

Table 6. Selected methodologic details from cohort studies

Draft Final for ACCLPP Review

Quality Assurance Comments

Study Population	Quality Assurance Comments	
	Blood-lead Measurement	Cognitive Function Measurement
Boston (6, 7, 34)	Samples were measured by capillary and venous and were analyzed by ASV and GFAAS. Blood specimens for 6-, 12-, 18, and 24-month specimens were collected in capillary tubes by trained technicians. Blood samples were assayed in duplicate or triplicate. The analytical system was calibrated with aqueous standards of known lead concentrations. Each batch of samples was accompanied by a blood sample of known lead concentrations to quantify intralaboratory reliability. Several standardized blood samples with lead concentrations also were included after they became available in 1982 from CDC. (Rabinowitz, et al., 1985) 57-month venous blood samples were obtained. Lead was measured in duplicate by GFAAS. An aliquot of a standardized blood sample provided by the National Bureau of Standards was included in each batch of samples. (Bellinger, et al., 1991)	MDI was administered at 6-month intervals beginning at 6 months of age, by examiners blind to the infants' lead levels. (Bellinger, et al., 1985) For WISC-R, most children were tested in a single session, 2 were seen in a second session to complete testing, and 7 were tested in their homes by parental request. Psychologists were blind to all aspects of child's developmental and lead exposure histories.
Cincinnati (13)	Samples were measured by venipuncture, heel stick, and finger stick for infants and were analyzed by ASV. Blood samples were obtained using either venipuncture or heel stick. Approximately 72% of all samples are venipuncture. For heel stick, two capillary tubes were filled for duplicate PbB determination. If venipuncture was possible, pediatric vacutainer tubes were filled, one for PbB determination and a second for serum iron and total iron binding capacity (TIBC) analyses. The sample was aliquoted and duplicate analyses performed according to a predetermined protocol using ASV. The laboratory participates in both the CDC and PA State Blood Lead and Protoporphyrin Programs. A series of bench-top QC samples and blind QC samples were analyzed with each run. (Bornschein et al., 1985)	For WISC-R, one experienced psychometrician performed all the assessments. Children were tested at a pediatric clinic. The examiner was blind to the exposure levels of the child. For MDI, all assessments took place in a prenatal and child welfare clinic. Psychometric tests were administered at an inner-city health clinic by the study leader or trained assistant with whom inter-tester reliability had been previously established. Testers were blind to children's blood-lead levels.
Cleveland (14, 15, 16)	Samples were measured by venous and were analyzed by GFAAS. Blood samples were collected in heparinized plastic syringes which had been determined to be free of trace metals. The concentration of lead in whole blood samples was determined by GFAAS. All samples were run in duplicate. The within-run (same day) reproducibility was evaluated for a sample of adult whole blood. The obtained values were 55.2 ug/dl, 1.34, and 2.4%, respectively, for the mean, SD, and coefficient of variation. Regular assessment of accuracy and precision using CDC samples of bovine blood were conducted and found to be within the certified range. Two inter-laboratory reviews were conducted for further determination of accuracy. Blood-lead levels were not adjusted for hematocrit. (Ernhart, et al., 1985)	WPPSI, MDI, and Stanford Binet IQ tests were conducted by well-trained examiners blind to all risk and background information. Home testing was used to control attrition, to minimize bias in attrition, and to facilitate administration of the HOME Inventory. Inter-observer agreement was checked through observation and duplicate scoring by a supervisor for approximately one out of every 26 examinations. Agreement was maintained at r=.99. Answer sheets were checked for possible irregularities by the supervisor within a few days of each administration.
Costa Rica (41)	Samples were measured by venous and were analyzed by GFAAS. Venipuncture samples were taken and red blood cells were promptly separated and frozen for future analysis in the U.S. The frozen red cells were analyzed using GFAAS in a laboratory that participates in CDC's Maternal and Child Health Resources Development Proficiency Testing Program for Blood Lead. Quality control was monitored through certified controls obtained from the National Bureau of Standards. Red cell lead values were converted to whole blood-lead levels using the formula of Rosen et al.(1974).	Spanish versions of Bayley MDI and WPPSI were used in the assessment. A single tester, trained by one of the primary investigators and the most senior research psychologist in the country, administered the assessments. The tester was blind to the children's iron status and never knew the blood-lead levels (these were performed in the U.S.). (Lozoff, personal communication)
Kosovo (37, 38)	Samples were measured by venous and were analyzed by GFAAS. All blood specimens were refrigerated on site and transported on wet ice to Columbia University where all assays were performed. The laboratory participates in CDC's PBB QC program and is certified by OSHA. Over the study period, interclass correlation with QC values was computed, with correlation coefficients of .95 for PbB.	Three Yugoslavian psychologists scored the WISC-R and the McCarthy GCI independently. All interviews and assessment instruments were translated and administered in the two dominant languages of the region, Serbo-Croatian and Albanian. Training and reliability visits occurred. The average interclass correlation for 96 tests over study period was calculated.
Mexico City (31)	Samples were measured by venous and were analyzed by ASV. Samples were analyzed at Environmental Sciences Associates (ESA) Laboratories, Inc., which is a CDC reference lab for the Blood Lead Proficiency Testing Program and also participates in the New York State Department of Control Program. All samples were analyzed using ASV. Samples with mean duplicate values < 5 ug/dl were reanalyzed in duplicate by graphite furnace AAS. Mean values of the duplicates were used as data. (Rothenberg, et al., 1994)	Four trained psychologists blind to children's lead levels administered the McCarthy GCI. As there were no norms for the McCarthy scale in the Mexican population, the U.S. norms were used to calculate GCI, with a Spanish translation of the test. Interexaminer reliability was assessed by calculating the correlation in GCI scores assigned by two of the psychologists with the scores of a third psychologist whom they observed applying the test in all possible combinations with 10 subjects for each combination. Mean observer-examiner correlation was .99.

Draft Final for ACCLPP Review

Quality Assurance Comments

Study Population	Blood-lead Measurement	Cognitive Function Measurement
Port Pirie (23, 35)	Samples were measured by capillary & venous and were analyzed by ETAAS. Capillary samples were obtained by finger prick using a rigorous cleansing and collection protocol. A pilot study had demonstrated that blood-lead concentrations measured in capillary samples were highly correlated with simultaneously determined venous lead concentrations in 47 children in metropolitan Adelaide. Internal and external QC procedures were used. Interbatch accuracy and standardization were monitored. The laboratory participated in 3 QC programs: Standards Assoc of Australia, Pennsylvania Health Dept., and Wolfson Research Labs.	Full-time, trained examiners, blind to past or current PbB, performed assessments in a clinic setting. The Bayley (2 yrs), McCarthy GCI (4 yrs) and WISC-R (7, 11, & 13 yrs) were assessed. At ages 2, 4, and 7 years all children were assessed by a single research psychologist blind to their exposure status. At ages 11 and 13, the subjects were evaluated by a single trained examiner who had not participated in earlier phases of the cohort study and who was unaware of the children's exposure and developmental histories. The assessment and the blood sampling were carried out on different days.
Rochester (11)	Samples were measured by venous and were analyzed by ETAAS. Blood-lead values were calculated as the means of six analyses of each venous sample. The results of the repeated analyses, separated by 5 days, were extremely consistent (SD=0.40 ug/dl) for blood-lead concentrations below 20 ug/dl. Values below the limit of detection (1.0 ug/dl) were set to 1.0 ug/dl.	A different examiner administered an abbreviated Stanford-Binet at each age and was blinded to a child's lead status.
Sydney (12)	Samples were measured by venous and capillary and were analyzed by Flame and ETAAS. At six months, capillary blood samples were obtained, but at later ages venous sample were collected wherever possible to reduce the risk of sample contamination. Up to 24 months, approximately half the samples were capillary, but almost all subsequent samples were venous. When an elevated capillary reading was obtained (>25 ug/dl after 1985), a venous sample was collected as soon as possible. All postnatal blood samples were collected in the children's homes. All assay runs included 6 calibration standards ranging from 0-100 ug/dl, and samples were assayed in duplicate. Lyophilised whole blood controls from two commercial supplies were routinely used. The laboratory regularly submits blood samples to the Wolfson UK QA Scheme. Other QC measures are periodically assaying samples received from the Standards Association of Australia, as well as from other national and international QC programs.	Examinations using McCarthy GCI were performed by trained psychologists who were blinded to actual blood-lead levels. All examinations were conducted in the children's homes by trained psychologists within 7 days of blood sampling. Reliability checks were carried out on the psychologists at regular intervals by an independent clinical psychologist, who also was responsible for their training on the tests. Inter-observer correlations exceeded .95.