead paint abatement is the next best option but is often difficult and prohibitively expensive, taking many months to complete. The final option, and the one adopted by this trial, is to provide interim control measures aimed at reducing exposure to lead in deteriorating paint and lead dust through in-place management of sources.

This protocol establishes standards of environmental assessment and intervention to be followed by all Clinical Centers. Each Center will meet or exceed applicable local, state, and federal guidelines for the clinical management of children with lead toxicity. See Appendix 3 for copies of the relevant laws, regulations, and guidelines. As resources permit, individual Centers may elect to provide environmental management beyond the common core. TLC efforts are not meant to substitute for lead paint abatement that would be required or encouraged by local health departments. See Appendix 4 for supplemental environmental protocols from the TLC Clinical Centers.

The TLC clean-up protocol does not, and is not intended to, substitute for the legally mandated activities carried out by local or state agencies in each city. TLC activities will be carried out independently of and in addition to municipal or state activities. TLC participation will not relieve anyone of the responsibility to abate. All participants in the Trial will have more clean-up activities done to their homes than they would otherwise have.

6.2. Environmental Assessment and Monitoring

6.2.1. Initial Home Assessment

At the first clinic visit (V1), environmental assessment will begin with a residential questionnaire designed to help determine eligibility for the trial. Children may be excluded because of the reported quality of current housing, high frequency of changing residences, or extended periods of time spent by the child at two or more secondary residences. In addition, the parent or guardian will be asked several questions related to any lead paint problems in their current dwelling. This information will be of value to the Assessor at the time of the first home visit (H1).

At the first home visit (H1), trained TLC personnel will determine whether the child will be excluded from the Trial based on the condition of the housing, will estimate the amount of work required to clean the residence, and will assess the likelihood that efforts at lead dust suppression will fail within an unacceptably short interval. An assessment will be made of the likely risks of lead exposure based on

(1) condition of painted surfaces
(2) accessibility of non-intact painted surfaces

(3) condition of painted substrates
(4) ease with which surfaces can be cleaned
(5) overall structural integrity of the dwelling, both interior and exterior.

Standardized assessment forms will be used in all Clinical Centers to assess the residential dwelling unit, common areas (such as hallways and stairwells), and porches. Frequency of access by the child to each area will be considered in the environmental assessment and clean-up plan. If the housing unit meets eligibility criteria, the TLC Assessor will sketch a floor plan, record room sizes and number of windows, note the type of flooring with particular attention to carpeting, estimate the amount of time required to prepare and clean the unit, and determine if it will be necessary to contact the building owner or manager prior to any planned clean-up activities.

During the first home visit, the family will be informed as to what will be done, when the cleaning and paint stabilization will be conducted, how long it will take, what they should do in preparation, and what they should do during cleaning and other work. In some cases, a child with an elevated blood lead may be found to live in relatively lead-free housing or to have moved to relatively lead-free housing after the detection of the blood lead elevation and prior to study enrollment. In such cases, the TLC Assessor may elect to implement a less aggressive clean-up plan, if the age and condition of the housing so warrant.

6.2.2. Collection of Environmental Lead Monitoring Data

There are several needs for measuring the amount of lead in the child's environment. These data are needed to describe the average level of dust lead exposure across cities. This can be accomplished, for a minimal expenditure of resources, by measuring dust lead levels in a random subset of all study residences in each city. Monitoring data are also needed to assure that the residence has been appropriately cleaned and is relatively lead-safe. This monitoring should be performed as soon as possible following clean-up. Finally, lead measurements may serve as covariates in analyses which attempt to characterize the effectiveness of succimer in reducing blood lead levels. Such data could also be used to explain anomalous responses to succimer therapy and to quantify the extent of residential lead reduction.

Evaluation of contractor performance with respect to the clean-up protocol will be based on post-clean-up visual inspection and a "white glove" test. Since we do not know if our clean-up protocol is adequate to attain Housing and Urban Development (HUD) clearance levels, these guidelines should not be used to monitor clean-up. Similarly, we have no basis for specifying a particular percent reduction in lead loading of dust samples.

To determine and document the effectiveness of the clean-up strategy, pre- and post-clean-up dust wipe samples will be collected from approximately 50 homes in each site. Half of these homes will be evaluated during the first two months of recruitment, analyzed quickly, and reviewed by the Environmental Subcommittee. If the lead loadings increase following clean-up activities, this information will be used to evaluate the clean-up protocol and the performance of the cleaning crew. The remaining homes will be evaluated over the rest of the year.

A single composite wipe from the floor areas will be collected from each residence approximately three to six months after clean-up. This sample will document the exposure of each study participant following clean-up and treatment. These samples will be archived pending availability of funds to analyze the samples.

The measures of lead loading will be obtained by using the HUD wipe method. This is a standard measure which is relatively inexpensive to collect and analyze. It cannot be used on carpets and provides only a measure of loading; however, these constraints are not seen as serious limitations in the context of the TLC Trial.

6.3. Lead Dust Suppression Procedures

A TLC cleaning crew will return to the home of each eligible child before randomization to clean that child's house according to a standardized protocol. As resources permit, the family will be provided with plastic bags or cardboard boxes several days prior to cleaning, so that they can pick up items on the floor for easy removal by the cleaning crew.

A strict series of contamination control procedures will be in force throughout the dust suppression process to ensure that contaminated furnishings, cleaning water, and dust are handled appropriately on-site and transported to the designated disposal site as appropriate without loss or spread of material. Vacuum cleaners equipped with high-efficiency particulate accumulator (HEPA) filters will be used to abate interior dust. If the vacuum cleaner bag breaks while a vacuum cleaner is operating or if the vacuum cleaner is operated without a bag, the second stage filter must be changed prior to any further use of the vacuum cleaner.

Each cleaning crew will consist of two or three individuals. This crew will be responsible for the temporary removal of the furnishings and carpeting to other locations within the housing or to a lockable van brought to the housing site for this purpose. Moving the furniture will permit more efficient use of time in cleaning. Removal of all furniture is not necessary; however, furniture remaining in a room during cleaning will be covered in plastic. The crew is also responsible for vacuuming and washing household surfaces including the floors and ledges (e.g., window wells and sills) and restoring the furniture and personal belongings to their original locations.

The first step in cleaning will be the preparation of an area for temporary storage of household belongings from other rooms. This preparation will include an initial one-pass vacuuming. After the temporary storage area has been prepared, the rooms will be cleaned in a sequence which begins with rooms located furthest from the entrance. All ledges (e.g., sills, tops of baseboards) will be washed with a detergent solution. Window wells, if accessible, will be vacuumed to remove paint chips and dust and then wiped clean with a damp sponge. Other dust traps (e.g., venetian blinds, cold air return registers, baseboards) will be inspected and cleaned as appropriate. The family will be encouraged to wash curtains and dispose of old carpets and blinds.

Carpeting will be vacuumed as follows. The carpet will be folded in half and the bottom side of the carpet will be vacuumed and the exposed floor will be vacuumed and damp mopped with the detergent solution. The carpet will then be folded to the opposite side of the room and the same procedures will be carried out on the other half of the carpet and exposed floor. If there is padding beneath the carpet, it will be cleaned in a manner similar to the carpets, if possible. The last step in the cleaning process will be a final vacuuming of the carpet. The carpet will be vacuumed three times at the rate of one minute per square yard each time. Workers will be required to time this vacuuming with a watch. All carpets will be vacuumed with an approved HEPA equipped vacuum and an approved beater bar. In rooms where the carpeting is permanently installed (e.g., wall to wall carpeting), the carpeting will not be folded back and the floor beneath the carpeting will not be cleaned. The carpet will be vacuumed at the rate indicated above. At the completion of the vacuuming, the furniture and personal belongings will be replaced in their original positions.

If there is no carpeting on the floor, the floor will be vacuumed at the rate of one minute per square yard. After the first vacuuming, the floor will be damp mopped with a detergent solution and then vacuumed a second time at the specified rate. This second vacuuming may only be needed in the worst situations where the floor surface is in very poor condition and is therefore likely to retain large quantities of dust.

Badly deteriorated carpets or padding will be permanently removed, if possible. Disposal of the carpet or padding is left to the discretion of the TLC Home Assessor. When disposal or

replacement of carpets or padding is indicated, the existing carpet or padding should be rolled into a tight roll and wrapped with 4 mil polyethylene plastic and taped securely with duct tape or a similarly durable strapping tape prior to removal from the room. If new carpet or padding is to be installed, it should not be installed until all cleaning and paint stabilization in the housing unit has been completed.

Common areas (e.g., hallways, stairs) will be included in the cleaning effort to increase the effectiveness of the dust suppression efforts. Similarly, porches and other exterior entryways will be included in the clean-up program. The limited paint stabilization effort will also be applied to the common areas, porches, and entryways. Particular attention will be given to deteriorated painted surfaces on porches, including ceilings. All surfaces will be vacuumed to remove loose paint.

Door mats at the interior entry to the residential unit will be used to minimize the amount of dust which enters the living space. These mats will be periodically cleaned or replaced to prevent them from becoming a reservoir of lead dust that can contaminate the house. Outdoor mats or indoor-outdoor carpet are recommended. The thickness of indoor mats and their placement must not interfere with the normal opening of the entry door; otherwise, they are likely to be removed by the resident.

A two-bucket system will be used for washing floors. The cleaning solution will be mixed in one bucket; the second bucket will contain rinse water for cleaning the mop head. The water in both buckets will be changed after cleaning approximately every 75 to 100 square feet of floor and after each room is completed. Wash water will be disposed of in the toilet. It will not be disposed of in other places such as sinks, bath tubs, street gutters, or back yards.

6.4. Paint Stabilization

It is not the objective of this trial to carry out or oversee comprehensive lead paint abatement activities. However, the interim dust control procedures will be rapidly negated if no attention is given to deteriorated paint surfaces. If the deterioration is extensive and proper paint abatement is not an immediate possibility, then relocation must be sought or the child will be excluded from participation in the trial. If the deterioration is localized to one or two surfaces (e.g., window sills or frames), then in-place management is an appropriate interim option to be carried out under this trial. Loose, peeling paint will be gently brushed with a damp towel or damp sponge to remove the flakes or these can be removed with a vacuum cleaner with an appropriate attachment. Contact paper or a coat of paint may be applied over the deteriorated surface to provide a short term stabilization of the surface. All loose chips must be vacuumed and the surrounding surfaces washed. It is important that the family and landlord understand that this is an emergency measure only. Without adequate preparation of the painted surface, any form of encapsulant will have a short life expectancy. Constant reinspection by the family is required. The family will be instructed to keep children away from the repaired area until more complete abatement can be provided by the owner.

The parent or guardian will be instructed to contact the TLC representative if the surface deteriorates further or if the landlord performs her or his own repairs or repainting. In the latter case, the parent will be instructed to request that the workers clean the area thoroughly by damp mopping and wiping up any dust. The parent should further remove any dust left behind by repair workers.

6.5. Followup

Each family will be provided with educational materials and information on lead poisoning and how to minimize its occurrence. As needed and within the constraints of available funds, families will be supplied with cleaning materials, such as a bucket, mop, sponges, and detergent.

Cleaning by TLC personnel beyond the baseline clean-up will occur at a minimum when a subject changes residence. Frequency of recleaning beyond this minimum will be within the constraints of available funds and proportional to the perceived rate of lead dust reaccumulation and rate of deterioration of painted surfaces. The condition of painted surfaces should be assessed periodically. If the temporary stabilization does not appear to be satisfactory, other measures, such as owner-provided abatement or relocation, should be considered.

6.6. Quality Control Procedures

To standardize the home visual assessment process, assessors from each city will undergo common training and will use a common assessment form. Photographs of various painted surface conditions with varying degrees of surface degradation will be used.

Training for cleaning and paint-stabilization personnel will include relevant parts of the four-day EPA-approved *Lead Abatement Course for Workers, Supervisors, and Contractors* or its equivalent as developed specifically for this trial. Prior to the enrollment of the first subject, pilot cleaning will occur in each community in housing selected specifically for this purpose. Workers will be supplied with uniforms to wear during working hours and a facility for changing clothes and cleaning up at the end of the day to eliminate the potential for carrying lead dust into their cars or homes. Work crews will not engage in any paint removal activities unless they have received appropriate training in lead paint abatement procedures and are provided with respirators and other safety equipment and supplies in accordance with local requirements.

7. STUDY PROCEDURES

7.1. Pre-Randomization Evaluation

7.1.1. Introduction

The pre-randomization evaluation schedule includes two pre-randomization clinic visits (V1 and V2) and two home visits (H1 and H2), for a total of four pre-randomization visits. Table 6 summarizes the activities during the pre-randomization period.

Table 6. Visit Schedule for Pre-Randomization Evaluation

VISIT	V1		H1	V2	H2	T0
WEEK	-6 → -5	-6 → -5	-6 → -2	-2 → -1	-4 → -1	0
DAY	-42 → -35	-41 → -34	-28 → -8	-14 → -7	-27 → 0	0
Eligibility Checklist	✓		✓	✓		
Informed Consent	✓			✓		
PbB	✓			✓		✓*
CBC, Differential, Platelet Count	✓					
Serum Chemistries	✓					
Creatinine	✓					
Urine Dip (protein, glucose)	✓					
Ferritin	✓			✓**		
Physical Examination	✓					
Multivitamin + Minerals + Iron	✓**					Stop

3 mg/kg/day Fe		✓****				Stop
Assess Compliance				✓		✓
Dispense Drug						✓
Psychometric Testing						✓
Home Visual Assessment			✓			
Home Clean-up					✓	

* If V2 > 14 days prior, repeat CDC PbB and reschedule T0.
** Repeat if V1 ferritin < 12 ng/dL.
*** Prescribed for all children.
**** Prescribed for children with hemoglobin between 9 and 10 with increased RDW.

7.1.2. Management of Iron Status

Because iron deficiency increases lead absorption and is independently associated with poor developmental outcomes,[41] careful management of the child's iron status is required. Children whose hemoglobin at V1 is less than 9 g/dL from any cause will be excluded from further participation. Children whose hemoglobin at V1 is greater than or equal to 9 g/dL but less than 10 g/dL will be checked for iron deficiency on the basis of the red cell distribution width (RDW). If the RDW is normal, the child will be enrolled. If the RDW is increased, the child will be treated with a therapeutic iron supplement of 3 mg/kg/day and their hemoglobin rechecked in one month. Further TLC activities, such as home visits, will be deferred until the results from the repeat testing are known. If the repeat hemoglobin is 10 g/dL or greater, the child will be enrolled, otherwise, excluded. If a three-month course of therapeutic iron is not completed before study treatment begins, iron supplementation will be interrupted and resumed after the completion of study treatment until a full three months of iron supplementation have been completed. Children whose hemoglobin at V1 is 10 g/dL or greater will be considered to be iron sufficient by virtue of a month or longer course of multivitamin plus iron supplement prior to randomization.

7.1.3. Pre-randomization Visit 1 (V1)

Each Clinic will identify potential subjects with elevated blood lead levels whose projected age at enrollment is 12 to 32 months and whose family's language is English (English or Spanish in the Newark Center). At Pre-randomization Visit 1 (V1) or over the phone prior to V1, the Clinic Coordinator will explain the trial to the family and assess initial eligibility. At V1, informed consent for the pre-randomization evaluation will be sought from the parent or legal guardian of children who satisfy the initial eligibility requirements. See Appendix 2 for Stage I Informed Consent Forms from each of the Clinical Centers. If informed consent is given, a medical history will be obtained and a physical examination performed. Height, weight and head circumference will be measured by standardized procedures. Blood pressure will be obtained. A TLC physician will review and verify the child's eligibility.

Blood will be drawn for determination of blood lead concentration and ferritin by the central laboratory and for local laboratory determination of hemoglobin, red cell distribution width, absolute neutrophil count, platelet count, alkaline phosphatase, ALT, AST, and serum creatinine. A urine dip stick test will be performed in the clinic for proteinuria and glucosuria.

All children will be given a multivitamin with minerals including iron and the caregivers will be instructed as to their administration. A vitamin diary will be provided for parents to record vitamins taken each day. The diary will assist TLC staff in the assessment of compliance. Appointments will be

scheduled for the home visual assessment visit (H1) in one to two weeks and for Pre-Randomization Visit 2 (V2) in approximately one month.

Local laboratory results will be available shortly after V1. Children whose hemoglobin is less than 9 g/dL will be excluded from the study. Children whose hemoglobin is equal to or greater than 9 g/dL and less than 10 g/dL and whose red cell distribution width is increased will be provided with three months of supplemental iron therapy and will undergo repeat testing at their next visit (approximately one month). Children who are not iron deficient on the basis of the RDW or whose hemoglobin is greater than or equal to 10 g/dL will be enrolled. Children who show abnormalities on their liver function studies will be brought back to the Clinic for repeat testing of the abnormal values in approximately two to three weeks. If the repeat values are normal, the child may be enrolled. Children whose serum creatinine is greater than 1.0, who show proteinuria of 2+ or greater, or who show glucosuria will be referred for evaluation. If these conditions resolve and the child is otherwise eligible, she or he may be entered in the study at a later time but will be required to repeat the appropriate laboratory tests. In all cases, further TLC activities, such as H1 or V2, will be deferred until the abnormality resolves.

CDC PbB results will be available approximately one week following V1. Children whose PbB from V1 is 45 μg/dL or greater will be referred for immediate treatment according to the local standards of care and excluded from the study. Children whose PbB from V1 is less than 20 μg/dL will be excluded from the study.

Families of excluded children will be appropriately notified, any scheduled study visits will be cancelled, and they will be provided with appropriate followup based on their lead status.

7.1.4. Home Visit 1 (H1): Home Visual Assessment

The Home Visit 1 (H1) will take place as soon as possible after V1 for eligible children. This initial visual assessment will be used to determine whether the child should be excluded from the trial based on poor condition of the housing and to estimate the amount of work required to clean the residence. An assessment will be made of the likely risks of exposure to lead in paint and dust based on the following criteria:

(1) condition of painted surfaces
(2) accessibility of non-intact painted surfaces
(3) condition of painted substrates
(4) ease with which surfaces can be cleaned
(5) overall structural integrity of the dwelling, both interior and exterior.

Attention will be given to the immediate dwelling unit, common areas such as hallways and stairwells, and porches. Frequency of access to the hazardous areas by the child will be considered in the environmental assessment and clean-up plan. An attempt will be made to do visual assessments of secondary residences so that the condition of supplemental residences can be taken into account in determining eligibility.

The assessor will sketch a floor plan, record room sizes and number of windows, note presence and condition of carpeting and other flooring, estimate the amount of time required to prepare the unit for cleaning and determine if it will be necessary to contact the building owner or management prior to any planned clean-up activities.

A Home Visual Assessment Report will be issued and the child's eligibility on the basis of residence reassessed. Families of children who are excluded on the basis of the home visual assessment will be appropriately notified, any scheduled study visits will be cancelled, and they will be provided with appropriate followup based on the child's lead status.

If the child is still eligible, an appointment will be scheduled before the projected date of randomization for Home Visit 2 (H2) for home cleaning.

7.1.5. Home Visit 2 (H2): Home Cleanup

If the child's residence(s) meets eligibility criteria, a second home visit will be made for lead dust suppression. This visit will ordinarily take place sometime between H1 and T0. If H2 has not occurred before T0, randomization may proceed with home clean-up to take place as soon as possible after T0. If it is not possible to clean the child's home within one week of initiation of treatment, the child will be excluded.

7.1.6. Pre-Randomization Visit 2 (V2)

At Pre-Randomization Visit 2 (V2), eligibility will be reviewed. Ability of the family to attend scheduled study visits and to give study medications will be assessed through compliance with the TLC schedule and with multivitamin supplementation. Families whose children are excluded from the TLC Trial on the basis of compliance will be provided with appropriate followup based on the child's lead status.

If the child remains eligible for the Trial, informed consent for participation in the Trial will be sought. See Appendix 2 for Stage II Informed Consent Forms from each of the Clinical Centers. Demographic information on the subject's family will be obtained. An interim medical history will be obtained and a brief physical examination performed. Height, weight, and blood pressure will be measured by standardized procedures. Blood will again be drawn for central laboratory determination of blood lead level. Children whose ferritin level at V1 was less than 12 ng/dL or who required iron supplementation will also have their ferritin rechecked by the Central Laboratory. If the child's home has not yet been cleaned, an appointment for the home clean-up will be scheduled at the earliest possible date. All eligible children will be scheduled for Treatment Visit 0 (T0) in one week.

7.2. Randomization

A few days before T0, eligibility will be reviewed and randomization to treatment group made. Children whose PbB from V1 is 45 μg/dL or greater will be referred for immediate treatment according to the local standards of care and excluded from the study. Children whose PbB from V1 is less than 20 μg/dL will be excluded from the study. Families will be notified before T0 and provided with appropriate followup.

7.3. Treatment

7.3.1. Treatment Visit 0 (T0): Initiation of Treatment

Treatment Visit 0 (T0) will be scheduled for approximately one week after V2. If the Data Coordinating Center notifies the Clinical Center that the child is ineligible, then this visit will be cancelled, the parent will be told the blood lead result, and appropriate follow-up will be provided based on the child's lead status. Table 7 shows the activities during the treatment phase.

Table 7. Activities During Treatment Phase

	CLINIC VISITS					
All Rounds	T0 / T4 / T8		T1 / T5 / T9		T2 / T6 / T10	T3 / T7 / T11

DAY OF DRUG (within course)	0	1	7	26	28	42
PbB			✓		✓	✓
CBC			✓		✓	✓
Chemistries			✓		✓	✓
Dispense Study Drug	✓					
Treatment		start		stop		
Brief Physical Exam			✓		✓	✓
Psychometric Testing	✓*					

* Psychometric testing will take place at T0 only (initial round of treatment).

If not already signed, the second informed consent for randomization and treatment will be obtained at this time. If V2 was more than 14 days earlier, blood will be drawn and shipped to CDC for an additional PbB and the T0 visit will be rescheduled for the following week, when the more recent PbB results become available.

Baseline psychometric testing using the Bayley Scales of Infant Development II and the Minnesota Child Development Index will be performed at T0.

Study drug will be dispensed and dosage reviewed with parent(s). Training in drug administration will be provided to the parent or appropriate caregiver. Using placebo capsules, the TLC nurse will demonstrate how to open the capsule and mix the drug beads with a small amount of fruit juice or soda. After briefly mixing the beads with the liquid, the child will be given the liquid to drink. The parent will be instructed to rinse the medicine cup with additional liquid twice and give to the child to ensure that all beads are administered. If the child refuses to take the drug in a liquid, the beads can be mixed with about one teaspoonful of applesauce or jelly and then given to the child. Before leaving the clinic, the parent will be asked to demonstrate this procedure for the TLC nurse. Parents will be shown how to record doses and any adverse events or problems in the medication diary. Problems in administration and use of diary will be identified and solutions proposed. The parent will be instructed to administer the study drug on an empty stomach. Subjects will begin taking drug on the following morning so that 3 doses can be given that day. Caregivers will be instructed to return with the pill bottle and the medicine diary at each visit.

Parents will be told to stop giving multivitamins and/or iron therapy to the child for the duration of the treatment period. They will also receive an emergency card with a 24-hour phone number to call should emergency unblinding be necessary. A subject and/or family incentive will be provided. These incentives will be determined by each Clinical Center. Appointments will be made, if possible, for all three Treatment Visits. The parent or guardian will be given a calendar showing scheduled appointments through the end of the treatment course (T1, T2, T3).

7.3.2. Treatment Visit 1 (T1)

Treatment Visit 1 (T1) will be scheduled on day 7 of study drug administration. A brief history and physical examination will be performed by the TLC nurse or physician. Any abnormalities will be

reviewed by a physician. The TLC nurse will review the medication diary and record study data. Dosing and administration of study drug will be reviewed, problems identified and solutions proposed. In addition, the caregiver will be reminded to reduce the dose starting the following day. Blood will be drawn and sent to the local laboratory for safety monitoring and to CDC for PbB. Monitoring will consist of absolute neutrophil count, platelet count, AST, ALT, and alkaline phosphatase. The appointment for the next visit, in three weeks, will be reviewed. A subject and/or family incentive will be provided.

7.3.3. Treatment Visit 2 (T2)

Treatment Visit 2 (T2) will be scheduled on day 28 of the treatment phase. The TLC nurse will review the medication diary and record study data. All pill bottles will be collected and returned to the Drug Distribution Center for pill counts and appropriate disposal. Blood will be drawn and sent to the local laboratory for safety monitoring and to CDC for PbB. Monitoring will consist of absolute neutrophil count, platelet count, AST, ALT, and alkaline phosphatase. The results of the T2 venipuncture are necessary to assess how well the child has tolerated the study drug in anticipation of further courses of treatment, should these be necessary on the basis of the PbB. The appointment for the next visit, in two weeks, will be reviewed. A subject and/or family incentive will be provided.

7.3.4. Treatment Visit 3 (T3)

Treatment Visit 3 (T3) will be scheduled for 2 weeks after the end of the treatment period, on day 42 of the treatment phase. A brief history and physical examination will be performed by the TLC nurse or physician. Any abnormalities will be reviewed by a physician. Blood will be drawn and sent to the local laboratory for safety monitoring and to CDC for PbB. Monitoring will consist of absolute neutrophil count, platelet count, AST, ALT, and alkaline phosphatase. The results of the T3 venipuncture are necessary to assess how well the child has tolerated the study drug in anticipation of further courses of treatment, should these be necessary on the basis of the PbB. Results of the PbB measurement obtained at T3 will determine whether a child is retreated or enters follow-up. The appointment for the next visit, in one week, will be reviewed. A subject and/or family incentive will be provided.

The appointment for T4 in one week will be scheduled before the PbB result is available, in anticipation that most children will need more than one course of study drug. If the Data Coordinating Center notifies the clinic that additional therapy is not indicated, the parent will be notified and the appointment will be rescheduled for the first follow-up visit. The family will be instructed to resume multivitamin plus mineral supplements and iron therapy, if prescribed.

7.3.5. Subsequent Treatment Visits

If the PbB measurement obtained at T3 or T7 is 15 μg/dL or greater, drug treatment will be readministered. Subsequent treatment visits (T4, T5, T6 and T7 for the second course of treatment, and T8, T9, T10 and T11 for the third course of treatment) will follow the schedule of the initial treatment phase, excluding psychometric testing. Except for psychometric testing, which will be administered at T0 only, the protocol for retreatment will be the same as for the initial course of treatment. No more than three courses of treatment will be given to any child.

7.3.6. Off Protocol

Children may be taken off the TLC treatment protocol for a number of different reasons, as discussed above. Such children will remain enrolled in the TLC Trial. In particular, followup and psychometric visits will occur on the originally projected schedule.

7.4. Followup Schedule

Once treatment has been completed, children will resume taking nutritional supplementation for the duration of the trial. Children who were found to be iron deficient during the enrollment phase will resume iron therapy, for a total of three months of supplementation.

The followup schedule will be timed with reference to randomization, rather than to end of treatment. This will keep the followup schedule in synch with the timing of psychometric followup. All children will be seen every three months through the 24-month post-randomization visit. After that visit, followup visits will occur every four months. In cases where the six-month post-randomization date occurs later than three months following the end of treatment, an additional followup visit will be scheduled between the end of treatment and the six-month post-randomization date. In particular, children who require only one round of treatment will have their first followup visit scheduled for one month after day 42 (T3). Any children who, for whatever reason, do not follow the standard TLC treatment schedule will still follow this schedule for followup, i.e., they will be seen at six months post-randomization regardless of their treatment status.

Children will be followed until the age of 72 months or the end of the study. A reminder call will be made or a card mailed to the family one week prior to each scheduled visit.

At each followup visit, a brief history and physical examination will be performed by the TLC nurse or physician. Any abnormalities will be reviewed by a physician. The subject will be given an adequate supply of multivitamins and the parent will be instructed to continue their administration. Blood will be drawn and sent to CDC for determination of PbB. A subject and/or family incentive will be provided. An appointment will be made for the next visit.

8. LABORATORY PROCEDURES

8.1. Introduction

Blood samples for blood lead and serum ferritin determination will be shipped to the Nutritional Biochemistry Branch, CDC, in Atlanta, which will serve as the Central Laboratory for the trial. All other blood work will be done locally, following local protocols. Samples for blood lead and ferritin analysis will be collected by venipuncture by personnel trained and experienced in pediatric venipuncture using proper sterile technique and following universal precautions and CDC guidelines.

Samples will be shipped to the CDC the same day they are collected. During the treatment phase of the trial, blood sample will be shipped via overnight delivery. During the followup phase of the trial, shipping need not be shipped overnight. Routine turn-around time, i.e., the time from the receipt of the sample at CDC to the reporting of results to the Data Coordinating Center, will be five working days (i.e., one week). The shipping and reporting system will include a means of identifying and expediting samples requiring analysis on an urgent or STAT basis. Urgent samples will be processed so that results are available no less than two days before the next visit; these will include PbB samples at V1, V2, and T3. STAT samples will be processed so that results are available within 24 hours of receipt of sample; these will include confirmation of PbBs greater than 44 μg/dL or confirmation of increase in PbB greater than 15 μg/dL.

All analytical results will be reviewed by both the study analyst and the study laboratory supervisor at the central laboratory. All quality control materials will be reviewed by the laboratory supervisor. Data will be transmitted to the Data Coordinating Center via Internet on a daily basis as needed. Data will also be recorded onto floppy disks and optical disks for archiving.

Residual TLC blood samples will be stored at CDC for a minimum of one year following publication of trial results.

8.2. Blood Lead Analysis

Lead will be measured in blood by atomic absorption spectrometry based on the method described by Miller *et al.*[42] The lead content will be determined by using a Perkin-Elmer Model 4100-ZL graphite furnace atomic absorption spectrophotometer with Zeeman-effect background correction. Lead contamination must be carefully avoided throughout all procedures. All materials used for collecting and processing specimens will be pre-screened for possible lead contamination. All laboratory processing work will be performed under clean conditions, including laminar flow hoods.

8.3. Ferritin Analysis

Ferritin, like hemoglobin, is a major iron storage protein. Circulating plasma ferritin is most like the L-isoferritin. Serum ferritin provides a much more sensitive indicator of iron body stores than a traditional serum iron assay. Serum ferritin is increased in iron overload, aging, infection, inflammation, liver disease, juvenile rheumatoid arthritis, leukemia, and Hodgkin's disease. Serum ferritin is reduced in iron deficiency.

Ferritin will be measured by using the Bio-Rad Laboratories "Quantimmune Ferritin IRMA" kit which is a single-incubation two-site ^{125}I-immunoradiometric assay (IRMA) based on the general principles of assays as described by Addison *et al.*[43] and Miles[44] and modified by Jeong *et al*[45].

8.4. Quality Control Procedures

8.4.1. Lot Testing of Supplies for Lead Contamination

Lot testing for lead contamination is a critical part of the accurate evaluation of lead in whole blood. Lead may contaminate most commercial blood collection devices (e.g., "Vacutainers") from a variety of sources, including the container materials themselves (glass, stainless steel, rubber, or plastic) and the anticoagulants used. EDTA is a particularly common source. To assure that blood lead values obtained are accurate and not falsely elevated from contamination, CDC will undertake a screening program to evaluate the lead levels in Vacutainer tubes for the TLC Trial and any and all devices that contact the TLC blood specimens, including disposable syringes, stainless steel needles, skin cleaning devices or solvents (such as isopropanol in alcohol pads).

8.4.2. Laboratory Analyses

Estimates of imprecision will be generated from long-term quality control pool results. A quality control system of "bench" quality control specimens will be inserted by the analyst in each analytical run (a set of consecutive assays performed without interruption) so that judgements may be made on the day of analysis. All levels of blood lead concentration are assessed by taking these samples through the complete analytical process. The data from these materials will then be used in estimating methodological imprecision and in assessing the magnitude of any time-associated trends.

The "bench" quality control pools are prepared in sufficient quantity to last the duration of the trial. The levels chosen are in the low range (approximately 20 µg/dL) as well as elevated range (approximately 40-44 µg/dL) so as not to be obvious to the analyst. In every batch of 20 specimens analyzed, either one low or high concentration quality control pool will be randomly inserted. Limits will be established for new pools after 20 runs.

If, after reviewing the analytical and quality control data, the system is declared "out of control" by the supervisor, the entire run will be repeated. If the "out-of-control" condition still exists for ferritin, a new kit will be used and the autodiluter evaluated for pipetting precision and accuracy. If the "out-of-control" condition exists for blood lead, all instrumental parameters will be reverified, and matrix modifier and all other reagents will be checked for possible contamination. National Institute of Standards and Technologies (NIST) Standard Reference Material (SRM) 955a "Lead In Blood" materials[46] will be analyzed in addition to normal bench quality control pools in order to confirm accuracy and precision has been reestablished. Specimens for any analytical run held in question will be reassayed after the system has been reverified to be "in control."

8.4.2.1. Blood Lead Analysis

The blood lead analysis method to be used in the TLC Trial has been used for several years in the Nutritional Biochemistry Branch, CDC, for environmental and occupational health studies, as well as for the Third National Health and Nutrition Examination Survey (NHANES III). The method has proven to be accurate, precise, and reliable. The primary standard used is a NIST SRM lead nitrate, and the NIST SRM 955a "Lead In Blood" materials will also be used as external standards. Bench quality control materials are prepared by CDC as EDTA-whole blood from lead-dosed cows.

8.4.2.2. Serum Ferritin Analysis

The serum ferritin method has also been used in the Nutritional Biochemistry Branch for a number of years, including the NHANES III Study. The method has been proven to be highly comparable to the International Committee for Standardization in Hematology (ICSH) reference enzyme immunoassay method. The ICSH International Reference Ferritin Standard from the National Institute of Biologicals, Standards, and Chemicals, U.K., is used as the external validation material for accuracy and precision.

Because of reliability and availability, four levels of Bio-Rad Laboratories ECS Division "Lyphochek" lyophilized human serum controls will be used as bench quality control materials for ferritin analysis. Approximate values will be 5, 50, 150, and 400 ng/mL. Bench quality control pools as well as blind quality control pools may also be made from filter-sterilized fasting human serum.

9. DRUG DISTRIBUTION

9.1. Trial Medications

As described in Section 4.2, children will be randomly assigned to active drug or placebo. The dosing regimen will be based on six categories of body surface area. The total number of bottles needed is projected to be 1,332 bottles of active drug and 1,332 bottles of placebo, based on the assumption that each participant will need an average of two treatments (two bottles per participant). An additional 30 bottles each of succimer and placebo will be retained by the Drug Distribution Center for quality assurance samples. Study drug, both active and placebo, will be packaged in bottles of 95 and 130.

All trial medication, both active and placebo, will be provided by the manufacturer, McNeil Consumer Products Company, to the Drug Distribution Center. The Drug Distribution Center will receive, inspect, store, repackage and ship all trial medications.

9.1.1. Repackaging of Trial Medications

The Drug Distribution Center will repackage the medications in amber color glass unit-of-use containers, with child-resistant safety caps and a tamper-evident seal. The Drug Distribution Center will prepare two-thirds of the projected drug requirements before enrollment begins. When half of the

projected total has been dispensed, the Drug Distribution Center will repackage the remaining one-third of the drug in proportions to be specified by the Data Coordinating Center based on actual trial experience.

In order to provide placebo with an odor comparable to that of succimer, the Drug Distribution Center will place a two cm^2 piece of filter paper which has been soaked with Mucomyst 20% solution into each bottle of placebo drug. An unsoaked piece of filter paper will be placed inside each bottle of succimer so that all bottles will appear the same.

Each bottle of drug will be assigned a unique number in random sequence at the Drug Distribution Center. Equal numbers of active and placebo drug will be placed in sequential order in shipping cartons. Each shipping carton will be assigned a unique identifying number. The Drug Distribution Center will provide to the Data Coordinating Center a database containing the bottle number, the carton number, and a code indicating whether active or placebo. This database will be used with a randomization algorithm different from that which was used at the Drug Distribution Center to further randomize drug assignments for trial participants.

9.1.2. Labelling of Trial Medications

The Drug Distribution Center will label all repackaged bottles of trial medications according to a double-blinded design. Neither the clinic nor the patient will know the contents of any bottle. The primary label affixed by the Drug Distribution Center will state that the bottle may contain succimer or placebo; will include a detachable, tamper-evident sealed packet containing identification of the drug in the bottle which can be used in cases of emergencies which require unblinding of the patient; and will include a standard, detachable bar-code with the unique Control Number of the bottle of drug. This bar code will be transferred to the patient record after the bottle of drug is assigned.

The Drug Distribution Center will provide each clinic with secondary labels that conform to local regulations. Clinic personnel will complete the label with the requisite dosing information when dispensing the drug. The secondary label will provide space for the date dispensed, dosing directions, Principal Investigator's name, address and emergency phone number. Secondary labels will be available in Spanish as required for individual patients. Clinical Centers will be responsible for providing the information on local regulations for the secondary label.

9.2. Vitamins and Mineral Supplements

Each child will receive a supply of multivitamins plus mineral supplements to be taken throughout the study except during treatment. Estimated total multivitamins plus mineral supplements is 1,391,366 tablets. This total assumes a 7% attrition rate each year of followup to treatment.

The Drug Distribution Center will purchase in bulk 1.5 million daily doses of multivitamins plus mineral supplements for the Trial. The Drug Distribution Center will receive, inspect, store, and ship containers of multivitamins plus mineral supplements to the Clinics. The Data Coordinating Center will recommend which vitamins to purchase.

Multivitamins plus mineral supplements will be repackaged in unit-of-use bottles.

9.3. Storage, Shipping and Inventory Control

The Drug Distribution Center will store all containers of trial medication and multivitamins plus mineral supplements for shipment and will maintain computerized inventory records of all available quantities of trial medication. The Data Coordinating Center will also maintain records of available drug in all clinics and at the Drug Distribution Center.

The Drug Distribution Center will ship the study drug and multivitamins plus mineral supplements to the clinics as needed. Copies of shipping invoices will be given to the Data Coordinating Center.

The Drug Distribution Center will distribute all orders for trial medication and multivitamins plus mineral supplements to the clinical sites using a delivery service that tracks shipments. Trial medication will be shipped to the Clinical Centers on an as-needed basis, upon request from the Coordinating Center, within two business days of request. Shipments of multivitamins plus mineral supplements will be sent to the Clinical Centers when requested by Clinical Centers and within five business days of request.

Trial drug and multivitamins plus mineral supplements will be dispensed at six clinics in four Clinical Centers: Baltimore (2 clinics), Newark (1 clinic), Ohio (2 clinics), and Philadelphia (1 clinic).

9.4. Documentation

The Drug Distribution Center will provide the Data Coordinating Center with:

- A statement of methods to be used for maintaining accurate and complete records of drugs dispensed.
- Assurance of proper storage and inventory control of drugs.
- A statement that dispensing and labelling of drugs and multivitamins plus mineral supplements are handled in accordance with local regulatory requirement for each Clinical Center.
- A listing on paper and 3½" disk in ASCII format, specifying for each bottle of drug or placebo:
  - Control Number
  - whether drug is active or placebo
  - carton number.
- Invoices and packing slips for each study medication shipment specifying the Control Numbers of all bottles shipped.
- Invoices and packing slips for multivitamins plus mineral supplements shipped.
- Specification of method used for generating Control Numbers, e.g. the name of the software used to randomly assign numbers and copies of relevant pages from the software manual describing the random sequence generator.
- The name and telephone number of a contact person with whom the Data Coordinating Center can work.

9.5. Return and Disposal of Unused Medication

The Clinical Centers will return all used and unused bottles of study drug to the Drug Distribution Center. Unused capsules will be counted and the counts reported to the Data Coordinating Center. The Drug Distribution Center will account for and dispose of all unused active drug and placebo capsules and bottles.

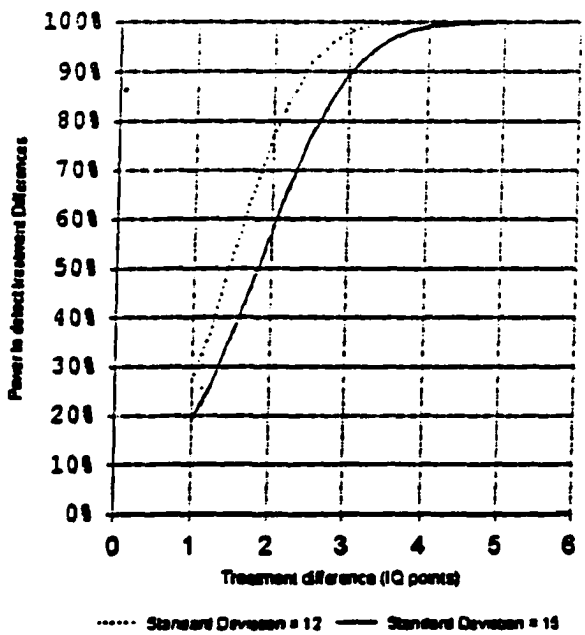
10. STATISTICAL METHODS

10.1. Power Calculations

The primary hypothesis of the TLC trial is that succimer treatment of children with elevated levels of blood lead will improve developmental status three years after treatment begins. Although the primary hypothesis will be tested by an analysis of covariance (see below), we assume for the purposes of the sample size calculation that the hypothesis will be tested by an unadjusted comparison of the mean developmental status at the three-year followup visit in the succimer and placebo groups. We assume that the standard deviation of the standardized WPPSI-R test scores in the study sample will be 15 and that 1,040 randomized children (78% of those enrolled) will complete the three-year followup visit successfully. The variance assumption should be conservative, both because test scores in the study sample may have lower variance than that in the normative population and because adjustment for baseline developmental status through analysis of covariance will reduce the error variance.

Study power with respect to the WPPSI-R can be calculated as a function of the difference in mean test scores between treatment groups. Assuming a Type I Error rate of 0.05 (two-sided) and a sample size of 1,040 evaluable children, Figure 1 shows the power of the study as a function of the difference. In particular, a difference of three IQ points implies a power of 90% for a standard deviation of test scores of 15 (solid line). This power improves to 98% if we assume a standard deviation of 12 (dashed line).

Figure 1. Power as a function of achieved difference in mean IQ score



Relatively little is known about the potential effects of chelation on other measures of developmental status (CDI, CPRS, Neuropsychological Battery), height and weight. The power of the study to detect differences in mean values of these outcome variables between treatment groups can,

however, be described in a generic way. Table 8 presents the smallest detectable difference for a standardized test score for a fixed sample size of 1,040 as a function of power and standard deviation of the test score. For example, for a score with a standard deviation of 10, the study will detect a mean difference in score of 1.7 with a power of 80%.

Table 8. Smallest detectable difference for standardized test scores.

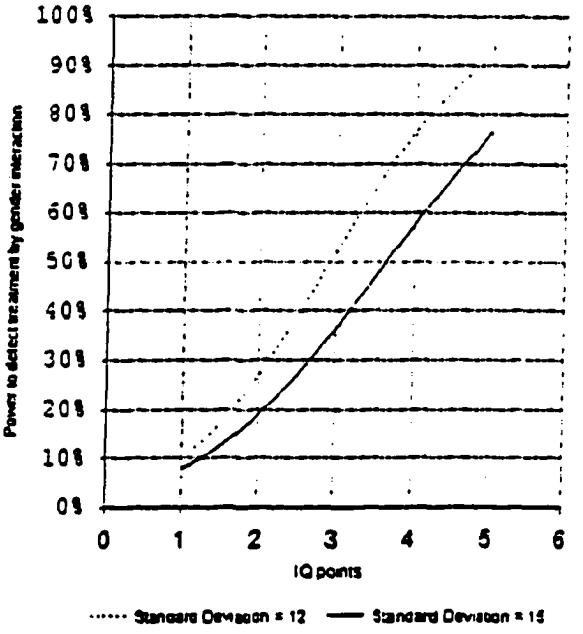
	Standard Deviation						
Power	4	6	8	10	12	14	16
20%	0.3	0.4	0.6	0.7	0.8	1.0	1.1
30%	0.4	0.5	0.7	0.9	1.1	1.2	1.4
40%	0.4	0.6	0.8	1.1	1.3	1.5	1.7
50%	0.5	0.7	1.0	1.2	1.5	1.7	1.9
60%	0.5	0.8	1.1	1.4	1.6	1.9	2.2
70%	0.6	0.9	1.2	1.5	1.8	2.2	2.5
80%	0.7	1.0	1.4	1.7	2.1	2.4	2.8
90%	0.8	1.2	1.6	2.0	2.4	2.8	3.2

Although the primary hypothesis of this study concerns the effects of chelation therapy in the study sample as a whole, questions about differential effects of chelation by race and gender are of scientific interest. Because approximately 85% or more of study participants are expected to be African American heritage, the study will provide little information about differential effects by race. The study will, however, provide some information about differential effects by gender. This question will be investigated by first testing for an interaction between gender and treatment in the analysis of covariance model. If a statistically significant interaction is detected, it will be necessary to estimate the treatment effect separately for boys and girls. If the test for interaction does not achieve statistical significance, the effect in each subgroup should be estimated by the overall estimate of the effect.

Because the sample must be divided into four subgroups for a test for interaction, the variance of the estimated difference in effect between boys and girls will have variance four times larger than the estimate of the overall effect. Figure 2 presents the power of the study to detect a gender by treatment interaction as a function of the size of that difference.

If we assume that test scores have a between-child standard deviation of 15 points, a test for interaction at the 0.05 level of significance will have power of approximately 76% to detect a difference in effect sizes between boys and girls of 5 points. With a standard deviation of 12, approximately the same power is achieved for differences of 4 IQ points. Given that the study is designed to detect an overall difference of 3 IQ points between treatment groups, it seems implausible that chelation therapy would have differential effects of that magnitude in boys and girls. The study will have power of 50% or less to detect interactions of 3 points or less.

Figure 2. Power to detect a gender by treatment interaction as a function of achieved difference in mean IQ score



10.2. Baseline Comparisons

Following standard practice in the analysis of parallel group randomized clinical trials, the analysis will begin with an assessment of the comparability of the two treatment groups at baseline. The Bayley scales of Infant Development II (BSID II) and the Child Development Inventory (CDI) will provide baseline measures of developmental status. Although randomization will ensure that any differences in the distribution of baseline characteristics are due to chance, exact and Student's t-tests will be used to compute p-values testing the equality of distributions and mean values for categorical and continuous variables, respectively. These p-values will be helpful in screening the baseline distributions for comparability.

10.3. Evaluation of Efficacy

10.3.1. Test of Primary Hypothesis

The primary hypothesis of the TLC Trial is that chelation with succimer will result in an increase in the mean IQ at three-year followup, as measured by the WPPSI-R full-scale deviation IQ. This hypothesis will be tested by an analysis of covariance. The dependent variable for this analysis will be WPPSI-R score at the three-year followup visit when that measurement is obtained, and WPPSI-R score at the 18-month followup visit when it is available and the three-year assessment is not. Independent variables will include indicator variables for clinic, treatment group, body surface area group, baseline blood lead level group, and baseline scores on the BSID II. Irrespective of compliance, each study participant for whom a WPPSI-R score is available will be included in the analysis according to their treatment assignment (an "intent-to-treat" analysis).

10.3.2. Tests of Secondary Hypotheses

Secondary outcome variables to be assessed in the TLC Trial include the other developmental measures described in Section 5, as well as height, weight, head circumference, systolic blood pressure, and diastolic blood pressure, as measured at the three-year followup examination. The hypotheses that chelation has a beneficial effect on these outcome variables will also be tested by analyses of covariance. Each ANCOVA will included clinic, treatment group, body surface area group, baseline blood lead level group, and baseline measures of developmental status, height, or weight most appropriate for and highly correlated with the dependent variable. These analyses will also employ the intent-to-treat principle.

10.3.3. Analysis of Repeated Measures

Height, weight, and the CDI will be measured at each regular examination, and IQ (using either the BSID II or the WPPSI-R) will be measured at baseline, six, 18, and 36 months. Longitudinal methods will be used to compare the rates of change in these outcome variables during the three-year followup period. Specifically, linear models with unrestricted covariance structures[47] will be used to test the hypothesis of equality of rates of change in the two treatment groups. These hypotheses will be tested by fitting models of the form

$$y_{ij} = a + b_1 * t_{ij} + b_2 * group_i + e_{ij}$$

where y_{ij} is the developmental score for the ith child at the jth followup visit, t_{ij} is the elapsed time from baseline at this visit, "$group_i$" represents the child's treatment group, and e_{ij} is the error term. Two considerations lead to the decision to use longitudinal analyses as secondary rather than primary analyses. First, two different measures of IQ will be obtained in this study, the BSID II and the WPPSI-R, raising concerns about changes in measure in a repeated measures analysis. The second and most important consideration, however, is that the comparison of greatest interest in this trial is that at the three-year followup examination. Previous studies suggest that the beneficial effect of chelation may be largest at this examination, and developmental status at this examination is also most relevant to the long-term effect of chelation on development. The analysis of covariance of the WPPSI-R at the three-year examination, adjusting for baseline BSID II score, will retrieve most of the information about trend that would be available from longitudinal analysis of the three followup examinations.

10.3.4. Other Analyses

Additional analyses will be performed to compare blood lead levels during and after treatment in the two treatment groups, investigate the relation between blood lead level and developmental status at the three-year followup examination, investigate the relation between change in blood lead level and development status at the three-year followup examination, and evaluate the association between compliance-adjusted measures of treatment and developmental outcome.

10.4. Monitoring for Efficacy and Safety

All TLC participants will complete the treatment phase of the TLC trial before participants begin the three-year follow-up visits at which the primary outcome variable, the full-scale IQ will be measured by the WPPSI - R. Thus, it will not be necessary to develop formal sequential monitoring procedures for early termination of the enrollment and treatment phase of the trial on the basis of demonstrated efficacy. The investigators, the NIEHS Project Office, and the Data and Safety Monitoring Committee (DSMC) will nevertheless be responsible for monitoring the progress of the study closely for evidence of both efficacy and possible adverse effects of treatment.

FDA regulations for investigational new drugs include specific requirements for reporting of adverse drug experiences (ADEs). All serious ADEs will require an immediate telephone call by the TLC physician to the Data Coordinating Center (DCC), the FDA, the Project Office, and other TLC physicians. FDA notification must occur within three days of recognition of a possible serious ADE. Any death or hospitalization will be considered a serious ADE. In addition, the DCC will routinely gather data on all possible ADEs for regular reporting to the DSMC and the FDA.

All available information on efficacy and safety will be presented to the DSMC as part of the DCC report prepared for each Committee meeting, and annual reports will be prepared for submission to the FDA as required by the Investigational New Drug authorization. Because no single endpoint will be specified in advance as a primary endpoint for assessment of toxicity, no formal statistical stopping rules will be established for monitoring toxicity. The DCC will prepare, as part of its regular statistical report to the DSMC, an interpretation of any statistically significant finding regarding possible side effects of active treatment.

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Appendix 3. Dust Data for Cleaning Intervention Analysis

Table A3.1 Dust Lead Levels in Bedrooms of the Accident Prevention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	5.34	-1.079	0.487
1	2	5.90	-0.605	0.403
1	3	5.69	-0.778	0.440
2	1	6.49	-1.733	-1.313
2	2	5.38	-3.274	-1.749
2	3	5.95	-1.879	-0.921
3	1	5.96	-0.631	0.313
3	2	5.83	-0.393	0.682
3	3	5.47	-0.972	0.466
4	1	7.93	-1.605	-2.631
4	2	8.09	-0.290	-1.474
4	3	8.46	-0.285	-1.839
5	1	6.68	-2.263	-2.033
5	2	6.64	-1.720	-1.452
5	3	6.38	-2.022	-1.492
6	1	5.52	-3.605	-2.216
6	2	7.17	-1.657	-1.917
6	3	6.01	-3.055	-2.154
7	1	5.78	-1.983	-0.856
7	2	6.15	-2.141	-1.378
7	3	6.35	-1.814	-1.259
8	1	5.73	-0.865	0.314
8	2	8.60	0.025	-1.671
8	3	7.47	-1.451	-2.010
9	1	6.13	-1.710	-0.929
9	2	5.08	-2.874	-1.050
9	3	5.61	-3.073	-1.778
10	1	6.69	-2.360	-2.146
10	2	7.80	-1.683	-2.577
10	3	6.36	-2.783	-2.235
11	1	6.56	-1.408	-1.064
11	2	7.17	-2.075	-2.333
11	3	6.55	-1.905	-1.551
12	1	6.31	-1.151	-0.550
12	2	8.37	2.071	0.612
12	3	6.10	-0.963	-0.153
13	1	5.95	-2.900	-1.945
13	2	8.16	-1.080	-2.333
13	3	6.92	-1.813	-1.826

Table A3.1 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.29	-1.061	-0.445
14	2	5.61	-1.134	0.168
14	3	5.85	-0.678	0.379
15	1	6.90	-2.202	-2.189
15	2	9.06	1.845	-0.302
15	3	4.59	-2.471	-0.151
16	1	5.37	-0.928	0.608
16	2	7.01	-0.109	-0.212
16	3	6.93	0.058	0.036
17	1	7.31	-1.719	-2.120
17	2	7.09	-1.862	-2.040
17	3	5.86	-2.493	-1.440
18	1	6.70	-1.313	-1.103
18	2	6.73	-1.548	-1.366
18	3	6.30	-2.094	-1.487
19	1	6.85	-2.576	-2.513
19	2	6.83	-2.265	-2.189
19	3	6.03	-2.430	-1.546
20	1	6.41	-1.614	-1.112
20	2	5.24	-1.979	-0.315
20	3	6.82	-0.885	-0.792
21	1	6.78	-0.276	-0.144
21	2	5.74	-0.244	0.924
21	3	7.07	0.416	0.253
22	1	5.89	-2.904	-1.884
22	2	5.26	-3.178	-1.528
22	3	6.70	-1.801	-1.590
23	1	6.26	-0.889	-0.238
23	2	6.33	-0.342	0.233
23	3	6.54	-1.206	-0.837
24	1	5.78	-1.076	0.054
24	2	6.35	0.141	0.702
24	3	6.16	-1.244	-0.494
25	1	6.12	-0.636	0.152
25	2	6.55	0.163	0.518
25	3	6.53	-0.703	-0.327
26	1	6.02	-0.883	0.004
26	2	6.07	-0.180	0.662
26	3	6.34	-2.304	-1.732

Table A3.1 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
27	1	7.07	-1.397	-1.556
27	2	7.00	-1.917	-2.010
27	3	6.04	-2.756	-1.890

Table A3.2 Dust Lead Levels in Living Rooms of the Accident Prevention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	6.31	-1.772	-1.171
1	2	6.07	-2.033	-1.191
1	3	6.20	-1.441	-0.736
2	1	7.02	-3.854	-3.963
2	2	5.45	-3.387	-1.924
2	3	6.06	-2.061	-1.214
3	1	5.76	-2.348	-1.204
3	2	5.80	-2.781	-1.677
3	3	5.29	-2.998	-1.382
4	1	6.12	-0.079	0.709
4	2	5.90	-0.026	0.980
4	3	5.89	-0.393	0.627
5	1	6.04	-0.777	0.092
5	2	6.27	-0.286	0.348
5	3	6.14	-0.227	0.541
6	1	5.98	-2.911	-1.988
6	2	6.59	-1.493	-1.178
6	3	6.41	-3.216	-2.718
7	1	4.12	-4.457	-1.666
7	2	6.49	-1.646	-1.228
7	3	6.49	-1.498	-1.076
8	1	5.10	-4.605	-2.797
8	2	5.47	-3.080	-1.645
8	3	6.33	-2.999	-2.419
9	1	7.12	-1.997	-2.207
9	2	7.38	-1.277	-1.749
9	3	6.81	-1.913	-1.814
10	1	5.33	-2.899	-1.317
10	2	6.59	-3.371	-3.058
10	3	5.77	-2.753	-1.619
11	1	5.90	-1.451	-0.439
11	2	5.68	-1.299	-0.074
11	3	5.91	-0.219	0.777
12	1	5.56	-2.122	-0.779
12	2	7.13	-0.602	-0.828
12	3	6.74	-2.469	-2.303
13	1	6.76	-0.620	-0.468
13	2	5.99	-1.445	-0.528
13	3	5.61	-1.776	-0.481

Table A3.2 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.77	-1.634	-1.501
14	2	7.66	0.184	-0.573
14	3	8.14	0.070	-1.158
15	1	8.70	0.886	-0.904
15	2	7.31	-1.063	-1.465
15	3	6.95	-1.294	-1.336
16	1	6.63	-2.364	-2.087
16	2	6.75	-2.952	-2.797
16	3	6.25	-2.080	-1.427
17	1	8.25	-1.762	-3.101
17	2	5.95	-3.658	-2.703
17	3	6.70	-1.525	-1.317
18	1	5.55	-2.372	-1.011
18	2	6.63	-1.565	-1.287
18	3	5.84	-1.957	-0.892
19	1	6.63	0.367	0.642
19	2	5.62	-0.891	0.401
19	3	7.09	-0.425	-0.605
20	1	6.10	-1.978	-1.168
20	2	6.84	-1.030	-0.957
20	3	6.34	-1.298	-0.734
21	1	5.37	-1.191	0.351
21	2	6.39	-1.892	-1.370
21	3	6.24	-2.419	-1.749

Table A3.3 Dust Lead Levels on Windowsills of the Accident Prevention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	7.56	0.930	0.280
1	2	8.01	2.010	0.900
1	3	7.98	1.850	0.780
2	1	6.43	-2.610	-2.130
2	2	5.43	-3.400	-1.920
2	3	6.57	-1.170	-0.820
3	1	5.38	-1.060	0.470
3	2	5.63	-0.320	0.960
3	3	5.14	-2.470	-0.700
4	1	7.23	-1.720	-2.030
4	2	5.66	-0.460	0.790
4	3	6.16	-0.860	-0.110
5	1	6.17	-2.630	-1.880
5	2	5.64	-2.050	-0.780
5	3	6.45	-2.240	-1.780
6	1	4.39	-0.460	2.060
6	2	5.02	-0.740	1.150
6	3	6.71	-1.010	-0.820
7	1	5.44	-0.420	1.050
7	2	5.59	-1.430	-0.110
7	3	6.31	-1.770	-1.170
8	1	5.04	-2.760	-0.890
8	2	4.72	-2.590	-0.400
8	3	4.84	-3.150	-1.080
9	1	6.10	-1.780	-0.980
9	2	6.21	-2.140	-1.440
9	3	6.79	-1.800	-1.680
10	1	5.43	-0.820	0.660
10	2	5.60	-1.850	-0.540
10	3	8.01	1.780	0.670
11	1	7.18	2.140	1.860
11	2	7.64	2.350	1.620
11	3	8.17	2.650	1.380
12	1	7.00	-0.890	-0.980
12	2	10.81	3.450	-0.450
12	3	7.17	1.120	0.860
13	1	6.10	-0.790	0.020
13	2	5.45	-1.620	-0.160
13	3	5.20	-2.350	-0.640

Table A3.3 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.74	0.040	0.210
14	2	5.70	-1.400	-0.190
14	3	5.83	-0.870	0.210
15	1	6.07	-1.060	-0.210
15	2	6.41	-1.080	-0.590
15	3	7.38	1.300	0.830
16	1	5.06	-1.620	0.230
16	2	6.21	-1.040	-0.340
16	3	7.21	-0.280	-0.590
17	1	7.99	-0.830	-1.910
17	2	6.34	-2.360	-1.790
17	3	6.59	-1.770	-1.440
18	1	8.36	1.330	-0.120
18	2	9.34	2.460	0.030
18	3	8.43	1.190	-0.330
19	1	8.18	0.280	-0.990
19	2	7.46	0.340	-0.210
19	3	7.28	-0.060	-0.430
20	1	8.46	1.690	0.140
20	2	8.33	-0.200	-1.630
20	3	7.42	-0.630	-1.150
21	1	6.22	-0.870	-0.180
21	2	5.82	-1.350	-0.250
21	3	5.75	-1.940	-0.790
22	1	5.70	-1.890	-0.690
22	2	6.27	-1.990	-1.360
22	3	5.18	-2.820	-1.090
23	1	8.22	-0.010	-1.320
23	2	6.36	-1.720	-1.170
23	3	5.75	-1.460	-0.300
24	1	6.25	0.290	0.950
24	2	6.37	-0.100	0.440
24	3	6.68	0.530	0.760
25	1	6.74	-0.610	-0.430
25	2	9.40	2.680	0.180
25	3	7.49	-0.230	-0.810
26	1	6.67	-0.520	-0.280
26	2	8.66	-0.450	-2.200
26	3	9.20	2.650	0.360

Table A3.3 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
27	1	6.73	-1.520	-1.340
27	2	8.82	-0.930	-2.850
27	3	8.59	-2.230	-3.910
28	1	6.18	-0.610	0.120
28	2	8.48	0.170	-1.400
28	3	8.29	-0.400	-1.780
29	1	7.20	-0.960	-1.250
29	2	7.30	0.230	-0.160
29	3	7.23	0.020	-0.300
30	1	6.62	-1.930	-1.640
30	2	6.07	-1.010	-0.180
30	3	6.70	-1.090	-0.880
31	1	7.75	-1.120	-1.970
31	2	7.15	-0.950	-1.190
31	3	6.71	-1.470	-1.270
32	1	7.37	-0.340	-0.800
32	2	6.37	-0.870	-0.340
32	3	6.44	-1.660	-1.190
33	1	6.31	-1.130	-0.520
33	2	6.97	-1.100	-1.170
33	3	8.01	1.010	-0.090
34	1	9.13	3.010	0.790
34	2	8.53	0.400	-1.220
34	3	8.17	-1.020	-2.280
35	1	5.96	-1.590	-0.640
35	2	6.81	-2.160	-2.060
35	3	6.25	-1.460	-0.810

Table A3.4 Dust Lead Levels in Kitchens of the Accident Prevention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	7.78	0.020	-0.850
1	2	5.72	-2.890	-1.700
1	3	6.77	-0.700	-0.570
2	1	5.94	-1.190	-0.220
2	2	5.90	-2.110	-1.110
2	3	5.64	-1.480	-0.210
3	1	6.30	-0.510	0.100
3	2	6.84	-0.680	-0.610
3	3	5.97	-1.340	-0.400
4	1	6.17	-1.020	-0.280
4	2	5.73	-1.800	-0.630
4	3	5.56	-2.040	-0.690
5	1	6.60	-1.250	-0.940
5	2	6.07	-1.650	-0.810
5	3	5.48	-1.740	-0.310
6	1	6.81	-2.770	-2.670
6	2	6.56	-1.780	-1.430
6	3	6.86	-2.700	-2.650
7	1	6.37	-1.670	-1.130
7	2	6.72	-0.820	-0.620
7	3	6.48	0.390	0.820
8	1	7.62	1.350	0.640
8	2	9.06	0.230	-1.920
8	3	7.79	-1.010	-1.880
9	1	6.53	-1.780	-1.410
9	2	4.22	-2.740	-0.050
9	3	6.15	-2.360	-1.600
10	1	6.41	-1.490	-0.990
10	2	7.14	-0.140	-0.370
10	3	6.90	-1.450	-1.440
11	1	5.81	-1.810	-0.710
11	2	7.00	-0.980	-1.080
11	3	6.07	-1.640	-0.800
12	1	6.95	-1.310	-1.340
12	2	7.19	-1.000	-1.280
12	3	7.37	-5.060	-5.520
13	1	6.49	-2.570	-2.150
13	2	5.30	-3.540	-1.930
13	3	4.87	-3.250	-1.210

Table A3.4 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.76	-1.350	-1.210
14	2	6.29	-1.790	-1.170
14	3	6.25	-2.010	-1.350
15	1	6.73	-2.210	-2.030
15	2	6.90	-1.900	-1.890
15	3	5.47	-2.700	-1.260
16	1	6.55	-1.160	-0.800
16	2	6.91	0.240	0.240
16	3	6.78	0.240	0.360
17	1	5.82	-3.310	-2.220
17	2	5.65	-3.030	-1.770
17	3	4.48	-4.760	-2.330

Table A3.5 Dust Lead Levels in Carpets (Vacuum) of the Accident Prevention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	6.36	2.242	2.792
1	2	4.50	1.589	3.996
1	3	6.07	2.661	3.496
2	1	5.68	1.144	2.369
2	2	3.73	1.135	4.308
2	3	5.50	1.677	3.087
3	1	6.16	1.291	2.040
3	2	6.40	1.426	1.937
3	3	6.01	1.785	2.682
4	1	6.72	1.479	1.669
4	2	5.66	0.354	1.600
4	3	7.11	2.610	2.405
5	1	7.52	3.267	2.655
5	2	5.80	2.182	3.288
5	3	5.33	0.850	2.427
6	1	5.38	0.107	1.636
6	2	5.43	1.136	2.617
6	3	6.35	1.849	2.405
7	1	7.12	2.927	2.716
7	2	6.22	3.043	3.734
7	3	5.08	2.268	4.091
8	1	5.72	1.491	2.677
8	2	5.13	0.605	2.379
8	3	5.65	3.480	4.735
9	1	6.50	1.565	1.977
9	2	8.74	4.334	2.503
9	3	8.44	4.108	2.571
10	1	6.78	3.418	3.549
10	2	6.27	0.971	1.609
10	3	6.85	2.197	2.259
11	1	5.68	0.306	1.537
11	2	7.39	3.171	2.688
11	3	6.08	1.552	2.379
12	1	6.03	2.179	3.059
12	2	7.08	1.863	1.689
12	3	4.46	-0.918	1.525
13	1	6.01	0.947	1.840
13	2	6.41	1.586	2.079
13	3	6.33	1.760	2.341

Table A3.5 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	8.69	1.537	-0.244
14	2	6.48	0.177	0.608
14	3	8.61	1.900	0.198
15	1	6.48	0.516	0.943
15	2	6.57	0.585	0.920
15	3	5.07	1.241	3.082
16	1	6.58	-0.821	-0.491
16	2	7.72	0.699	-0.118
16	3	6.14	-0.889	-0.118
17	1	6.83	1.169	1.249
17	2	7.13	-0.850	-1.073
17	3	5.88	-1.794	-0.767
18	1	6.86	2.898	2.944
18	2	5.09	2.295	4.108
18	3	6.17	3.611	4.348
19	1	5.77	1.090	2.225
19	2	5.36	1.284	2.835
19	3	5.32	1.446	3.030
20	1	6.90	1.894	1.897
20	2	7.70	2.020	1.225
20	3	5.96	1.829	2.777
21	1	7.10	3.142	2.954
21	2	6.28	1.610	2.241
21	3	6.28	1.673	2.297
22	1	6.93	2.425	2.400
22	2	6.29	2.023	2.643
22	3	6.80	0.841	0.949
23	1	4.40	-0.778	1.725
23	2	4.99	-0.265	1.649
23	3	4.25	-1.711	0.947
24	1	5.80	1.030	2.142
24	2	5.09	0.400	2.218
24	3	4.62	-2.155	0.129
25	1	5.39	-1.111	0.406
25	2	4.75	-2.539	-0.381
25	3	4.25	-1.059	1.603
26	1	5.35	-0.953	0.606
26	2	4.80	-1.721	0.383
26	3	5.46	0.810	2.262

Table A3.5 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
27	1	7.46	0.771	0.217
27	2	5.69	-0.795	0.420
27	3	5.62	-0.701	0.590
28	1	7.32	0.557	0.142
28	2	7.90	3.855	2.867
28	3	6.86	2.404	2.452
29	1	5.91	1.099	2.098
29	2	6.38	2.417	2.941
29	3	5.61	1.699	3.001
30	1	7.29	0.243	-0.141
30	2	6.76	-1.488	-1.339
30	3	7.81	0.344	-0.563
31	1	8.11	0.861	-0.343
31	2	6.89	-1.021	-1.007
31	3	3.71	-3.621	-0.418
32	1	7.62	0.337	-0.377
32	2	8.73	0.818	-1.006
32	3	6.16	-1.392	-0.646
33	1	5.64	0.254	1.526
33	2	5.14	0.342	2.108
33	3	7.12	2.306	2.091

Table A3.6 Dust Lead Levels in Bedrooms of the Lead Intervention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	5.37	-4.029	-2.489
1	2	4.78	-4.605	-2.477
1	3	4.54	-4.804	-2.430
2	1	5.27	-2.114	-0.472
2	2	5.23	-2.628	-0.949
2	3	5.62	-2.828	-1.542
3	1	5.19	-3.826	-2.104
3	2	5.22	-3.713	-2.025
3	3	6.22	-3.880	-3.194
4	1	6.96	-1.784	-1.839
4	2	6.57	-1.314	-0.978
4	3	5.82	-1.266	-0.179
5	1	5.27	-2.644	-1.008
5	2	5.24	-2.812	-1.143
5	3	6.33	-1.620	-1.038
6	1	5.81	-1.620	-0.523
6	2	5.79	-2.359	-1.245
6	3	6.85	-2.384	-2.323
7	1	5.87	-1.191	-0.154
7	2	5.29	-2.056	-0.440
7	3	6.08	-1.930	-1.100
8	1	6.34	0.804	1.374
8	2	7.58	1.009	0.341
8	3	6.51	-0.324	0.070
9	1	8.28	1.114	-0.259
9	2	7.01	-1.275	-1.374
9	3	6.31	0.078	0.674
10	1	8.10	0.087	-1.100
10	2	6.07	-2.211	-1.370
10	3	6.40	-2.711	-2.198
11	1	5.47	-2.215	-0.779
11	2	5.90	-2.430	-1.423
11	3	5.15	-3.385	-1.625
12	1	7.10	0.674	0.482
12	2	7.06	-0.464	-0.611
12	3	6.69	-1.360	-1.139
13	1	7.29	-0.043	-0.423
13	2	7.23	-1.168	-1.492
13	3	7.10	-1.686	-1.877

Table A3.6 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.13	-2.346	-1.570
14	2	5.99	-3.116	-2.198
14	3	6.56	-1.433	-1.088
15	1	7.25	-1.035	-1.378
15	2	6.92	-1.517	-1.528
15	3	7.01	-0.991	-1.091
16	1	5.70	-2.351	-1.146
16	2	6.70	-1.668	-1.457
16	3	5.18	-2.855	-1.130
17	1	5.46	-2.428	-0.978
17	2	5.44	-3.107	-1.640
17	3	5.51	-3.027	-1.625
18	1	6.96	-1.421	-1.474
18	2	5.05	-2.744	-0.887
18	3	5.74	-2.119	-0.949
19	1	6.60	0.457	0.770
19	2	5.60	-0.154	1.150
19	3	5.49	-0.443	0.974
20	1	6.06	-0.665	0.185
20	2	5.46	-0.774	0.671
20	3	5.39	-0.873	0.650
21	1	9.90	-2.612	-0.994
21	2	5.40	-2.851	-1.339
21	3	5.07	-3.544	-1.704
22	1	6.49	-2.084	-1.666
22	2	5.46	-3.243	-1.796
22	3	5.24	-2.787	-1.115

Table A3.7 Dust Lead Levels in Living Rooms of the Lead Intervention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	5.23	-3.330	-1.655
1	2	5.41	-3.455	-1.959
1	3	5.49	-3.339	-1.917
2	1	5.93	-2.682	-1.704
2	2	5.48	-1.749	-0.319
2	3	5.68	-1.718	-0.489
3	1	5.69	-2.146	-0.929
3	2	5.24	-1.816	-0.152
3	3	5.93	-1.984	-1.005
4	1	5.55	-4.075	-2.718
4	2	5.39	-1.879	-0.358
4	3	5.06	-1.546	0.299
5	1	5.39	-0.983	0.534
5	2	5.36	-2.152	-0.603
5	3	4.97	-2.432	-0.498
6	1	7.05	0.210	0.066
6	2	4.20	-1.950	0.758
6	3	6.37	-0.923	-0.386
7	1	5.49	-0.830	0.590
7	2	6.10	-0.658	0.151
7	3	5.66	-1.131	0.120
8	1	6.39	-2.968	-2.453
8	2	5.82	-3.594	-2.501
8	3	6.50	-2.021	-1.609
9	1	5.73	-1.673	-0.496
9	2	6.25	-1.447	-0.787
9	3	5.95	-1.486	-0.531
10	1	10.51	-0.664	-4.269
10	2	7.04	-1.937	-2.071
10	3	7.09	-0.600	-0.777
11	1	6.09	-0.945	-0.130
11	2	6.34	-0.493	0.078
11	3	6.25	-0.612	0.052
12	1	5.95	-2.509	-1.546
12	2	5.33	-2.538	-0.960
12	3	5.13	-2.426	-0.650
13	1	6.68	-0.585	-0.358
13	2	5.44	-1.090	0.378
13	3	5.25	-1.035	0.622

Table A3.7 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.39	-2.207	-1.687
14	2	5.22	-2.147	-0.457
14	3	5.48	-2.837	-1.406

Table A3.8 Dust Lead Levels on Windowsills of the Lead Intervention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	4.82	-0.900	1.190
1	2	4.58	-3.490	-1.160
1	3	5.35	-1.940	-0.380
2	1	5.37	-3.040	-1.500
2	2	5.34	-2.690	-1.120
2	3	5.03	-2.980	-1.100
3	1	5.71	-3.320	-2.130
3	2	5.83	-1.140	-0.060
3	3	5.86	-1.830	-0.780
4	1	5.02	-1.260	0.630
4	2	6.32	-2.440	-1.850
4	3	5.28	-3.100	-1.470
5	1	6.70	-0.080	0.130
5	2	7.15	-1.930	-2.180
5	3	6.26	-1.480	-0.840
6	1	5.67	-1.470	-0.230
6	2	5.92	-1.440	-0.450
6	3	7.99	-0.040	-1.120
7	1	6.15	0.210	0.970
7	2	6.21	-1.960	-1.260
7	3	5.61	-2.400	-1.090
8	1	7.59	0.520	-0.170
8	2	9.12	-1.330	-3.540
8	3	6.91	-3.510	-3.510
9	1	7.60	0.360	-0.330
9	2	7.52	-2.220	-2.830
9	3	7.99	-1.170	-2.250
10	1	7.67	1.200	0.440
10	2	5.56	-0.440	0.900
10	3	10.55	2.330	-1.310
11	1	5.67	-1.920	-0.680
11	2	6.07	0.510	1.350
11	3	6.00	-3.120	-2.220
12	1	5.56	-1.810	-0.460
12	2	6.41	-1.600	-1.100
12	3	4.28	-2.720	-0.100
13	1	8.31	1.110	-0.290
13	2	7.82	0.100	-0.810
13	3	7.75	0.330	-0.510

Table A3.8 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	9.44	3.130	0.600
14	2	8.70	0.810	-0.990
14	3	9.05	0.360	-1.780
15	1	5.49	-1.880	-0.450
15	2	6.17	-3.170	-2.430
15	3	6.34	-1.340	-0.760
16	1	7.08	0.500	0.320
16	2	8.02	-0.230	-1.340
16	3	7.21	-1.420	-1.720
17	1	10.11	1.570	-1.630
17	2	9.23	0.450	-1.880
17	3	6.01	-2.650	-1.750
18	1	5.01	-2.190	-0.290
18	2	6.41	-2.400	-1.900
18	3	6.36	-0.580	-0.040
19	1	6.88	0.440	0.470
19	2	5.20	-1.810	-0.100
19	3	5.42	-3.000	-1.510
20	1	9.55	2.340	-0.300
20	2	9.14	0.360	-1.860
20	3	7.68	-0.950	-1.720
21	1	8.15	0.960	-0.280
21	2	8.30	0.600	-0.790
21	3	7.99	-0.010	-1.090
22	1	6.18	-0.910	-0.180
22	2	5.23	-2.830	-1.150
22	3	5.21	-3.140	-1.450
23	1	7.30	0.400	0.010
23	2	6.09	-2.220	-1.390
23	3	5.73	-2.920	-1.740
24	1	7.49	-0.340	-0.930
24	2	7.11	-1.560	-1.770
24	3	6.62	-2.080	-1.790
25	1	6.95	-0.320	-0.350
25	2	5.58	-1.700	-0.370
25	3	4.79	-1.910	0.210
26	1	6.13	-2.040	-1.270
26	2	6.46	-2.260	-1.810
26	3	6.17	-2.310	-1.570

Table A3.8 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
27	1	6.54	-1.490	-1.120
27	2	6.17	0.030	0.760
27	3	5.12	-2.100	-0.320

Table A3.9 Dust Lead Levels in Kitchens of the Lead Intervention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	5.19	-3.800	-2.080
1	2	4.53	-3.690	-1.310
1	3	4.84	-3.970	-1.900
2	1	4.96	-4.610	-2.660
2	2	5.67	-2.820	-1.580
2	3	6.24	-3.020	-2.350
3	1	5.96	-1.720	-0.770
3	2	5.86	-0.480	0.570
3	3	5.75	-0.100	1.060
4	1	5.19	-2.680	-0.960
4	2	5.03	-2.230	-0.350
4	3	5.66	-2.240	-0.990
5	1	7.24	-1.780	-2.110
5	2	5.78	-2.630	-1.510
5	3	6.39	-1.920	-1.400
6	1	8.38	0.780	-0.690
6	2	6.39	-1.530	-1.010
6	3	6.21	-1.850	-1.140
7	1	2.93	-5.500	-1.520
7	2	5.84	-3.560	-2.490
7	3	7.77	-1.790	-2.650
8	1	6.52	-1.680	-1.290
8	2	8.13	1.830	0.610
8	3	6.71	-1.710	-1.510
9	1	5.47	-2.110	-0.670
9	2	6.36	-0.830	-0.280
9	3	5.69	-1.350	-0.130
10	1	5.38	-0.940	0.600
10	2	6.25	-3.040	-2.380
10	3	6.09	-3.250	-2.430
11	1	5.80	-1.940	-0.830
11	2	6.37	-2.640	-2.100
11	3	6.74	-2.600	-2.430
12	1	6.01	-2.920	-2.020
12	2	6.87	-1.530	-1.490
12	3	5.35	-3.020	-1.450
13	1	7.17	-1.490	-1.750
13	2	5.66	-3.430	-2.180
13	3	6.53	-2.350	-1.970

Table A3.9 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	6.02	-1.040	-0.160
14	2	6.37	-1.100	-0.560
14	3	6.27	-1.740	-1.100
15	1	7.06	-0.120	-0.270
15	2	7.12	-3.010	-3.220
15	3	6.42	-0.460	0.030
16	1	7.65	1.170	0.430
16	2	6.69	-0.750	-0.530
16	3	7.10	0.760	0.580
17	1	6.36	-1.960	-1.410
17	2	6.80	-0.210	-0.100
17	3	6.88	-1.000	-0.970
18	1	4.86	-4.000	-1.950
18	2	6.05	-2.800	-1.940
18	3	5.13	-3.530	-1.750
19	1	5.63	-2.220	-0.940
19	2	5.14	-2.820	-1.060
19	3	4.77	-2.730	-0.590
20	1	6.52	-1.200	-0.810
20	2	5.14	-3.410	-1.640
20	3	4.94	-3.360	-1.390
21	1	6.08	-2.060	-1.230
21	2	5.21	-2.850	-1.150
21	3	4.80	-2.850	-0.740

Table A3.10 Dust Lead Levels in Carpets (Vacuum) of the Lead Intervention Homes with Three Sequential Home Visits.

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
1	1	5.78	0.637	1.764
1	2	5.53	0.960	2.336
1	3	4.79	0.186	2.302
2	1	6.94	1.570	1.539
2	2	6.08	0.793	1.622
2	3	5.18	1.190	2.915
3	1	5.92	1.885	2.872
3	2	6.59	2.769	3.083
3	3	6.15	2.974	3.737
4	1	7.18	2.987	2.717
4	2	7.93	3.713	2.694
4	3	7.88	3.275	2.306
5	1	5.74	0.578	1.746
5	2	8.94	4.346	2.312
5	3	6.93	1.883	1.863
6	1	5.36	-0.439	1.107
6	2	5.96	0.873	1.822
6	3	5.49	0.458	1.877
7	1	7.14	3.136	2.900
7	2	7.06	3.021	2.873
7	3	6.32	1.843	2.426
8	1	5.23	-0.141	1.541
8	2	5.71	1.177	2.375
8	3	5.66	-0.525	0.724
9	1	5.87	1.186	2.225
9	2	6.47	2.284	2.723
9	3	4.48	-2.487	-0.062
10	1	6.12	1.928	2.713
10	2	6.61	2.329	2.626
10	3	7.50	0.793	0.197
11	1	5.28	0.893	2.524
11	2	5.29	1.968	3.591
11	3	7.07	0.471	0.309
12	1	7.04	0.614	0.482
12	2	6.51	1.379	1.779
12	3	8.23	-0.892	-2.211
13	1	5.57	0.145	1.480
13	2	4.47	-0.875	1.564
13	3	4.25	-1.221	1.437

Table A3.10 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
14	1	3.77	-0.086	3.055
14	2	4.48	-0.699	1.731
14	3	5.78	-0.972	0.155
15	1	3.14	-0.809	2.961
15	2	4.73	-0.966	1.212
15	3	6.86	-0.025	0.018
16	1	5.98	0.919	1.846
16	2	10.48	2.798	-0.775
16	3	6.09	-1.187	-0.365
17	1	6.37	0.292	0.831
17	2	8.51	1.721	0.116
17	3	5.85	-0.601	0.453
18	1	6.38	1.793	2.320
18	2	6.44	-0.016	0.455
18	3	5.93	-0.645	0.337
19	1	6.49	3.075	3.496
19	2	6.29	0.419	1.040
19	3	6.63	1.430	1.706
20	1	5.82	2.390	3.480
20	2	5.17	-0.164	1.577
20	3	5.05	1.306	3.166
21	1	5.66	2.298	3.544
21	2	5.71	0.498	1.696
21	3	6.07	0.897	1.733
22	1	5.51	2.028	3.423
22	2	6.77	1.437	1.579
22	3	5.71	0.256	1.453
23	1	7.14	2.791	2.555
23	2	6.45	0.730	1.193
23	3	7.05	1.040	0.897
24	1	7.98	3.711	2.640
24	2	6.95	1.631	1.593
24	3	6.26	0.134	0.784
25	1	8.12	2.371	1.158
25	2	4.87	-3.838	-1.797
25	3	6.82	0.579	0.664
26	1	5.67	0.319	1.553
26	2	6.86	-0.329	-0.276
26	3	5.37	-1.754	-0.214

Table A3.10 (Continued).

Subject	Home Visit	Natural Log Pb Concentration (μg/g)	Natural Log Pb Loading (mg/m^2)	Natural Log Dust Loading (g/m^2)
27	1	5.10	1.406	3.216
27	2	6.51	2.482	2.876
27	3	7.09	1.196	1.011
28	1	6.77	3.408	3.549
28	2	6.04	1.819	2.688
28	3	7.32	0.923	0.512
29	1	6.44	2.055	2.525
29	2	7.17	2.793	2.536
29	3	7.04	1.992	1.861
30	1	7.07	3.366	3.205
30	2	7.08	2.980	2.812
30	3	7.30	2.587	2.191
31	1	7.73	3.194	2.370
31	2	7.26	2.724	2.370
31	3	7.19	1.492	1.207

Appendix 4. Blood and Dust Data for Stepwise Regression Analysis (CLEARS)

Table A4.1 Blood and Dust Lead Levels for Stepwise Regression Analysis.

Average Blood Pb Conc (µg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Average Carpet (Log_{10})			Floor Surfacing Type
	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
0.48	2.59	-0.75	-1.16							Uncarpeted
0.43	2.59	-0.75	-1.16	2.90	0.22	0.12				Uncarpeted
0.93	2.54	-0.60	-1.06	3.46	0.34	0.80				Uncarpeted
0.65				2.79	-0.92	-1.13				Uncarpeted
0.75	3.02	-1.49	-1.47	3.18	-0.12	0.06				Uncarpeted
0.86	2.79	-0.50	-0.71	2.72	0.25	-0.02				Uncarpeted
1.25	2.63	0.22	-0.15	2.45	0.42	-0.14				Uncarpeted
1.21	2.55	0.22	-0.23	2.23	-0.30	-1.07				Uncarpeted
0.97				2.68	-0.05	-0.37				Uncarpeted
0.81	2.89	-0.37	-0.47							Uncarpeted
1.38	2.85	-0.48	-0.64	1.75	0.01	-1.24				Uncarpeted
0.71	2.44	-1.05	-1.62	2.29	-0.10	-0.81				Uncarpeted
1.38	3.73	0.09	0.81	3.23	0.51	0.74				Uncarpeted
1.34	3.16	-0.05	0.10	3.17	0.51	0.68				Uncarpeted
1.39	3.06	-0.16	-0.10	3.04	-0.42	-0.39				Uncarpeted
1.49	3.83	-0.87	-0.03	4.70	-0.20	1.50				Uncarpeted
1.40	3.26	-0.76	-0.51	3.11	0.37	0.49				Uncarpeted
0.95	2.76	-0.51	-0.75	3.22	0.51	0.73				Uncarpeted
1.05	2.66	-0.83	-1.17							Uncarpeted
0.87	2.85	-0.61	-0.76	2.93	0.09	0.02				Uncarpeted
1.03	3.20	-0.76	-0.56	2.47	-0.08	-0.61				Uncarpeted
0.92	2.87	-0.76	-0.89	2.53	0.09	-0.38				Uncarpeted
0.86	2.61	-0.33	-0.72	2.63	-0.09	-0.46				Uncarpeted
0.90	2.83	-0.13	-0.30	2.78	-0.25	-0.47				Uncarpeted
1.14	2.68	-0.07	-0.39	3.20	0.36	0.56				Uncarpeted
1.17	2.51	-0.50	-0.99	2.20	0.10	-0.70				Uncarpeted
1.01	3.23	-0.61	-0.39	2.70	-0.15	-0.45				Uncarpeted
0.99	2.86	-0.71	-0.86	3.13	-0.25	-0.12				Uncarpeted
0.76	2.07	-0.39	-1.32	2.03	-0.66	-1.63				Uncarpeted
1.27				3.66	-0.14	0.52				Uncarpeted
1.03	2.98	-0.73	-0.74	3.70	-0.42	0.28				Uncarpeted
1.29	2.91	-0.99	-1.08	3.24	-0.09	0.15				Uncarpeted
1.18	2.91	-0.99	-1.08	3.16	-0.19	-0.02				Uncarpeted
1.31	2.67	-0.50	-0.83	2.47	-0.26	-0.79				Uncarpeted
1.18	2.75	-0.68	-0.93	2.50	-0.22	-0.71				Uncarpeted
1.23	3.07	0.22	0.29	3.50	-0.08	0.43				Uncarpeted
1.03	3.06	-0.06	-0.01							Uncarpeted
1.34	3.11	-0.36	-0.25							Uncarpeted
1.14	3.01	-0.28	-0.27							Uncarpeted
1.08	2.62	-0.40	-0.78	2.47	0.78	0.25				Uncarpeted
0.91	2.75	-0.48	-0.73	2.43	-0.56	-1.13				Uncarpeted
1.01	2.84	-0.55	-0.71	2.76	-0.51	-0.75				Uncarpeted
1.03	2.66	-0.54	-0.88	2.50	-0.13	-0.63				Uncarpeted
1.18	1.98	0.11	-0.91	2.77	-0.66	-0.89				Uncarpeted
0.84				3.38	0.04	0.43				Uncarpeted
0.76	2.66	-0.98	-1.32	3.73	-1.70	-0.97				Uncarpeted
0.83				2.55	-0.33	-0.77				Uncarpeted
1.13	2.89	-0.14	-0.25							Uncarpeted

Table A4.1 (Continued).

Average Blood Pb Conc (µg/dl)	Average Floor (Log_{10}) Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Average Sill (Log_{10}) Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Average Carpet (Log_{10}) Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Floor Surfacing Type
0.98	2.45	0.02	-0.53							Uncarpeted
1.16	3.04	-0.18	-0.15							Uncarpeted
1.25	2.76	-0.35	-0.59	3.37	-0.85	-0.49				Uncarpeted
1.40	2.91	-0.07	-0.16	3.26	-0.65	-0.39				Uncarpeted
1.32	2.85	-0.17	-0.33	2.63	-0.66	-1.03				Uncarpeted
0.48	1.95	-1.01	-2.07	3.14	-0.28	-0.14				Uncarpeted
0.98	2.63	-0.08	-0.45	3.28	0.03	0.31				Uncarpeted
0.90	2.81	-0.13	-0.32	3.33	-0.71	-0.38				Uncarpeted
0.91	2.72	-0.54	-0.82	3.13	-0.67	-0.54				Uncarpeted
1.30	2.61	-0.63	-1.01	3.15	-0.61	-0.45				Uncarpeted
0.55	0.90	0.71	-1.39	2.81	-0.59	-0.78				Uncarpeted
0.83	3.53	-0.61	-0.09	3.13	-0.53	-0.40				Uncarpeted
0.52	2.53	-0.30	-0.77				2.48	1.31	0.79	Carpeted
0.70	3.96	0.24	1.20	2.86	-0.01	-0.15	2.71	1.60	1.31	Carpeted
1.03	2.82	-0.28	-0.47	3.36	-0.13	0.23	2.51	1.43	0.94	Carpeted
0.36	2.54	-0.60	-1.06	3.48	0.39	0.87	2.06	1.43	0.49	Carpeted
1.24	2.54	0.10	-0.36	2.92	0.37	0.29	2.61	1.16	0.78	Carpeted
1.03	3.03	0.16	0.19	2.94	0.31	0.25	2.43	1.49	0.92	Carpeted
0.72	3.38	-0.22	0.17	2.61	-0.31	-0.71	2.63	0.61	0.24	Carpeted
0.48	3.07	0.30	0.37	2.82	0.31	0.13	2.95	1.02	0.97	Carpeted
0.85	2.41	-0.52	-1.10	2.98	-0.37	-0.40	2.44	1.28	0.72	Carpeted
0.85	2.45	-0.33	-0.88	2.85	-0.36	-0.51	2.54	1.05	0.59	Carpeted
0.79	2.86	-0.41	-0.54	3.14	-0.88	-0.74	2.79	1.17	0.96	Carpeted
0.92	2.64	-0.35	-0.72	2.46	0.34	-0.20	2.46	1.33	0.79	Carpeted
0.85	2.38	-0.13	-0.76	2.68	-0.05	-0.37	2.33	1.92	1.25	Carpeted
0.88	3.03	-1.01	-0.98				2.88	1.20	1.08	Carpeted
1.11	3.02	-0.45	-0.43	2.68	-0.78	-1.10	3.26	0.89	1.15	Carpeted
0.97	3.31	-0.94	-0.63				3.32	1.05	1.37	Carpeted
0.87	3.21	-0.65	-0.45				3.17	0.89	1.06	Carpeted
0.92	2.88	0.03	-0.09	2.76	-0.09	-0.33	2.72	1.03	0.75	Carpeted
1.11	2.88	0.29	0.17	2.95	0.46	0.41	2.99	1.25	1.23	Carpeted
0.93	2.42	0.03	-0.55	3.01	0.27	0.28	2.29	0.85	0.14	Carpeted
1.03	2.89	-0.80	-0.91	2.89	-0.69	-0.81	3.19	0.35	0.54	Carpeted
0.99	2.89	-0.34	-0.45	2.76	-0.24	-0.47	2.80	0.58	0.38	Carpeted
0.82	2.89	-0.37	-0.47	2.80	-0.77	-0.97	3.24	0.61	0.85	Carpeted
1.25	3.20	-0.08	0.12	1.58	0.50	-0.92	3.09	1.25	1.33	Carpeted
1.28	3.62	-0.51	0.11	3.21	0.37	0.57	3.45	1.18	1.63	Carpeted
1.23	2.90	0.36	0.26	3.46	-0.06	0.39	2.91	1.59	1.50	Carpeted
0.87				2.13	0.68	-0.19	2.32	0.76	0.08	Carpeted
0.99				2.30	0.22	-0.47	2.97	0.25	0.22	Carpeted
0.67				2.83	-0.43	-0.60	2.21	1.44	0.65	Carpeted
0.95	2.91	-0.43	-0.52	2.56	-0.10	-0.53	3.22	1.27	1.49	Carpeted
1.12	2.80	-0.15	-0.36				2.81	0.97	0.78	Carpeted
0.85	2.80	-0.15	-0.36				2.81	0.97	0.78	Carpeted
0.81	3.20	-0.76	-0.55	2.70	-0.63	-0.93	3.23	-0.26	-0.03	Carpeted
0.49	2.96	-0.79	-0.83	2.95	-0.73	-0.78	2.61	-0.19	-0.58	Carpeted
1.14	2.69	-0.18	-0.49	3.55	0.50	1.06	2.63	1.42	1.05	Carpeted
1.07	2.41	-0.47	-1.06	2.74	0.55	0.29	2.50	1.60	1.10	Carpeted

Table A4.1 (Continued).

Average Blood Pb Conc (µg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Average Carpet (Log_{10})			Floor Surfacing Type
	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.05	2.63	-0.62	-0.99	3.51	0.45	0.96	2.50	1.60	1.10	Carpeted
1.45	2.27	0.49	-0.24	3.47	0.52	0.99	2.71	0.88	0.58	Carpeted
0.83	2.17	-0.27	-1.09	2.26	-0.28	-1.02	2.66	1.10	0.76	Carpeted
0.93	3.11	-0.59	-0.49				2.18	0.40	-0.42	Carpeted
0.81	2.77	0.12	-0.11				2.72	1.35	1.07	Carpeted
0.97	3.38	-1.23	-0.85	2.76	0.06	-0.18	2.34	1.15	0.49	Carpeted
0.83	2.40	-0.97	-1.57	2.32	0.00	-0.68	2.30	0.84	0.13	Carpeted
0.86	2.98	0.01	-0.01	2.71	-0.26	-0.55	2.89	1.30	1.18	Carpeted
0.81	2.61	0.04	-0.35	2.75	-0.78	-1.02	2.73	1.15	0.88	Carpeted
1.26	2.47	0.01	-0.52	2.86	-0.63	-0.77	2.95	0.40	0.35	Carpeted
1.09	2.64	-0.20	-0.56	3.14	0.32	0.45	2.62	1.89	1.52	Carpeted
1.13	2.47	-0.17	-0.70	3.10	0.23	0.33	2.42	1.67	1.09	Carpeted
1.14	3.94	0.41	1.35	3.63	-0.05	0.58	3.46	1.15	1.61	Carpeted
1.29				4.06	0.01	1.07	2.97	-0.22	-0.26	Carpeted
0.94				3.10	0.61	0.71	2.73	0.62	0.35	Carpeted
1.07	3.09	-0.62	-0.53				2.47	0.85	0.32	Carpeted
1.08	2.65	-0.22	-0.56	2.67	-0.22	-0.55	2.71	1.18	0.90	Carpeted
1.01	2.61	-0.36	-0.75				2.55	1.63	1.18	Carpeted
0.97							2.24	1.20	0.44	Carpeted
1.07	2.98	0.27	0.24	3.67	0.61	1.28	3.00	1.56	1.57	Carpeted
1.11	3.17	0.10	0.28	3.47	0.27	0.73	3.32	2.00	2.32	Carpeted
0.63	2.59	-1.17	-1.59	2.53	-0.11	-0.58	2.19	0.84	0.03	Carpeted
0.66	2.91	-0.57	-0.66	2.50	-0.34	-0.84	1.93	0.23	-0.84	Carpeted
1.44	2.48	0.22	-0.31	3.40	-0.45	-0.05	3.37	0.35	0.71	Carpeted
0.90	2.82	-0.94	-1.12	2.48	-0.30	-0.82	2.33	0.22	-0.45	Carpeted
0.94	2.30	-0.84	-1.54	2.72	-0.59	-0.87	2.07	0.00	-0.93	Carpeted
0.89	2.12	-0.53	-1.41	2.25	-0.47	-1.22	2.11	0.84	-0.05	Carpeted
0.86	2.50	-0.41	-0.90	2.61	-0.30	-0.69	2.50	1.00	0.49	Carpeted
0.93				2.42	-0.51	-1.09	2.25	0.43	-0.32	Carpeted
1.10	2.59	0.18	-0.23	2.82	0.09	-0.09	2.64	0.58	0.22	Carpeted
1.11				2.85	0.03	-0.12	2.64	0.58	0.22	Carpeted
0.93				3.54	-0.23	0.31	2.40	0.83	0.23	Carpeted
1.12	3.68	-0.20	0.48	3.99	0.22	1.20	3.65	0.96	1.60	Carpeted
0.81	2.80	-1.08	-1.28	2.92	-0.58	-0.66	2.95	0.26	0.20	Carpeted
0.81	3.19	-1.34	-1.15	3.83	-1.24	-0.41	2.77	0.63	0.40	Carpeted
1.26	2.92	-0.88	-0.96	2.91	-0.25	-0.34	3.36	-0.12	0.24	Carpeted
1.42	2.99	-0.82	-0.83	3.43	-0.34	0.09	3.24	-0.49	-0.24	Carpeted
1.63	2.38	-0.55	-1.17	3.37	-0.45	-0.08	2.56	-0.24	-0.68	Carpeted
1.12				2.93	0.46	0.39	3.10	0.18	0.28	Carpeted
0.89	2.34	-0.12	-0.78	2.71	0.16	-0.13	2.17	1.09	0.25	Carpeted
0.64	2.02	-0.09	-1.07	2.59	-1.28	-1.68	2.17	1.00	0.17	Carpeted
0.93	2.64	-0.77	-1.13	2.90	-0.27	-0.36	2.77	0.58	0.36	Carpeted
0.78	2.73	-0.85	-1.12	2.56	-0.61	-1.05	2.18	1.32	0.50	Carpeted
1.06	3.19	-0.84	-0.65	3.48	-0.29	0.19	3.06	0.95	1.01	Carpeted
1.02	2.61	-0.80	-1.20	3.05	-0.35	-0.31	3.12	0.96	1.08	Carpeted
1.13	2.61	-0.35	-0.74	2.87	-0.71	-0.84	2.45	0.66	0.11	Carpeted
1.09	2.31	-0.63	-1.32	2.64	-0.08	-0.44	2.23	0.92	0.15	Carpeted
1.10	2.74	-0.35	-0.61	2.91	-0.38	-0.47	3.09	0.91	1.00	Carpeted

Table A4.1 (Continued).

Average Blood Pb Conc (µg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Average Carpet (Log_{10})			Floor Surfacing Type
	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
0.77	2.95	-1.00	-1.05	2.97	-0.29	-0.32	2.32	0.46	-0.22	Carpeted
0.66	2.45	-0.77	-1.31	2.90	-0.33	-0.43	1.83	0.31	-0.86	Carpeted
1.18	3.31	-0.66	-0.35	2.75	0.19	-0.06	2.39	1.15	0.55	Carpeted
0.72	2.17	-0.20	-1.03	2.09	0.09	-0.82	2.17	1.06	0.23	Carpeted
1.08	2.74	0.33	0.06	3.23	0.24	0.47	2.69	0.87	0.56	Carpeted
0.83	2.20	-0.27	-1.07	3.38	-0.37	0.01	3.21	0.46	0.66	Carpeted
1.11	2.80	-0.12	-0.32	3.48	-0.30	0.18	2.20	0.19	-0.61	Carpeted
0.79	2.03	-0.22	-1.20	2.51	-0.13	-0.62	1.67	1.04	-0.29	Carpeted
0.63	2.26	-0.49	-1.23	2.40	-0.39	-0.98	1.74	0.54	-0.72	Carpeted
1.14	2.28	-0.82	-1.53				2.07	0.15	-0.78	Carpeted
0.88	2.43	-0.68	-1.25	2.44	-0.84	-1.40	2.29	-0.06	-0.76	Carpeted

Appendix 5. Blood Data for Floor-Surfacing Analysis

Table A5.1 Blood Lead Levels in the Carpeted and Uncarpeted Homes of Accident Group with Three Visits.

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
1	uncarpeted	1	0.34
1	uncarpeted	2	0.58
1	uncarpeted	3	0.43
2	uncarpeted	1	1.03
2	uncarpeted	2	0.82
2	uncarpeted	3	0.82
3	uncarpeted	1	1.37
3	uncarpeted	2	1.38
3	uncarpeted	3	1.25
4	uncarpeted	1	1.23
4	uncarpeted	2	0.99
4	uncarpeted	3	0.81
5	uncarpeted	1	0.73
5	uncarpeted	2	0.81
5	uncarpeted	3	0.49
6	uncarpeted	1	1.47
6	uncarpeted	2	1.42
6	uncarpeted	3	1.31
7	uncarpeted	1	1.23
7	uncarpeted	2	1.49
7	uncarpeted	3	1.40
8	uncarpeted	1	0.69
8	uncarpeted	2	0.78
8	uncarpeted	3	0.54
9	uncarpeted	1	1.03
9	uncarpeted	2	1.34
9	uncarpeted	3	1.14
10	uncarpeted	1	1.15
10	uncarpeted	2	1.30
10	uncarpeted	3	1.21
11	uncarpeted	1	0.85
11	uncarpeted	2	0.63
11	uncarpeted	3	0.82
12	uncarpeted	1	1.00
12	uncarpeted	2	0.94
12	uncarpeted	3	0.89
13	uncarpeted	1	1.32
13	uncarpeted	2	1.12

Table A5.1 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
13	uncarpeted	3	1.14
14	uncarpeted	1	0.81
14	uncarpeted	2	0.79
14	uncarpeted	3	0.63
15	uncarpeted	1	1.13
15	uncarpeted	2	0.98
15	uncarpeted	3	1.16
16	uncarpeted	1	1.36
16	uncarpeted	2	1.40
16	uncarpeted	3	1.49
17	uncarpeted	1	0.98
17	uncarpeted	2	0.90
17	uncarpeted	3	0.91
1	carpeted	1	0.04
1	carpeted	2	0.60
1	carpeted	3	0.53
2	carpeted	1	1.37
2	carpeted	2	1.33
2	carpeted	3	1.24
3	carpeted	1	0.65
3	carpeted	2	0.85
3	carpeted	3	0.83
4	carpeted	1	1.09
4	carpeted	2	1.19
4	carpeted	3	1.29
5	carpeted	1	0.74
5	carpeted	2	0.88
5	carpeted	3	0.88
6	carpeted	1	0.89
6	carpeted	2	1.11
6	carpeted	3	1.07
7	carpeted	1	1.34
7	carpeted	2	1.31
7	carpeted	3	1.09
8	carpeted	1	1.34
8	carpeted	2	1.19
8	carpeted	3	1.08
9	carpeted	1	1.12
9	carpeted	2	1.17

Table A5.1 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
9	carpeted	3	1.21
10	carpeted	1	0.89
10	carpeted	2	0.88
10	carpeted	3	1.26
11	carpeted	1	1.14
11	carpeted	2	0.93
11	carpeted	3	0.90
12	carpeted	1	0.85
12	carpeted	2	1.04
12	carpeted	3	0.92
13	carpeted	1	1.17
13	carpeted	2	1.01
13	carpeted	3	0.99
14	carpeted	1	0.75
14	carpeted	2	1.23
14	carpeted	3	1.19
15	carpeted	1	1.03
15	carpeted	2	1.29
15	carpeted	3	1.18
16	carpeted	1	0.93
16	carpeted	2	0.93
16	carpeted	3	0.88
17	carpeted	1	0.88
17	carpeted	2	1.01
17	carpeted	3	1.03
18	carpeted	1	1.10
18	carpeted	2	0.93
18	carpeted	3	0.84
19	carpeted	1	0.81
19	carpeted	2	0.81
19	carpeted	3	0.76
20	carpeted	1	1.26
20	carpeted	2	1.42
20	carpeted	3	1.63
21	carpeted	1	0.87
21	carpeted	2	0.83
21	carpeted	3	1.11

Table A5.1 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
22	carpeted	1	0.89
22	carpeted	2	0.64
22	carpeted	3	0.83
23	carpeted	1	0.93
23	carpeted	2	0.78
23	carpeted	3	0.68
24	carpeted	1	1.16
24	carpeted	2	1.02
24	carpeted	3	1.05
25	carpeted	1	1.16
25	carpeted	2	1.09
25	carpeted	3	1.10
26	carpeted	1	0.77
26	carpeted	2	0.66
26	carpeted	3	0.48

Table A5.2 Blood Lead Levels in the Carpeted and Uncarpeted Homes of Lead Group with Three Visits.

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
1	uncarpeted	1	0.72
1	uncarpeted	2	0.43
1	uncarpeted	3	0.51
2	uncarpeted	1	0.18
2	uncarpeted	2	0.58
2	uncarpeted	3	0.41
3	uncarpeted	1	1.16
3	uncarpeted	2	1.00
3	uncarpeted	3	1.07
4	uncarpeted	1	0.95
4	uncarpeted	2	1.09
4	uncarpeted	3	1.09
5	uncarpeted	1	1.04
5	uncarpeted	2	0.96
5	uncarpeted	3	0.76
6	uncarpeted	1	0.90
6	uncarpeted	2	1.16
6	uncarpeted	3	1.19
7	uncarpeted	1	1.09
7	uncarpeted	2	1.13
7	uncarpeted	3	1.06
8	uncarpeted	1	1.26
8	uncarpeted	2	1.09
8	uncarpeted	3	1.02
9	uncarpeted	1	1.21
9	uncarpeted	2	1.33
9	uncarpeted	3	1.13
10	uncarpeted	1	1.19
10	uncarpeted	2	1.27
10	uncarpeted	3	1.16
11	uncarpeted	1	1.18
11	uncarpeted	2	1.16
11	uncarpeted	3	1.05
12	uncarpeted	1	1.09
12	uncarpeted	2	0.90
12	uncarpeted	3	1.19
13	uncarpeted	1	1.10
13	uncarpeted	2	0.93

Table A5.2 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
13	uncarpeted	3	0.98
14	uncarpeted	1	1.25
14	uncarpeted	2	0.91
14	uncarpeted	3	0.89
15	uncarpeted	1	0.86
15	uncarpeted	2	0.76
15	uncarpeted	3	0.56
16	uncarpeted	1	0.88
16	uncarpeted	2	0.56
16	uncarpeted	3	0.61
17	uncarpeted	1	0.98
17	uncarpeted	2	0.86
17	uncarpeted	3	0.93
18	uncarpeted	1	1.27
18	uncarpeted	2	1.11
18	uncarpeted	3	0.65
19	uncarpeted	1	1.23
19	uncarpeted	2	1.06
19	uncarpeted	3	1.09
20	uncarpeted	1	1.01
20	uncarpeted	2	0.78
20	uncarpeted	3	0.66
21	uncarpeted	1	1.48
21	uncarpeted	2	0.97
21	uncarpeted	3	0.91
1	carpeted	1	1.00
1	carpeted	2	0.93
1	carpeted	3	0.83
2	carpeted	1	0.92
2	carpeted	2	1.36
2	carpeted	3	1.13
3	carpeted	1	1.20
3	carpeted	2	1.20
3	carpeted	3	0.95
4	carpeted	1	0.76
4	carpeted	2	1.03
4	carpeted	3	1.16
5	carpeted	1	0.54
5	carpeted	2	0.94

Table A5.2 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
5	carpeted	3	0.88
6	carpeted	1	0.82
6	carpeted	2	0.79
6	carpeted	3	0.71
7	carpeted	1	1.06
7	carpeted	2	1.08
7	carpeted	3	1.14
8	carpeted	1	1.42
8	carpeted	2	1.27
8	carpeted	3	1.30
9	carpeted	1	1.29
9	carpeted	2	1.21
9	carpeted	3	1.52
10	carpeted	1	0.77
10	carpeted	2	0.85
10	carpeted	3	0.58
11	carpeted	1	1.21
11	carpeted	2	1.33
11	carpeted	3	1.03
12	carpeted	1	1.12
12	carpeted	2	0.85
12	carpeted	3	1.10
13	carpeted	1	0.73
13	carpeted	2	0.88
13	carpeted	3	0.64
14	carpeted	1	1.06
14	carpeted	2	1.15
14	carpeted	3	1.02
15	carpeted	1	0.98
15	carpeted	2	1.06
15	carpeted	3	0.96
16	carpeted	1	1.37
16	carpeted	2	1.32
16	carpeted	3	1.31
17	carpeted	1	1.13
17	carpeted	2	1.06
17	carpeted	3	1.15
18	carpeted	1	0.89
18	carpeted	2	0.76

Table A5.2 (Continued).

Subject	Floor Surfacing	Visit	Blood (Log_{10}) Concentration (μg/dl)
18	carpeted	3	0.59
19	carpeted	1	1.18
19	carpeted	2	0.83
19	carpeted	3	0.76
20	carpeted	1	1.15
20	carpeted	2	1.04
20	carpeted	3	0.94
21	carpeted	1	1.11
21	carpeted	2	1.13
21	carpeted	3	0.87

Appendix 6. CLEARS and TLC Blood and Dust Data for Stepwise Regression Analysis

Table A6.1 CLEARS and TLC Blood and Dust Lead Levels for Stepwise Regression Analysis.

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.40	1.12	-0.35	-2.23	3.00	-2.22	-2.22	TLC
1.62	1.64	-0.17	-1.54	2.38	-0.96	-1.58	TLC
1.36	1.59	0.14	-1.27	1.94	0.62	-0.44	TLC
1.41	1.66	-0.37	-1.71	1.59	-0.86	-2.27	TLC
1.49	2.10	-0.18	-1.08	2.99	0.36	0.35	TLC
1.04	1.98	-1.06	-2.08	1.17	0.44	-1.39	TLC
1.45	3.10	-0.07	0.03	4.19	-0.42	0.78	TLC
1.40	3.10	-0.07	0.03	4.19	-0.42	0.78	TLC
1.15	2.76	-0.06	-0.31	3.47	-0.10	0.37	TLC
1.40	3.45	-0.33	0.12	4.01	0.13	1.14	TLC
1.36	2.89	-0.61	-0.72				TLC
1.43	3.37	-0.55	-0.18	4.42	-0.08	1.33	TLC
1.38	3.37	-0.55	-0.18	4.42	-0.08	1.33	TLC
1.46	2.54	-0.21	-0.67	2.76	-1.19	-1.42	TLC
1.41	2.96	0.34	0.30	4.65	0.17	1.82	TLC
1.41	2.79	-0.01	-0.22	4.00	-0.46	0.55	TLC
1.34	2.88	-0.76	-0.88	3.24	-0.15	0.09	TLC
1.49	3.24	-0.85	-0.62	2.84	-0.59	-0.75	TLC
1.46	4.15	-1.42	-0.27	3.63	-0.28	0.35	TLC
1.30	3.40	-0.31	0.08	5.18	-0.41	1.77	TLC
1.64				3.37	-1.15	-0.78	TLC
1.36	3.25	0.61	0.86	2.99	0.11	0.10	TLC
1.49	3.36	-0.59	-0.24	2.45	0.87	0.32	TLC
1.40	2.86	-0.24	-0.39	3.05	-0.29	-0.24	TLC
1.36	2.86	-0.24	-0.39	3.05	-0.29	-0.24	TLC
1.36	2.44	-0.86	-1.41	2.57	0.19	-0.24	TLC
1.30	2.50	-0.43	-0.93	3.40	0.23	0.63	TLC
1.30	2.50	-0.43	-0.93	3.40	0.23	0.63	TLC
1.36	3.26	-0.56	-0.30	4.40	0.03	1.42	TLC
1.40	2.86	-0.66	-0.80	2.69	-0.22	-0.53	TLC
1.40				2.59	-0.07	-0.48	TLC
1.48	2.37	-0.20	-0.83	3.00	-0.83	-0.84	TLC
1.45	3.33	-0.22	0.11	4.27	-0.02	1.26	TLC
1.30	2.32	0.23	-0.45	2.12	0.26	-0.62	TLC

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.59	2.57	-0.50	-0.93	3.27	0.22	0.49	TLC
1.30	3.22	-0.69	-0.48	4.76	-0.04	1.72	TLC
1.63	4.28	0.00	1.28	5.41	0.40	2.82	TLC
1.40	2.96	0.03	-0.01	3.67	0.82	1.49	TLC
1.43	3.00	-0.45	-0.45	4.21	0.28	1.49	TLC
1.43	3.68	0.04	0.72	4.41	0.69	2.10	TLC
1.40	3.36	-0.65	-0.29				TLC
1.28	3.44	0.15	0.59	3.39	0.46	0.85	TLC
1.32	3.44	0.15	0.59	3.39	0.46	0.85	TLC
1.34	3.28	0.06	0.34	4.66	0.58	2.24	TLC
1.45	3.40	-0.61	-0.21	3.87	-0.83	0.05	TLC
1.34	1.17	-0.43	-2.26	2.09	-0.18	-1.08	TLC
1.60	3.47	0.82	1.29	4.15	0.91	2.06	TLC
1.67	2.79	-0.34	-0.54	4.42	0.29	1.71	TLC
1.58	2.79	-0.34	-0.54	4.42	0.29	1.71	TLC
1.54	4.49	0.44	1.94	3.75	0.35	1.11	TLC
1.38	4.49	0.44	1.94	3.75	0.35	1.11	TLC
1.40	3.14	-0.19	-0.04	3.93	0.57	1.51	TLC
1.49	2.85	-0.49	-0.65	4.32	0.36	1.68	TLC
1.49	3.03	-0.40	-0.37	2.63	0.45	0.08	TLC
1.48	1.99	0.04	-0.96	2.64	0.52	0.16	TLC
1.36	1.18	0.51	-1.31	2.40	0.01	-0.59	TLC
1.56	2.19	0.16	-0.65	2.97	-0.20	-0.23	TLC
1.34	2.80	-0.42	-0.62	4.09	-0.05	1.03	TLC
1.52	2.73	-0.33	-0.60	2.74	0.04	-0.23	TLC
1.52	3.37	-0.21	0.16	4.19	-0.02	1.17	TLC
1.36	3.34	0.03	0.37	2.93	0.42	0.35	TLC
1.32	2.32	0.26	-0.42	3.12	-0.16	-0.03	TLC
1.38	3.32	-0.44	-0.12	3.98	-0.31	0.67	TLC
1.34	2.80	0.65	0.45	2.72	-0.18	-0.46	TLC
1.36	2.91	-0.52	-0.61	3.23	-0.11	0.13	TLC
1.36	3.52	-0.63	-0.12	5.49	0.13	2.62	TLC
1.50	3.17	0.04	0.21	4.97	0.17	2.15	TLC
1.38	2.43	0.22	-0.35	2.43	0.18	-0.39	TLC
1.43	2.87	0.38	0.26	4.84	-0.97	0.87	TLC
1.50	3.21	0.12	0.34	4.32	0.88	2.20	TLC
1.45	3.33	0.16	0.49	3.81	-0.13	0.68	TLC

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.38	3.03	0.05	0.08	2.83	-0.01	-0.17	TLC
1.34	2.80	-0.63	-0.83	2.87	-0.29	-0.42	TLC
1.54	3.90	-0.10	0.80	5.22	0.52	2.74	TLC
1.32	3.66	-0.46	0.20	3.60	-0.29	0.31	TLC
1.43	2.71	-0.44	-0.73	3.62	-0.19	0.43	TLC
1.45	2.78	-0.06	-0.28	2.53	0.77	0.30	TLC
1.53	2.69	-0.51	-0.82	4.28	-0.59	0.69	TLC
1.45	3.63	-0.26	0.37	3.74	0.11	0.85	TLC
1.49	2.91	-0.25	-0.35	3.68	0.07	0.75	TLC
1.45	3.12	-0.69	-0.58	4.24	-0.03	1.21	TLC
1.38	3.13	-0.59	-0.45	3.59	0.61	1.19	TLC
1.62	2.43	-0.25	-0.82	4.44	-0.25	1.19	TLC
1.34	2.68	-0.91	-1.22	3.52	-0.49	0.03	TLC
1.60	3.97	-0.56	0.41	4.48	-0.22	1.26	TLC
1.30	2.55	0.02	-0.43	4.06	-0.74	0.32	TLC
1.36	3.08	-0.10	-0.02				TLC
1.57	2.99	0.42	0.41	2.86	0.26	0.12	TLC
1.41	3.43	0.09	0.51	3.72	-0.02	0.69	TLC
1.65	3.99	0.16	1.15	3.32	-0.17	0.15	TLC
1.58	3.99	0.16	1.15	3.32	-0.17	0.15	TLC
1.38	3.18	-0.83	-0.65	3.94	-0.33	0.62	TLC
1.58	2.86	0.11	-0.03	4.79	0.33	2.12	TLC
1.40	3.04	-0.35	-0.31	4.45	0.12	1.57	TLC
1.57	3.23	0.32	0.55	2.88	-0.05	-0.17	TLC
1.38	3.51	-0.65	-0.15	3.78	-0.12	0.66	TLC
1.45	2.74	-0.54	-0.80	3.46	0.01	0.47	TLC
1.36	3.23	-0.26	-0.03	4.58	0.19	1.77	TLC
1.40	3.28	0.06	0.34	3.26	0.43	0.69	TLC
1.50	3.28	0.06	0.34	3.26	0.43	0.69	TLC
1.50	3.00	-0.24	-0.25	3.62	0.18	0.80	TLC
1.48	2.85	-0.84	-0.99	2.69	0.14	-0.17	TLC
1.50	3.24	-0.44	-0.19	4.40	-0.16	1.24	TLC
1.32	2.72	-0.97	-1.24	3.15	0.38	0.54	TLC
1.56	3.41	-0.31	0.10	3.52	0.24	0.77	TLC
1.41	2.78	-0.38	-0.59	3.87	0.14	1.01	TLC
1.36	3.12	-0.26	-0.14	2.92	-0.04	-0.12	TLC
1.38	2.95	-0.10	-0.15	4.24	0.41	1.66	TLC

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.49	2.87	-0.66	-0.79	2.60	-0.20	-0.60	TLC
1.41	3.35	0.45	0.80				TLC
1.50	2.71	-0.50	-0.79				TLC
1.46	3.13	-0.18	-0.05	5.21	-0.26	1.96	TLC
1.46	3.44	0.09	0.53	3.44	0.25	0.69	TLC
1.52	3.16	-0.29	-0.13	3.63	0.38	1.01	TLC
1.50	2.39	-0.26	-0.87	3.18	0.34	0.52	TLC
1.34	3.00	-0.61	-0.61	2.91	-0.46	-0.55	TLC
1.54	2.98	-0.13	-0.14	3.14	0.72	0.87	TLC
1.49	2.70	0.04	-0.26				TLC
1.43	3.61	0.06	0.67	3.64	0.42	1.05	TLC
1.58	3.45	0.01	0.46				TLC
1.41	3.04	-0.07	-0.03	3.93	-0.04	0.90	TLC
1.32	3.23	0.38	0.61	3.39	-0.14	0.26	TLC
1.38	2.44	-0.20	-0.75	2.82	-0.36	-0.54	TLC
1.40	2.87	-0.03	-0.16	2.78	0.34	0.12	TLC
1.46	3.08	-0.37	-0.29	3.49	-0.08	0.42	TLC
1.40	2.74	-0.50	-0.77	3.65	0.19	0.84	TLC
1.32	2.88	0.41	0.29	3.42	0.04	0.47	TLC
1.38	2.70	-0.23	-0.53	3.27	0.15	0.43	TLC
1.32	2.70	-0.23	-0.53	3.27	0.15	0.43	TLC
1.38	2.80	-0.03	-0.23	4.63	0.04	1.67	TLC
1.34	3.12	-0.97	-0.85	4.29	0.53	1.83	TLC
1.52	3.09	-1.12	-1.03	2.33	0.23	-0.45	TLC
1.48	2.80	-0.68	-0.88	4.61	-0.54	1.06	TLC
1.38	2.81	-0.44	-0.63	3.83	-0.28	0.55	TLC
1.53	2.56	0.06	-0.38	3.33	0.64	0.97	TLC
1.32	2.78	-0.19	-0.41	2.87	0.15	0.02	TLC
1.30	3.34	-0.10	0.23	4.22	0.16	1.39	TLC
1.50	3.76	0.04	0.80	2.52	0.33	-0.15	TLC
1.50	3.50	0.11	0.61				TLC
1.53	3.15	-0.50	-0.35	4.10	0.38	1.48	TLC
1.54	3.50	-0.67	-0.17	5.33	0.15	2.48	TLC
1.30	3.18	0.48	0.66	4.35	0.09	1.43	TLC
1.59	2.63	0.03	-0.35	2.56	0.18	-0.25	TLC
1.38	2.11	-0.12	-1.01	2.10	0.13	-0.77	TLC
1.41	2.76	-0.05	-0.29	1.70	0.68	-0.63	TLC

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.30	2.92	0.09	0.01	3.62	0.57	1.20	TLC
1.32	2.11	0.38	-0.51	2.97	0.23	0.20	TLC
1.32	2.88	-0.09	-0.21	4.45	0.29	1.75	TLC
1.34	2.03	0.23	-0.74	3.12	-0.16	-0.03	TLC
1.41	2.47	-0.92	-1.45	2.82	-0.48	-0.66	TLC
1.34	2.31	-0.63	-1.32	1.98	0.22	-0.81	TLC
1.34	2.71	-1.11	-1.40	4.10	0.04	1.15	TLC
1.36	2.75	0.06	-0.18	3.67	-0.27	0.40	TLC
1.46	2.97	0.13	0.10				TLC
1.34	2.40	-0.28	-0.89	3.39	0.47	0.86	TLC
1.38	2.03	-0.51	-1.48	2.31	-0.42	-1.11	TLC
1.40	2.50	0.05	-0.45	3.91	0.23	1.13	TLC
1.46	2.62	-0.03	-0.40	3.13	0.86	0.99	TLC
1.56	3.12	-0.11	0.01	3.82	0.05	0.87	TLC
1.48	2.73	-0.48	-0.75	4.14	-0.53	0.62	TLC
1.38	3.28	-0.15	0.13	4.98	0.66	2.64	TLC
1.45	3.25	0.21	0.46	3.15	0.23	0.38	TLC
1.38	3.51	-0.63	-0.12	3.14	-0.09	0.05	TLC
1.43	3.19	0.32	0.51	4.04	0.35	1.38	TLC
1.40	3.28	-0.04	0.24				TLC
1.41	2.65	-0.77	-1.12	1.59	0.34	-1.08	TLC
1.58	2.48	-0.41	-0.94	3.10	0.00	0.10	TLC
1.49	3.19	-0.61	-0.42				TLC
1.54	2.11	-0.01	-0.89	3.21	0.34	0.55	TLC
1.45	4.37	-0.20	1.17	3.68	-0.79	-0.10	TLC
1.36	1.89	-0.41	-1.52	2.30	0.56	-0.15	TLC
1.40	2.74	-0.47	-0.72	2.36	0.10	-0.54	TLC
1.38	2.62	-0.86	-1.24	3.63	-0.30	0.33	TLC
1.36	3.86	0.31	1.17	4.14	0.04	1.18	TLC
1.36	3.16	-0.08	0.08	4.14	0.11	1.24	TLC
1.50	3.25	-0.36	-0.12	3.24	0.16	0.40	TLC
1.38	2.99	-0.43	-0.44	3.63	0.34	0.96	TLC
1.48	3.10	-0.43	-0.33	4.34	0.10	1.44	TLC
1.36	3.10	-0.43	-0.33	4.34	0.10	1.44	TLC
1.50	3.52	0.36	0.88	3.31	0.12	0.43	TLC
1.36	2.54	-0.64	-1.10	3.53	-0.13	0.40	TLC
1.32	2.66	-0.26	-0.60	2.67	-0.33	-0.66	TLC

Table A6.1 (Continued).

Average Blood Pb Conc (µg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (µg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.36	2.88	-0.03	-0.14	3.62	0.65	1.27	TLC
1.50	2.80	-0.54	-0.74	3.30	0.05	0.35	TLC
1.58	2.80	0.07	-0.13	3.32	0.52	0.84	TLC
1.66	2.80	0.07	-0.13	3.32	0.52	0.84	TLC
1.32	2.77	-0.16	-0.40	3.55	0.36	0.91	TLC
1.59	3.06	-0.27	-0.21	4.20	-0.35	0.85	TLC
1.43	3.12	0.19	0.31	3.84	0.35	1.18	TLC
1.40	2.16	1.18	0.34	3.13	-0.33	-0.20	TLC
1.32	2.53	-0.31	-0.78	2.52	0.52	0.04	TLC
1.46	2.36	0.06	-0.58	2.17	0.10	-0.73	TLC
1.50	3.53	0.12	0.64	3.36	-0.20	0.16	TLC
1.46	2.73	-0.33	-0.60	2.66	-0.74	-1.07	TLC
1.50	3.04	0.09	0.12	3.65	0.85	1.50	TLC
1.48	3.04	0.09	0.12	3.65	0.85	1.50	TLC
1.34	3.29	-0.62	-0.33	4.30	-0.40	0.90	TLC
1.48	2.67	-0.74	-1.06				TLC
1.34	2.61	0.21	-0.17	3.58	-0.10	0.48	TLC
1.34	3.05	-0.58	-0.53	3.10	-0.42	-0.32	TLC
1.53	2.72	-1.87	-2.15	3.44	-0.28	0.15	TLC
1.45				2.85	-0.72	-0.87	TLC
1.52	2.48	-0.39	-0.91	3.11	-0.35	-0.25	TLC
1.60	3.12	-0.47	-0.34	3.14	0.14	0.28	TLC
1.43	2.31	-0.40	-1.09	2.23	-0.37	-1.15	TLC
1.41	2.50	-0.31	-0.81	3.63	-0.21	0.42	TLC
1.43	3.06	0.12	0.18	3.37	0.09	0.46	TLC
0.48	2.58	-0.75	-1.16				CLEARS
0.43	2.58	-0.75	-1.16	2.90	0.23	0.12	CLEARS
0.93	2.54	-0.60	-1.06	3.47	0.34	0.80	CLEARS
0.65				2.79	-0.92	-1.13	CLEARS
0.75	3.02	-1.49	-1.47	3.18	-0.12	0.07	CLEARS
0.86	2.79	-0.50	-0.71	2.72	0.26	-0.02	CLEARS
1.30	2.63	0.23	-0.15	2.44	0.42	-0.14	CLEARS
1.19	2.63	0.23	-0.15	2.44	0.42	-0.14	CLEARS
1.12	2.55	0.22	-0.23	2.23	-0.30	-1.07	CLEARS
1.29	2.55	0.22	-0.23	2.23	-0.30	-1.07	CLEARS
0.98				2.67	-0.05	-0.37	CLEARS
0.95				2.67	-0.05	-0.37	CLEARS

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
0.81	2.89	-0.36	-0.47				CLEARS
1.38	2.84	-0.48	-0.63	1.75	0.01	-1.24	CLEARS
1.09	2.44	-1.06	-1.62	2.29	-0.10	-0.81	CLEARS
0.64	2.44	-1.06	-1.62	2.29	-0.10	-0.81	CLEARS
0.54	2.44	-1.06	-1.62	2.29	-0.10	-0.81	CLEARS
0.57	2.44	-1.06	-1.62	2.29	-0.10	-0.81	CLEARS
1.47	3.73	0.09	0.81	3.23	0.51	0.74	CLEARS
1.29	3.73	0.09	0.81	3.23	0.51	0.74	CLEARS
1.48	3.73	0.09	0.81	3.23	0.51	0.74	CLEARS
1.27	3.73	0.09	0.81	3.23	0.51	0.74	CLEARS
1.42	3.16	-0.05	0.10	3.17	0.51	0.68	CLEARS
1.26	3.16	-0.05	0.10	3.17	0.51	0.68	CLEARS
1.31	3.06	-0.16	-0.10	3.04	-0.43	-0.39	CLEARS
1.47	3.06	-0.16	-0.10	3.04	-0.43	-0.39	CLEARS
1.23	3.06	-0.16	-0.10	3.04	-0.43	-0.39	CLEARS
1.49	3.83	-0.87	-0.03	4.69	-0.20	1.50	CLEARS
1.40	3.26	-0.76	-0.51	3.11	0.37	0.49	CLEARS
1.21				3.47	0.53	0.99	CLEARS
1.09	2.76	-0.51	-0.75	3.22	0.51	0.73	CLEARS
0.79	2.76	-0.51	-0.75	3.22	0.51	0.73	CLEARS
0.77	2.76	-0.51	-0.75	3.22	0.51	0.73	CLEARS
1.14	2.76	-0.51	-0.75	3.22	0.51	0.73	CLEARS
1.21	2.66	-0.83	-1.17				CLEARS
0.90	2.66	-0.83	-1.17				CLEARS
0.84	2.85	-0.61	-0.76	2.93	0.09	0.02	CLEARS
0.99	2.85	-0.61	-0.76	2.93	0.09	0.02	CLEARS
0.78	2.85	-0.61	-0.76	2.93	0.09	0.02	CLEARS
1.02	3.20	-0.76	-0.56	2.48	-0.08	-0.61	CLEARS
1.04	3.20	-0.76	-0.56	2.48	-0.08	-0.61	CLEARS
0.92	2.87	-0.76	-0.89	2.53	0.09	-0.38	CLEARS
0.86	2.61	-0.33	-0.72	2.64	-0.09	-0.46	CLEARS
0.90	2.83	-0.13	-0.30	2.78	-0.26	-0.47	CLEARS
1.14	2.67	-0.07	-0.40	3.20	0.36	0.56	CLEARS
1.17	2.51	-0.50	-0.99	2.20	0.10	-0.70	CLEARS
1.01	3.23	-0.61	-0.39	2.70	-0.15	-0.45	CLEARS
0.99	2.86	-0.71	-0.86	3.13	-0.26	-0.12	CLEARS
0.76	2.07	-0.39	-1.32	2.03	-0.66	-1.63	CLEARS

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.35				3.66	-0.14	0.52	CLEARS
1.19				3.66	-0.14	0.52	CLEARS
1.03	2.98	-0.73	-0.74	3.70	-0.42	0.28	CLEARS
1.29	2.91	-0.99	-1.08	3.24	-0.09	0.15	CLEARS
1.18	2.91	-0.99	-1.08	3.16	-0.19	-0.03	CLEARS
1.31	2.67	-0.50	-0.83	2.47	-0.26	-0.79	CLEARS
1.31	2.75	-0.68	-0.93	2.51	-0.22	-0.71	CLEARS
1.06	2.75	-0.68	-0.93	2.51	-0.22	-0.71	CLEARS
1.23	3.07	0.22	0.30	3.50	-0.08	0.43	CLEARS
1.03	3.06	-0.07	-0.01				CLEARS
1.34	3.11	-0.36	-0.26				CLEARS
1.14	3.01	-0.28	-0.27				CLEARS
1.01	2.62	-0.40	-0.79	2.48	0.78	0.26	CLEARS
1.16	2.62	-0.40	-0.79	2.48	0.78	0.26	CLEARS
0.89	2.75	-0.48	-0.73	2.43	-0.56	-1.13	CLEARS
0.95	2.75	-0.48	-0.73	2.43	-0.56	-1.13	CLEARS
0.87	2.75	-0.48	-0.73	2.43	-0.56	-1.13	CLEARS
1.01	2.84	-0.55	-0.71	2.76	-0.51	-0.75	CLEARS
1.03	2.66	-0.54	-0.88	2.50	-0.13	-0.63	CLEARS
1.32	1.98	0.11	-0.91	2.77	-0.66	-0.89	CLEARS
0.96	1.98	0.11	-0.91	2.77	-0.66	-0.89	CLEARS
1.51	1.98	0.11	-0.91	2.77	-0.66	-0.89	CLEARS
0.86	1.98	0.11	-0.91	2.77	-0.66	-0.89	CLEARS
1.26	1.98	0.11	-0.91	2.77	-0.66	-0.89	CLEARS
0.84				3.38	0.04	0.43	CLEARS
0.76	2.66	-0.98	-1.32	3.73	-1.70	-0.97	CLEARS
0.87				2.93	0.46	0.39	CLEARS
0.67				2.55	-0.33	-0.77	CLEARS
1.00				2.55	-0.33	-0.77	CLEARS
0.81				2.55	-0.33	-0.77	CLEARS
1.13	2.89	-0.13	-0.25				CLEARS
0.98	2.45	0.02	-0.53				CLEARS
1.16	3.04	-0.18	-0.15				CLEARS
1.36	2.76	-0.35	-0.59	3.37	-0.86	-0.49	CLEARS
1.14	2.76	-0.35	-0.59	3.37	-0.86	-0.49	CLEARS
1.40	2.90	-0.07	-0.17	3.26	-0.66	-0.39	CLEARS
1.49	2.84	-0.17	-0.33	2.63	-0.66	-1.03	CLEARS

Table A6.1 (Continued).

Average Blood Pb Conc (μg/dl)	Average Floor (Log_{10})			Average Sill (Log_{10})			Intervention Project
	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	Pb Conc (μg/g)	Dust Loading (g/m^2)	Pb Loading (mg/m^2)	
1.15	2.84	-0.17	-0.33	2.63	-0.66	-1.03	CLEARS
0.48	1.95	-1.01	-2.07	3.14	-0.28	-0.14	CLEARS
0.98	2.63	-0.07	-0.45	3.27	0.03	0.31	CLEARS
0.90	2.81	-0.13	-0.32	3.33	-0.71	-0.38	CLEARS
0.91	2.72	-0.54	-0.82	3.13	-0.67	-0.54	CLEARS
1.30	2.61	-0.63	-1.02	3.15	-0.60	-0.46	CLEARS
0.73	0.90	0.71	-1.39	2.81	-0.59	-0.78	CLEARS
0.46	0.90	0.71	-1.39	2.81	-0.59	-0.78	CLEARS
0.46	0.90	0.71	-1.39	2.81	-0.59	-0.78	CLEARS
0.83	3.53	-0.62	-0.09	3.14	-0.53	-0.40	CLEARS

Appendix 7. Detection Limit of Analytical Instrument

Detection limit depends on the ratio of the magnitude of the analytical signal to the size of the statistical fluctuations in the blank signal. The minimum distinguishable analytical signal can be calculated from the following equation:

$$S_m = \bar{S}_{bl} + k\sigma_{bl}$$

S_m : minimum distinguishable analytical signal.

$\bar{S}_{bl}$: mean of blank signals.

σ_{bl} : standard deviation of blank signals.

k : a multiple of 3.

After S_m is calculated, the detection limit (C_m) can be derived by converting S_m to C_m using the following equation:

$$C_m = \frac{S_m - \bar{S}_{bl}}{m}$$

m is the slope of the calibration curve between concentration (C) and signal (S).

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1998	Lioy PJ, Yiin LM, Adgate J, Weisel C, Rhoads GG. The effectiveness of a home cleaning intervention strategy in reducing potential dust and lead exposure. Journal of Exposure Analysis & Environmental Epidemiology, 8(1):17-35 (1998).
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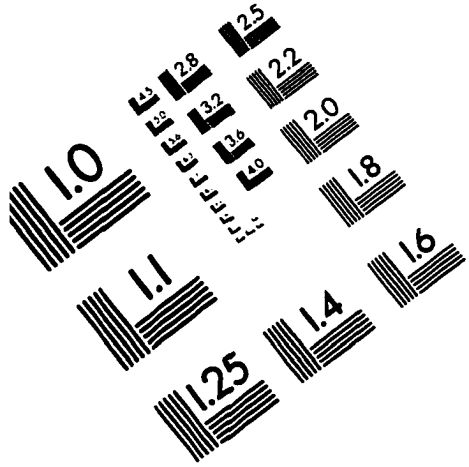
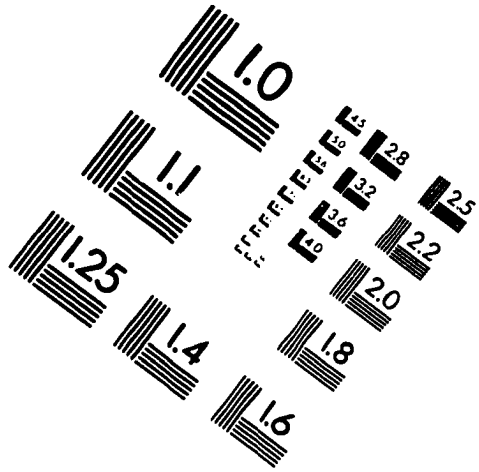
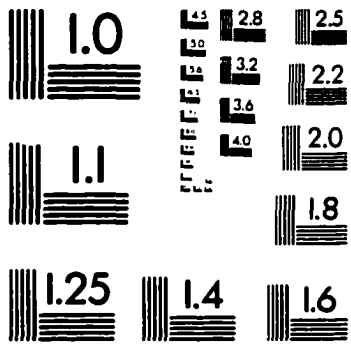
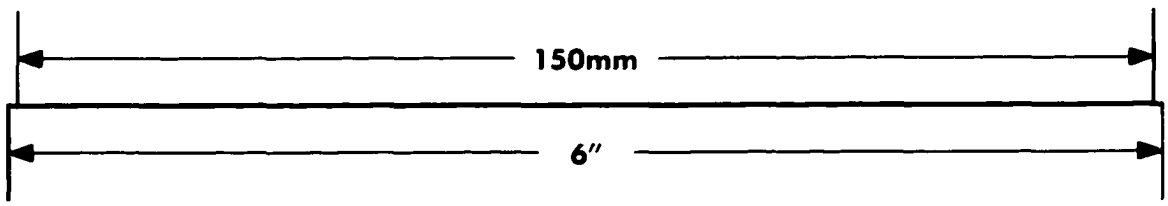
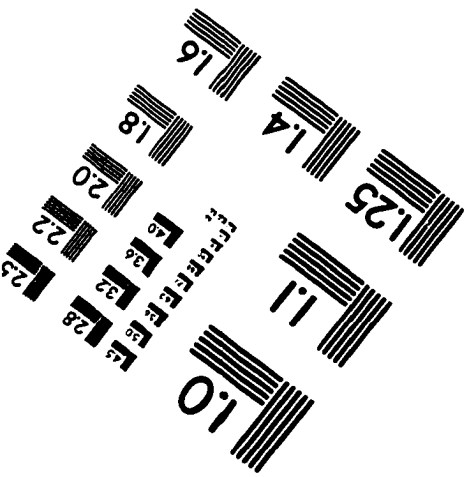
IMAGE EVALUATION TEST TARGET (QA-3)

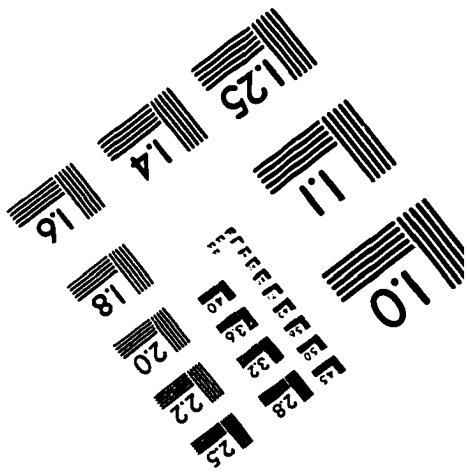












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