



VOLUME I

OCCUPATIONAL HEALTH SURVEILLANCE OF REPRODUCTIVE OUTCOMES:
A CASE CONTROL STUDY

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Dear Sirs/Madams:

I am please to present to you and the NIOSH the enclosed final report for the contract: "Occupational Health Surveillance of Reproductive Outcomes: A Case Control Study (No. 210-78-0057). The submission of this report represents the successful completion of this contract. Your office's efforts in helping us to fulfill our obligations within the designated time and costs constraints were most appreciated.

If you have any questions, please feel free to contact me at your earliest convenience.

Sincerely yours,

Stuart C. Hartz
Associate Professor
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SCH:er

Abstract

The present report describes the results of a case-control epidemiologic study of parental (both maternal and paternal) occupation during pregnancy in relation to selected "adverse" reproductive outcomes of pregnancy. This study uses information gathered as part of the Collaborative Perinatal Project (CPP), NINCDS, a large-scale study of some 55,000 pregnancies. A major purpose of the present study (of 14,038 pregnancies of the original CPP population) was to review the available CPP information on the parents' work histories (during gestation) and to identify and measure the effects of occupation on "poor" pregnancy outcome. The results are presented separately for maternal and paternal industries and occupations as recorded in the CPP data collection forms.

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Due to the relatively short time span of the project, a major consideration was obtaining a well-documented computer data file on the reproductive outcomes of the pregnancies. Fortunately, Drs. Dennis Slone and Samuel Shapiro, Co-Directors of the Drug Epidemiology Unit, Boston University Medical Center, graciously provided us with a duplicate computer file containing edited data on the reproductive outcomes of the CPP cohort. Mr. Len Gaetano of the DEU performed the relevant and important computer programming tasks.

Our thanks also go to Drs. Sheila Hoar, Philip T. Cole and Allen Morrison for making available to us the dictionary and coding scheme for classifying workers into industrial and occupational categories appropriate for data analysis.

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1.0 Introduction

1.1 An Overview

In the four decades since Gregg's discovery of the teratogenic effects of the rubella virus, the identification of environmental determinants of adverse reproductive outcomes was received increasing attention. Although the etiology of most birth defects and other poor pregnancy outcomes remain unknown, studies on the antenatal effects of the environment, and in particular occupation, have received greater priority only within the last decade (1). To a great extent, the impetus for the further study of teratogenic effects due to the environment is a result of the 1960-61 epidemic of phocomelia resulting from the antenatal use of the tranquilizer thalidomide (2).

More recently, researchers have directed their efforts to studying the role of occupation (both maternal and paternal) during pregnancy in regard to the outcomes of pregnancy. This interest is illustrated by the following statement in HEALTHY PEOPLE: THE SURGEON GENERAL'S REPORT ON HEALTH PROMOTION AND DISEASE PREVENTION:

Among critical areas that need study are the role of occupational exposures in producing birth defects and the special problems of women exposed to hazardous substances (3).

In addition to this statement, reflecting government policy, there is an increasing number of reports expressing similar concerns, either in the form of editorials or as results emanating from epidemiologic studies.

Aside from the interests of public health researchers and policy-makers, it is vital that clinicians obtain valid information on which to base their health care strategies when counseling pregnant women who are employed in possibly "harmful" occupations (4).

The major purpose of the present study was to explore the potential teratogenic and mutagenic effects of maternal and paternal occupation during pregnancy.

The study plans were to organize and review a large existing data base to identify occupations during early pregnancy associated with adverse reproductive outcomes. Specifically, the two major goals, which were developed together with the NIOSH, were:

- 1) To identify and measure the possible associations between both maternal occupational status during pregnancy and the father's prior work experience, and selected reproductive outcomes utilizing existing information collected as part of the Collaborative Study on Cerebral Palsy, Mental Retardation, and other Neurological and Sensory Disorders on Infancy and Childhood of the National Institute of Neurological Diseases and Stroke (Collaborative Perinatal Project, henceforth referred to as the CPP of the NINCDS).

2) To document the estimated relative risks associated with maternal occupational status during pregnancy and father's prior work experience on reproductive outcome, adjusted for potential influences on confounding variables; and, to summarize the results concisely in a format that can be useful in subsequent investigations of specific etiologic hypotheses, and in health planning and policy development.

Within the time and cost constraints of the present study, (discussed more fully below) the aim was to generate hypotheses which could be explored more intensively either in the CPP, or other data bases.

The CPP of the NINCDs is an epidemiologic study of some 50,000 pregnancies, which were registered from 1959 through 1965, with follow-up of the liveborn extending to the age of eight years. Extensive information was gathered on the parents, and the offspring (or outcomes) of pregnancy (described in detail below). Since the goals of the CPP were defined broadly, specific risk factors, such as drug use and occupation during pregnancy, were not specifically included as risk factors of major interest at the early design stages of the study. Reflecting this, the CPP collected information on occupational status of the mothers and fathers in two major data collection phases. These phases were distinguished by the two different data collection forms used. Despite this difficulty, for the purposes of the present study, it was still possible to extract certain items of occupational information from the forms. To use this information, however, it became necessary to reconcile much of the information gathered. As a result, employment information during pregnancy for the mothers and fathers included occupational exposure information common to both forms.

Since occupational information was not stored in computer retrievable form, it was necessary to abstract and code occupational exposure information from the original data collection records. Due to this significant methodologic consideration, it became impractical to access all fifty thousand medical records. Thus, although the original study design was a prospective-cohort (follow-up) epidemiologic study, it was deemed appropriate by the NIOSH to redesign and conduct the current investigation within the format of a case-control epidemiologic study. An advantage, in adopting this approach, was to minimize the required number of medical records to be accessed. The process of sampling from a prospective study in order to arrive at a case-control study design has been referred to as a synthetic retrospective study approach (5).

Consequently, various adverse reproductive outcomes were defined as the cases while "otherwise normal" outcomes of pregnancy were considered to be the controls. The adverse reproductive outcomes considered in this study include fetal and neonatal deaths, infant deaths, and physical congenital malformations. There were 5,333 cases selected, and for each of these two controls were frequency matched on several concomitant variables. Thus, in all, there was a total of approximately 15,000 pregnancy outcomes selected for study. The related criteria and sampling plan are discussed in greater detail in section 3.1.

The time period during which the present study on parental occupation and adverse reproductive outcomes was conducted was from October, 1978 to October, 1980.

1.2 Literature Review

1.2.1 Introduction

Previous studies of parental occupation in relation to adverse reproductive outcome have been restricted mainly to the employment histories of the mothers. The present discussion of the literature, thus, reflects this emphasis. It should be noted, however, that this emphasis is well placed since women have been entering the U.S. workforce in increasing numbers during the last four decades. For example, in 1974 the employment rate among American women was 45 percent accounting for 39.3% of the workforce (6).

A wealth of information on a broad spectrum of environmental factors which affect pregnancy has been reported; however, relatively few studies have been directed toward reproductive outcome and occupational exposures. It was primarily due to the non-decreasing rates of perinatal mortality and related outcomes in the 1950's that the CPP was designed and implemented. Therefore, this literature review presents an overview of trends in perinatal mortality and other "unfavorable" reproductive outcomes, followed by a summary of the state of knowledge on environmental risk factors and reproduction. These reviews provide a context for describing the available information on risks of "poor" pregnancy outcomes attributed to occupational exposures.

1.2.2 Adverse Reproductive Outcomes

In the first half of the 20th century, a sharp reduction in infant mortality rates occurred, largely due to decreasing mortality from infections, parasitic disease, influenza, and pneumonia. However, from 1950 through 1964 there were no significant changes in infant mortality. This trend was very similar for both male and female infants, although the chance of dying during infancy was approximately 30 percent greater for males relative to females. Whites and non-Whites showed similar trends up to 1950. Since 1950, non-Whites have shown a more erratic trend, with increases in rates observed for several years, although the overall trend is downward. For the period 1959-61, infant mortality for non-White children was 86 percent above the rate for White children (7).

Although a decrease in perinatal mortality was observed between 1942 and 1955, the number of fetal and neonatal deaths relative to infant deaths has declined more slowly. In 1956, this downward trend in perinatal mortality leveled off, and little change was observed through 1964. Specifically, males were subject to approximately a 22 percent higher risk of perinatal death than females from 1942 through 1964. Non-Whites had approximately a 75 percent higher risk than Whites throughout this period. During this time, there was no reduction in the sex or racial mortality ratios (7).

Infant and perinatal mortality rates provide a partial measure of the possible range of adverse outcomes associated with pregnancy. Accordingly, a "continuum" of adverse reproductive outcomes, in addition to infant and perinatal mortality, that may have similar etiologies has been proposed (8). This "continuum" includes spontaneous abortions and congenital anomalies. Since low birth weight may be a manifestation of similar etiology, it too may be considered a measure of reproductive efficiency, and could be included in the "continuum" of adverse reproductive outcomes.

It is commonly accepted that fetal loss of 20 weeks or more of gestation is only a small fraction of all perinatal deaths. Studies have estimated the magnitude of total fetal loss as being in excess of 20 percent of all pregnancies (9,10). In the Kauai Pregnancy Study (KPS), which consisted of an analysis of the outcome of all pregnancies in a single community (composed of 35 percent Japanese, 23 percent Filipino, 19 percent Hawaiian, and 14 percent Caucasian), 24 percent of all pregnancies with gestational age of 4 weeks or more terminated in fetal death; of these deaths, 91 percent occurred before the twentieth week of gestation. However, the generalizability of these results is weakened since infant mortality for Kauai is considerably lower than for the total population of the U.S. (11).

In a study of a population insured for comprehensive medical care, the Health Insurance Plan of Greater New York (HIP), it was found that about 14 percent of the pregnancies that were known to the physician terminated in a fetal death. Approximately one-half of these deaths occurred at gestational ages less than 12 weeks, 32 percent occurred at gestational ages 12-19 weeks, and 12 percent occurred at gestational ages of 20 weeks or more. These data may not be representative, since women under the care of HIP obstetricians had better reproductive outcomes than women under the care of private physicians in New York City (7).

Developmental birth defects, including congenital anomalies, may be defined as manifestations of developmental deviations of a structural or functional nature that usually originate before birth (12). However, there is no general agreement about what constitutes a malformation (13). The magnitude of the problem of congenital anomalies was documented in a 1954 report (14) which reported a rate of 7.5 physical congenital malformations per 100 children under 2 years of age. These results are supported by the findings of two subsequent studies, the HIP and the CPP, which reported malformation rates of 7 and 6.5 percent, respectively (7,13).

Birth weight is well recognized as being strongly related to high rates of congenital malformations and other developmental problem, regardless of race (13). In the CPP, malformation rates were demonstrated to be substantially higher among categories of liveborn with birth weight less than 2500 grams. The relative risk of malformations for White children weighing less than or equal to 1,499 grams (relative to White children weighing 2500 grams or more) was 4.7. The relative risks for the weight categories 1,500 - 1,999 and 2,000 - 2,499 grams

were 3.4 and 2.1, respectively. Relative risks for malformations among weight categories showed a similar trend for Black children, although they were reduced in magnitude (13).

Also, a higher risk of neonatal death has been observed for infants with lower birth weight. In particular, among infants weighing less than 2500 grams at birth, 174 per 1000 die within the first 28 days after birth. This is much higher than the rate for infants of all birth weights which is 7.8 per 1000. Although infants with low birth weight represent only about 7 percent of all live births, deaths among these children account for two-thirds of all neonatal deaths (7).

Race can be a relevant factor in determining the risk of an adverse reproductive outcome. Garn et al., for example, suggest a different course of prenatal development in those of African descent (15). Lower birth weights of Black infants have been documented in every category of maternal age, parity (16,17) weight, height, gestation (17), education, occupation (15,17) and income (15). In the CPP, Black and Puerto Rican mothers had a premature delivery rate twice that of the White mothers (15). Also, sudden infant death syndrome occurred more frequently in Black CPP children than in White children (18).

Pregnancies which occur at either extreme of the maternal reproductive age spectrum (approximately, below 15 and above 45 years) have been associated with suboptimal pregnancy outcome. The increased risk of the occurrence of Down's syndrome with advancing maternal age has long been established. In general, the highest risk of pregnancy complications exists for women 40 years and over; mothers aged 18 years or less are considered the group at second greatest risk (7). In an analysis of the CPP, Naylor found a correlation between risk of spontaneous abortion and increasing maternal age in White subjects (19). The relationship was not found in Black women.

The problem of reproductive and infant loss, as well as the frequency of developmental defects in the U.S. remains largely unresolved. For example, results of the KPS study indicate that for every 1000 live births there are 311 fetal deaths, 14 neonatal deaths, and 4 deaths of infants age 28 days through one year. Of 1000 live births, 35 have low birth weight requiring special care, 28 have handicaps requiring short-term care, 37 have handicaps requiring long-term care, while 32 others probably would require special educational services (11). Results of the HIP study show that of all pregnancies known to staff physicians, 14 percent end in a fetal death, 0.8 percent end in a neonatal death, 4.5 percent result in a significant physical or developmental anomaly that requires medical care, and 4 percent result in an infant with low birth weight (7). The statistics from both the KPS and HIP studies appear to underestimate the problem of the frequency of adverse reproductive outcomes in the general community.

1.2.3 Environmental Factors Related to Adverse Reproductive Outcomes

The etiology of human developmental defects is estimated to be unknown in 65-75 percent of the cases. The most important overall factor appears to be genetic transmission, which accounts for roughly twenty percent of all malformations, and for approximately two thirds of all defects with known etiology (12).

As regards many adverse reproductive outcomes not explained by known genetic determinants, environmental risk factors have been implicated as the possible etiologic agents.

Among these environmental factors is antenatal exposure to ionizing radiation, which presents a well-documented risk to the developing fetus. One study involving 500,000 infants from 30 U.S. hospitals showed a 30 percent increase in cancer, mainly leukemia and malignancy of the central nervous system, in children whose mothers were irradiated during pregnancy (20). In a case-control study of families of mongoloid children in Baltimore, Maryland, mothers of mongoloid children had been exposed to ionizing radiation seven times as frequently as those mothers in the control group (21). Furthermore, stillbirths, neonatal deaths, infant deaths, and congenital anomalies were all increased among pregnant women exposed to the atomic explosions at Hiroshima and Nagasaki (22,23).

A large number of chemical agents (pharmaceutical and others) have been related to congenital and developmental defects in humans. Prior to the thalidomide disaster during the early 1960's, it was commonly believed that the placental barrier effectively protected the fetus from drugs given to the mother (13). However, since that time a number of pharmaceutical agents have been documented as suspected teratogens.

The evidence implicating thalidomide is overwhelming. It is believed to be responsible for limb and other deformities among 6,000-8,000 children. This drug produced a well-defined pattern of musculoskeletal deformities, affecting mainly the extremities and face. Particularly striking were cases of phocomelia, usually a rare condition in which hands are attached directly to the shoulders (12,24).

Anticonvulsant drugs of various types have been suspected of having teratogenic effects. This group of drugs has been found to be primarily associated with cleft palate, cardiac, digital, central nervous and mental abnormalities (12,24).

The anticoagulant warfarin is also receiving attention as a potential teratogen. Defects such as nasal hypoplasia, optic atrophy, skeletal defects, and mental retardation have been related to the use of this drug (25).

Certain oral hypoglycemics are now included on the list of potential teratogens. Among diabetic mothers, the use of chlorpropamide during pregnancy has been associated with a three fold increase in the incidence of fetal death relative to that observed for diet or insulin therapy. Also, thrombocytopenia and hypoglycemia in the newborn have been reported as a result of tolbutamide use in the mother (26).

Hormonal pregnancy tests have been associated with congenital heart disease, neural tube defects, limb reduction deformities, and VACTERAL (vertebral, anal, cardiac, tracheoesophageal, renal and limb) syndrome. Sex hormones used during pregnancy have also been reported to cause masculinizing abnormalities in female infants (for a review of the teratogenic effects of hormonal drugs see (27)).

Oral contraceptives taken in early stages of an unrecognized pregnancy has been related to limb reduction deformities (28). A study involving the CPP data revealed a higher rate of cardiovascular defects among infants of mothers who used oral contraceptives in early pregnancy than among the unexposed (29).

The carcinogenic effect of diethylstilbestrol (DES) in daughters of women taking the drug to prevent miscarriages is well known. To this date, this is the only well-documented human transplacental carcinogen (24).

Antithyroid drugs have been shown to cross the placenta, and induce congenital goiter and hypothyroidism. Among these agents, iodine and thioureas are two agents which have been implicated (24).

Antibiotic drugs have been implicated as human teratogens. Tetracyclines have been shown to have a strong affinity for developing osseous and dental tissues; and, it has been related to discoloration of permanent as well as deciduous teeth in infants of mothers treated during pregnancy (24). Streptomycin has been associated with impaired hearing in infants whose mothers were treated during pregnancy. Furthermore, this agent is believed to be toxic to the labyrinth (24).

Many chemical exposures other than drugs appear to be associated with unfavorable reproductive outcomes. Maternal smoking is a well-known risk factor to the developing fetus, and has been linked to increased rates of spontaneous abortions (30), low birth weight (30,31), perinatal death (32), and congenital anomalies (33). Even at older ages, children of mothers who smoked in pregnancy appear to be physically smaller, and have reduced reading abilities as compared to their contemporaries whose mothers did not smoke during pregnancy (34). Ten percent of the perinatal deaths in the Ontario Perinatal Mortality Study was estimated to have been due to maternal smoking (35). In the CPP, sudden infant death syndrome was more frequent in the children of pregnant women who smoked relative to the non-smokers (18).

Recognition of the Fetal Alcohol Syndrome in infants of mothers who are heavy drinkers has received much attention (36,37,38,39). This syndrome includes the combination of fetal defects and deficiencies produced by chronic alcoholism of the mothers. It includes structural malformations of the face, limbs, and heart, mental retardation, intrauterine and postnatal growth deficiency (38). Jones et al. studied the infants of twenty-three CPP alcoholic mothers and reported varying degrees of mental deficiency as the most common disorder, in addition to increased perinatal mortality and visible physical abnormalities (40).

Polychlorinated biphenyls (PCB) have been shown to be associated with adverse reproductive outcome. Infants born to mothers with PCB poisoning (Yusho disease) from food cooked in contaminated rice oil had decreased birthweights. Another manifestation of Yusho disease was dark-brown staining of the skin (24).

It is also known that inorganic and organic mercury pass the placental barrier. Inorganic mercury is suspected of causing spontaneous abortions, although the evidence of the effects of mercury on the fetus is not clear (41). Results of the Minimata Bay "disaster" in Japan, a mass poisoning in the mid and late fifties resulting from consumption of fish contaminated with high concentrations of mercury from factory discharge, that infants of women who ingested methyl mercury had high rates of congenital defects. Cerebral palsy and mental retardation resulted in many cases (24,42).

1.2.4 Occupational Factors Related to Adverse Reproductive Outcome

The workplace environment may be related to poor pregnancy outcome through either maternal or paternal exposure. In these instances, fetal damage may result from a direct action on the fetus in-utero, and/or by damage to germ cells.

An early study of the effect of working during pregnancy indicated that the chance of a "successful pregnancy" is significantly lowered if a woman works during her pregnancy (43). An examination of 1318 records of first pregnancy indicated that the perinatal death rate for women gainfully employed in occupations that "did not appear to be either exceptionally dangerous or unusually exacting even when compared with housework" was higher than the rate for housewives. For women gainfully employed for more than 28 weeks during pregnancy, the perinatal death rate was 7.5 percent, while the rates for women employed less than 28 weeks and housewives were 4.9 and 2.8 percent, respectively. The rate of low birth weight among infants of women who were employed during pregnancy was also higher than among the infants of women who did only housework. In a sample of 152 women employed for more than 28 weeks during pregnancy and 152 housewives matched for age, social class, and marital status at time of conception, the incidence of prematurity was 7.3 percent for the employed women, and 1.3 percent for the housewives. In a similar matched sample for women working less than 28 weeks during pregnancy, the rates of prematurity were 4.9 percent for the employed women, and 2.1 percent for the housewives (43).

A 1958 study of maternal health and congenital defects indicated a slight excess of women working thirty or more hours a week at some time during pregnancy among mothers of children with major defects (44). Of women working 30 or more hours, 37 percent were clerical, 32 percent worked in factories, 11 percent in retail stores, 4 percent in domestic jobs, 3 percent in nursing, 3 percent in canteen or restaurants, and 2 percent in laundries; of 27 laundry workers, 4 (15%) had infants with major defects. Twenty percent of mothers of infants with major defects indicated that their work involved heavy lifting or pulling as compared with only 8 percent of mothers of normal infants.

Since the early 1900's, occupational exposure to lead has been known to affect reproductive outcome. Data obtained in 1897 from 77 female lead workers indicated that 212 pregnancies in this group resulted in 21 stillbirths, 90 miscarriages, and 40 infant deaths. Only 61 children survived the 212 pregnancies (45). In another report on pregnancy outcome among female lead workers, there were 271 deaths under one year of age per 1000 births. In contrast, the rate for mothers working in mills with no lead exposure was 214 deaths under one year of age per 1000 births (45).

A more recent report on pregnancies among Japanese female lead workers showed an increase in spontaneous abortions from 45.6 per 1000 pregnancies before exposure as compared with a rate of 84.2 per 1000 pregnancies after exposure. A spontaneous abortion rate for a similar number of comparable female employees not exposed to lead was 59.1 per 1000 pregnancies (46).

Paternal exposure to lead also adversely affects reproductive outcome. One early study reported a miscarriage and stillbirth rate of 25.5 percent in lead worker's wives (47). Another investigator noted sharply increased miscarriage and infant mortality rates in pregnancies where either parent was exposed to lead in the printing trade (48).

Clearly, exposure to lead poses a threat to the viability of the developing fetus. Increased risks of pregnancy wastage, sterility, and infant death have been documented repeatedly in pregnancies where either parent faced lead exposure (45-50). Lead appears to affect pregnancy through germ cell damage and/or by crossing the placenta and directly poisoning the fetal blood (48).

The risk to the fetus from maternal occupational exposure to anesthetic gases has been identified and described in the last decade. In one study, 29.7 percent of the pregnancies among operating room nurses exposed to anesthetic gas ended in spontaneous miscarriage as compared with only 8.8 percent in the control group (general duty nurses). A similar result was observed for anesthesiologists with 37.8 percent of the pregnancies ending in spontaneous abortion, while only 10.3 percent of the pregnancies in the control group (other physicians) ended in miscarriage. It was also observed that the miscarriages occurred earlier in both study groups (operating nurses and anesthesiologists) than in their respective control groups (51). A study from the U.K. reported a spontaneous abortion rate of 18.2 percent for female anesthesiologists who practiced during pregnancy; this rate was higher than the 14.7 percent rate of

other doctors. A 6.5 percent rate of congenital malformation in the children of practicing anesthetists was found. This rate was significantly increased relative to the rate of defects in offspring of non-working anesthetists, although not increased relative to the rate for other doctor's births (52). A survey in Michigan compared nurse anesthetists who practiced while pregnant with those who did not practice. There was a 16.4% birth defect rate in the offspring of the working mothers; non-working women gave birth to children with malformations in only 5.7% of the pregnancies (53).

In response to the growing concern over the risks posed by exposure to anesthetic gases, a committee appointed by the American Society of Anesthesiologists designed a study to evaluate the health status of all operating room personnel in the U.S. Thirty thousand "exposed" individuals were surveyed; a group of 10,000 other medical workers served as the reference group. A number of health hazards were identified, including significant risks to reproductive outcome for workers exposed to anesthetic gases. For example, relative risks of giving birth to children with congenital malformations ranged from 1.25 in male anesthesiologists' wives, to 2.0 in female anesthesiologists. All women working in the operating room had increased risks of spontaneous abortion (54). However, in the following year, 1975, a study in the U.K. failed to find an increased rate of major congenital malformations due to parental exposures to anesthetic gases (55). A 1977 study reported low birth weight as the most significant adverse pregnancy outcome experienced by female anesthesiologists (56).

In addition to personnel exposed to anesthetic gases, other groups of medical workers face conditions which may affect reproductive outcome. Haldane et al. conducted a study in Canada to determine the risk of giving birth to children with congenital malformations for nurses exposed to viral infections (57). Nurses who cared for infants with birth defects in the hospital or in the parents' homes had significantly higher rates of malformations in their own children. Home care for premature infants was also associated with elevated risk of abnormalities in the nurses' offspring. However, these results were based on a 54% response rate in the study. Nurses and other hospital employees may also face reproductive problems as a consequence of radiation exposure (58).

Laboratory technicians who are exposed to organic solvents have been shown to have significantly higher rates of chromosomal aberrations (59). Also apparently healthy children of women who worked during pregnancy had significant increases in these chromosomal abnormalities (59). A survey of female workers at a hospital laboratory noted the possibility of an increase risk of spontaneous abortion among laboratory staff (60).

In a study of dental offices, all were found to contain high levels of mercury (61). Assays for urinary mercury in office personnel revealed that dental assistants and dentists have significantly high risks of mercury vapor absorption. The inorganic mercury used in dental practice can be metabolized by the human body into organic mercury, including methyl mercury; the adverse in-utero effects of methyl mercury have been documented in the previously mentioned reports on the Minamata disease outbreak (24). Inorganic mercury is also suspected to be an abortifacient (24).

An occupational exposure which has been identified in recent years as potentially hazardous to workers is the manufacturing process of polyvinyl chloride. This process is accomplished by polymerization of the vinyl chloride monomer; this molecule has been causally linked with human carcinogenesis (62,63). Observations among workers exposed to vinyl chloride show a significant excess of chromosomal aberrations (64,65). A study of pregnancy outcome among wives of workers exposed to vinyl chloride indicated that, in comparison to controls, there was a significant excess fetal loss in the group whose husbands had exposure to vinyl chloride (66). The fetal death rate, adjusted for paternal age, in pregnancies fathered by exposed workers was 15.8 percent, compared with 8.8 percent in control pregnancies. The most striking difference occurred in husbands under 30 years of age. Fetal mortality was 20.0 percent for the exposed group compared with less than one percent for the control group.

The manufacture of polychloroprene, a synthetic rubber, is another polymerization process that has become suspect with regard to its adverse reproductive effects. The monomer used in this synthesis, chloroprene, has been associated with impaired spermatogenesis, chromosomal abnormalities, and spontaneous abortion in workers' wives (67).

Benzene exposure has been associated with chromosomal aberrations in male and female workers (59,68-70). In addition to its use in medical laboratories, benzene is used in various manufacturing processes. Exposure to arsenic has also been associated with chromosomal abnormalities in male workers, although the study group was small (71).

Currently, concern over the teratogenic and other adverse reproductive consequences of exposure to "Agent Orange" during the Vietnam War is increasing. This herbicide is contaminated with dioxin, which has been associated with increased frequencies of birth defects in the offspring of exposed veterans. However, this relationship has yet to be confirmed by epidemiological studies (72).

2.0 Description of Study Population

2.1 The Collaborative Perinatal Project (CPP)

2.1.1 CPP: An Overview and Background

The plan to undertake an epidemiologic study of factors in pregnancy related to cerebral palsy and other forms of damage to the central nervous system was first proposed in the early 1950's. The Collaborative Perinatal Project (CPP) was planned and developed at a time when perinatal mortality was declining more slowly than deaths in infancy (from 28 days to the end of the first year of life) in the U.S. In addition, in the years after World War II there was growing concern about those fetal deaths which occurred between the 20th week of gestation and the time of delivery, and deaths of live-born infants during the neonatal period. Against this background of perinatal mortality, more specific concerns arose regarding the relationships between factors affecting women during pregnancy and the neurological and sensory disorders of their offspring. However, it was recognized that in undertaking any study of neurological deficit in the offspring and risk factors during pregnancy, that information on many variables must be collected - such a study would be costly and extend over a long time period. Still, during the late 1950's and during the 1960's there was concern by public health authorities regarding the inability to reduce mortality in the perinatal period, as well as the increasing evidence that injuries or insults to the fetus could result in hazards to the long term physical and intellectual development, and growth.

After an extensive period of planning, the NINCDS was able to sharply define a set of appropriate study objectives. These goals were summarized in the Report of the NINCDS Perinatal Statistical Ad Hoc Committee in 1968.

A detailed history of the CPP can be found in (73). However, it is useful to restate the CPP objectives:

"Briefly, the data collected...are expected to provide additional knowledge on the relationships between perinatal factors and the subsequent development and cause of abnormalities in the offspring. The investigation is directed toward: 1) the examination, in depth, of the effects of factors already suspect; 2) the identification of factors not presently suspect; 3) the elucidation of mechanisms by which these factors operate.

"Prenatal factors and conditions to be investigated include: 1) the abnormal conditions of pregnancy itself, such as infection, trauma, drug reactions, or abnormal progress of labor; 2) the environmental factors - social and economic conditions; 3) the biological factors in parents - age, medical and reproductive history and immunologic characteristics.

"Other objectives include: 1) the evaluation of the relation of prenatal factors to early and late fetal loss, prematurity, infant and early childhood mortality as well as other aspects of the reproductive process and its outcome; 2) the dynamics of physical and mental development in early childhood, and the relationship of this development to genetic, biological and environmental factors; 3) the evaluation of the significance of events in the post natal environment in relation to later development of disturbances of structure and function of the nervous system and other systems."

Recognizing that many of the reproductive outcomes of interest were relatively rare, it was estimated that approximately 50-60,000 pregnant women were necessary to conduct a proper study. To enroll this many women, a collaborative multi-institutional prospective study was designed. The pretest period was 1958, during which time staff were hired and interview forms tested. Formal data collection began on 1 January 1959 and ended 7 years later on 31 December 1965. In all, a total of 55,908 women were enrolled in fourteen hospitals affiliated with 12 universities.

As the CPP project developed, its scope was increased until it was designed to collect data on a large number of antenatal and perinatal events in the mother, and post-natal events in the children. The purpose was "to define parameters of the broad problem of fetal wastage, to identify possible etiologic factors, and to pinpoint possible areas for intervention, or for further specific research."

2.1.2 The Sampling Frame

The specification of the sampling frame and the various sampling procedures used to identify study participants, and members of the final study cohort will be described briefly. A more detailed description can be found in (73). The final sample size determined in 1961 was approximately 60,000 registered pregnancies, and was determined, in part, on the basis of accumulating the necessary minimal number of those pregnancy outcomes, and events which occur with relatively low or rare incidence. Table 1 lists the collaborating institutions. For each institution, Appendix A gives the respective dates of registration of the women, the number of women in the original sampling frame and the eventual number of women selected to participate in the core study. Overall, there were 132,560 women in the original sampling frame which resulted in 55,908 pregnancies eventually included in the core study cohort. The average overall sampling ratio therefore was 2.4:1 (73).

Table 1

The Collaborating Institutions

<u>Observations</u>	<u>Collaborating Institutions</u>
BO	Boston Hospital for Women (Lying-In) Division and Children's Hospital Medical Center Harvard Medical Center Boston, Massachusetts
BU	Children's Hospital State University of New York at Buffalo Buffalo, New York
CH	Charity Hospital Tulane University School of Medicine and Medical Center, Louisiana State University New Orleans, Louisiana
CO	Columbia-Presbyterian Medical Center Columbia University College of Physicians and Surgeons New York, New York
JH	The Johns Hopkins Hospital The Johns Hopkins University School of Medicine Baltimore, Maryland
VA	Medical College of Virginia Virginia Commonwealth University Richmond, VA
MN	University of Minnesota Hospitals Health Sciences Center Minneapolis, Minnesota
NY	Metropolitan Hospital New York Medical College New York, New York
OR	University of Oregon Medical School Portland, Oregon
PA	Pennsylvania Hospital and the Children's Hospital of Pennsylvania University of Pennsylvania Philadelphia, Pennsylvania
PR	Child Study Center Brown University Providence, Rhode Island
TN	Gailor Hospital University of Tennessee College of Medicine Memphis, Tennessee

2.1.3 CPP Subject Selection Criteria and Procedures

Recruitment of the study participants lasted seven years, extending from 1 January 1959 to 31 December 1965. Participants were selected from pregnant women admitted to the collaborating hospital clinics. In ten medical centers, the obstetric and pediatric departments were in the same hospital, while in two centers, they were in separate hospitals; thus, twelve medical centers participated in collecting data.

The selection procedures were not uniform in all hospitals. They differed due to considerations such as the capacity of each center to commit its resources to the study for 15 years or more, the degree of interference with the different routines of the maternity clinics, and the individual interests of researchers in each institution.

In particular, the enrollment criteria differed by institution. The most important criterion was the patients' admittance to the hospital/clinic. However, the Children's Hospital in Buffalo differed in this respect since registrants were private patients of the participating obstetricians (of which there were 4 to 13, at various times in the study).

Additional constraints on the patients' recruitment included certain geographic restrictions. For example, the Johns Hopkins Hospital recruited only those patients who resided within the metropolitan Baltimore area. Nonetheless, during the progress of the study certain centers which originally did not impose geographic restrictions did so to maximize the follow-up capability by the center's staff.

The sampling procedures were designed to encompass the broad range of pregnancy conditions that could be considered generally representative of the more common pregnancies. A goal was to exclude those pregnancies which could be called "special", and which might otherwise reflect a particular specialization of any one university-affiliated medical center.

The sampling frame was designed to ensure roughly equal recruitment of white and black women, but no a priori ethnic exclusions were stipulated. In order for women to be placed in the sampling frame, a variety of constraints were imposed in all antenatal clinics. These constraints were introduced to restrict the study cohort to those women who did not have recognized poor prognosis for follow-up, and included categories of women such as unwed mothers who planned to place their babies for adoption, women who planned to leave the area, transients, and women who gave birth on the same day they registered in the study. The latter category of women were termed "walk-ins", and were excluded 17 months after the start of data collection.

With these pre-set limitations, there were 132,560 gravidas in the sampling frame and available for study, before the local selection plans for entry were applied.

In two of the hospitals, all presenting gravidas in the sampling frame were enrolled; in nine hospitals, systematic selection was based on, for example, the terminal digit of the recorded number, or the women's day of birth. In one hospital, random selection was used. If a woman had more than one pregnancy at a collaborating hospital within the stipulated time limits, she could be admitted as a participant more than once. See reference (73) for more specific details in the readmission criterion used by each institution.

Depending on the special interests of collaborating physicians in individual centers, it was permissible, to an agreed extent, to enroll and collect data as a routine part of the study for certain specified groups - for example, a (special group consisted of all gravidas under 16 years of age seen at the Johns Hopkins Hospital, and at Oregon all first trimester registrants were followed. Apart from these special groups, for gravidas registered according to the principal plan of the study, the sampling ratio was approximately two out of five eligible pregnancies at the hospital.

A total of 58,282 pregnancies were registered. Of these, 2,622 were members who were of special interest to particular hospital groups, 298 were "walk-ins" and 55,908 conformed strictly with the general selection rules.

Table 2 gives the racial distribution of the "core" pregnancies. Due to the small number of registrants who were other than White, Black or Puerto Rican, these cases were excluded from the study. The final composition of the study population reflected cases "lost to study". This determination was made if the gravida refused to continue participation in the study, or if she moved from the geographic region without being traced, or for other similar reasons.

Table 22

The CPP Gravidas by Ethnic Group

<u>Ethnic Group Of Gravidas</u>	<u>No. Core Pregnancies</u>	<u>(Percent)</u>
White	25,703	(46)
Black	25,837	(46)
Puerto Rican	3,795	(7)
Oriental	256	(*)
Other	317	(*)
	<u>55,908</u>	<u>(100)</u>

*Less than one percent.

The study (core) cohort includes repeat pregnancies. A discussion of the possible biases introduced by this inclusion have been discussed in (13). In general, it was felt that the estimated measures of association (odds ratios) were not unduly biased by including these pregnancies.

Over 2,000 selected registrations refused to participate. In addition, a small number of gravidas moved and could not be traced. Sometimes, for one reason or another, information concerning labor, delivery, or the child could not be obtained. In all, refusals and losses to follow-up amounted to 2,977 mother-child pairs (5.3%) which reduced the sample from 55,908 to 52,931. While there were no statistically significant differences between the non-responders and responders with regard to age, ethnic group, marital status, and weeks of gestation at registration, the non-responders were, overall, slightly more often well-educated, married, and over the age of 35 years. Differences, however, were not consistent by hospital (73).

A description of the exclusions specific to the present study is given below in section 3.1.

2.1.4 CPP Data Collection

The CPP represented an enormous undertaking during which approximately 55,000 pregnancies were registered over a 6-year period; and, subsequently the liveborn were followed during the first seven years of life. To accurately record information on the family, genetic, and obstetrical histories of the parents as well as to accurately document the outcomes of pregnancies together with the growth and development of the children, it was necessary to create standardized data collection forms which could be easily used by hospital clinic and study staff. A critical issue was that these data forms should permit easy transfer to computer retrievable forms, and correspondingly allow for easy coding and validation of the collected information. Appendix B lists the various data forms on which information was collected on the gravida, her pregnancy and delivery.

On entry to the study, usually while visiting the participating clinic the first time during pregnancy, each woman was interviewed by a specially trained examiner to obtain medical, genetic, social, and work history data. Specifically with regard to medications, the women were questioned about current drug use as well as drug use extending back beyond the date of the last menstrual period. Detailed, structured forms were used, and the data collection procedure was guided by the use of extensive manuals. Initially, at monthly visits to the clinic, and then at shorter intervals during the last trimester, interviewers and obstetricians continued to collect data. The completed study forms were then reviewed and compared with hospital records for completeness by another person. If the woman had received medical attention before entry into the study, further information on events taking place prior to registration was acquired from "non-study" physicians, and from other hospitals to complement and verify certain items of interview data. Completed forms were once more edited in the study hospital, this time by attending medical personnel. The assembled materials were then sent to a central facility where it was processed into computer files. Various precautionary measures were taken to prevent coding and punching errors in the massive flow of data. In addition, certain computer procedures were routinely used to identify and correct obvious mistakes in the original computer files.

Information routinely collected included data on maternal diseases during pregnancy, characteristics and abnormal conditions of pregnancy, reproductive history, and social and environmental characteristics of the mother.

Information on the offspring was collected from birth. Data concerning the child's birth, development, any diseases that occurred, and any congenital defects that were noted were collected, according to a systematic design, up to the eighth birthday.

The first period of systematic data collection covered the baby's stay in the hospital. Under surveillance, the baby was examined by a pediatrician every day during the first week after delivery, or weekly if the child remained in the hospital longer. In addition to the detailed forms, a summary for the nursery period was produced locally.

The mother was interviewed for what was termed an "interval history" when the child was 4, 8, 12, 18, and 24 months old, and thereafter, annually. If, in the interim, the child had been taken to a physician or a hospital, further data about the child's illness were acquired from these sources. An extensive, standardized pediatric examination was performed on the children at the age of one year. The response rate for the one-year examination was 91% in the surviving children. For most of the remaining children, an interval history was available. Finally, of 2,227 children who were stillborn, or who died before the fourth birthday, 81% came to autopsy; the autopsy rate did not vary appreciably according to the age at death.

Limited information on the child's siblings, father and other relatives was also obtained.

To help insure the collection of valid and reliable information the NINCDS conducted workshops for study staff members as well as creating films describing how to perform selected physical examinations. Close contact was maintained between the NINCDS and the various collaborating centers, to minimize difficulties arising in the collection of data and the follow-up of the women and their children.

One form of data validation was that a study case, once completed, had its information verified with the corresponding hospital records by an individual who was not part of the original data collection plan. Only after this check were the forms submitted to the Perinatal Research Branch, (PRB), and further edited by PRB medical personnel.

Accuracy of the collected data was assessed by the PRB and details describing this validation check can be found in (73). As a result of this validation review, it was determined that an insignificantly small number of patients had missing information from both the study and hospital records. This validation study described in (73) concluded that the CPP contained extensive and detailed information not available in other hospital records, and that the information gathered as part of the CPP had a high standard of completeness in the two centers which were evaluated.

From a methodologic point of view, it is significant to note that data collection efforts were not planned on the basis of a priori established hypotheses. Therefore, the issue of information bias for all practical purposes can be disregarded in the study of occupation and pregnancy outcome.

2.2 Occupational History Information: Questionnaire Description

For the purposes of the present study, the CPP cohort was subdivided into two groups for the required examination of occupational histories. This was necessary due to a change in the form on which occupational histories were collected midway through the period of data collection.

The original form, the FHHL form, sought information on work history of gravida and husband or father of the baby (see Appendix C). In section B of the FHHL form, questions pertaining to current or previous occupations of the gravida, such as job description, hours worked per week, length of time on the job, and the date that the gravida stopped working, if she is no longer working, were asked. Inquiries were also made into other previous occupations.

In section D of the FHHL form, the gravida was questioned about the work history of the husband or father of the baby. Questions were asked concerning the description of his occupation, length of time on the job, previous employment and unemployment.

The form which replaced the FHHL form, the SE1 form, sought similar information in the sections dealing with employment (see Appendix C). Section D of the SE1 form inquired about the gravida's work history. This included job description, hours worked per week, and length of time worked on the job for current or previous jobs, and the date that the gravida stopped working if she is not currently employed. Questions concerning past employment were also asked. In addition, the SE1 form has a section dealing with occupational hazards for the gravida.

Section G of the SE1 form describes the work history of the husband or father of the baby. Questions concerning current or previous employment were included along with questions about unemployment.

2.3 Reproductive Outcomes

A large amount of information was collected on each pregnancy outcome (livebirth or death). Among the array of outcomes recorded by the CPP were birthweight, stillbirth, neonatal or infant death, physical congenital malformations, and various psychomotor tests.

Of interest in the current study of occupation are well-defined outcomes, such as death or physical congenital malformation. A large number of congenital malformations were originally recorded in the CPP. Some of these malformations

were of minor importance, and their observation was likely to vary greatly due to their subjective nature. Examples of these, include dislocation of the fifth toe, cleft uvula, and accessory nipple. These malformations were excluded from analysis because of their variability by hospital, and their minor importance.

In addition, the distributions by hospital of all remaining malformations were compared to determine whether any of them showed grossly variable rates. Six malformations were found to vary considerably by hospital, but were considered important, and therefore, were included in analysis. The malformations, indicated as "non-uniform" malformations, (see reference 13), were inguinal hernia, club foot, cleft gum, pectus excavatum, urethral obstruction, and abnormalities of the hands and fingers. The vast majority of malformations, referred to as the uniform malformations, were more evenly distributed by hospital.

The malformations used in the present study were identified in: stillborn children of pregnancies lasting at least 5 lunar months; liveborn children during the first year of life, whether or not they died during that year; and children who died between the first and fourth birthday. Malformations were considered to be accurate when a diagnosis was noted in at least two of the following independent computer files: nursery period summary; summary of the period after discharge from the nursery up to and including the examination at one year of age; and the autopsy file. When diagnoses were not identical in the various files, or when they were only recorded in one of them, the original case records were reviewed by hand and the malformation was only considered to be acceptable if the record was unequivocal.

Malformations of the cardiovascular system were ascertained in a somewhat different manner than were the other malformations. This procedure has been well described elsewhere (76). Briefly this procedure included a detailed review of all files for diagnoses of definite or possible cardiovascular defects; a detailed search of medical clinic files to ensure that no cardiovascular defect escaped recording in the CPP data forms; re-examination of all children who were suspected of having any cardiovascular defect by a qualified cardiologist; inclusion of children in whom cardiovascular defects were first diagnosed after the age of four; and re-examination of the preserved hearts in 35% of the autopsied children.

2.4 Concomitant Variables

Together with abstracting information on parental occupation and outcomes of pregnancy, data on a number of other (concomitant) variables were reviewed, and stored on computer files for possible use during the data analysis stage of the project. These variables included information broadly categorized as:

- Characteristics and complications of the pregnancy (such as hyperemesis gravidarum, and single umbilical artery)
- Environmental factors (such as cigarette smoking or antenatal exposure to x-ray)
- Genetic factors (such as family history of malformations)
- Maternal diseases present during pregnancy (such as toxemia)
- Administrative Data (such as hospital and time of entry into study)
- Personal characteristics of mother (such as age and ethnic group)
- Reproductive history of the mother (such as parity and number of prior livebirths with birth defect(s))

Although a major purpose of the present study was to review the CPP data to generate hypotheses which can be more intensively studied, a central methodologic consideration was to eliminate selected concomitant (i.e., confounding) variables as possible explanations of any observed associations. As described below in section 3.3.2 for various reasons, the control of potential confounding bias was restricted to the "screening" stage of the project. A two-fold strategy was adopted, first in the design to (frequency) match cases and controls, and, secondly, in the analysis to adjust the estimated summary measures of association for selected concomitant variables.

3.0 Methods of Procedure

As mentioned above, the present study adopts a case-control epidemiologic study design to explore the association between parental occupation and adverse reproduction outcome. An analytic goal was to determine the prevalence of various occupations (and industries) within groups of pregnancies resulting in outcomes deemed to be either "adverse" or otherwise "normal". The case-control format adopted for these study purposes was based on data gathered as a result of a cohort study, whose duration was a total of 13 years (time to register women plus seven years to fully monitor the growth and development of the offspring). Under the time and cost constraints of the present study, this approach resulted in marked efficiencies with respect to the number of accessed (original medical) files to obtain information on parental occupation.

As part of the original protocol, associations identified during the screening stage were to be further explored using multivariate statistical procedures. However, this latter stage was eliminated due to the relatively small number of positive significant associations with adequate number of observations in the ("intersecting") group having a particular adverse outcome and having worked at a particular occupation or industry during pregnancy. Unlike many cohort studies, a motivation for applying multivariate statistical techniques is absent in the present case-control study - namely, the quantitative description of the epidemiology of an event. For a further discussion of the relevant aspects of this strategy, see (13). Consequently, the primary analytic approach which has been adopted is that related to stratification (described in section 3.3).

3.1 Selection of the Study Sample

3.1.1 Exclusions from Present Study

It was necessary to further restrict the available CPP cohort of 52,931 pregnancies. A total of 14,742 pregnancies were eliminated from the CPP cohort prior to the selection of the present study sample for a variety of reasons. These reasons are listed in table 3.

An additional twenty pregnancies were excluded due to the inability to match the pregnancy outcome information with the occupational information. After all the necessary exclusions were made, 38,169 CPP pregnancies were available as potential cases and controls.

Table 3

Exclusions from the CPP Cohort

<u>Description of Cohort</u>	<u>Reason for Exclusion</u>	<u>Number</u>	
		<u>Included</u>	<u>Excluded</u>
Total registered pregnancies		58,828	
	Non-care pregnancies		2,622
	Walk-in pregnancies		298
Pregnancies conforming to sampling scheme		55,908	
	Refusal and loss to follow-up		2,977
Available cohort		52,931	
	Exclusions for the purposes of this report (reasons may be overlapping):		14,742
	-small race groups		
	-multiple births		
	-clinical rubella during pregnancy		
	-congenital rubella syndrome		
	-therapeutic abortion		
	-complications of gestation		
	-not examined for malformation		
	-drug use unknown		
	-unknown sex of offspring		
	-birth weight unknown or less than or equal to 250 grams		
	-unknown previous pregnancy		
	-lack of occupational history form		
	-SE-1 form present prior to 1963		
	Unable to match information		20
Pregnancies available for study sample		38,169	

3.1.2 Selection of Cases

Any of the 38,169 available pregnancies that resulted in either an abortion, a stillbirth, a neonatal death, or an infant death, or any malformation (see Appendix E for the list of malformations included in this report) was

eligible for selection as a "case" pregnancy. It was possible for a mother to have more than one "case" pregnancy.

There were 5,333 eligible cases, and all were included in the study sample. These 5,333 "case pregnancies" included 3,186 malformed children and 2,569 deaths (these two categories are not mutually exclusive). The list of cases by death and major malformation categories is given in Table 4.

Table 4

Frequency of the Various Adverse Reproductive Outcome Categories among the Study "Cases" (Death and Malformation Categories are not Mutually Exclusive).

<u>Adverse Reproductive Outcome</u>	<u>Number</u>
Deaths under one year of age:	2,569
Abortions	659
Stillbirth	763
Neonatal Death	772
Infant Death	375
Total Malformations	3,186
Musculoskeletal malformations	871
Eye and ear malformations	119
Respiratory malformations	409
Gastrointestinal malformations	959
Cardiovascular malformations	408
Genitourinary malformations	404
Tumors	158
Central nervous system malformations	262
Syndromes	170

3.1.3 Selection of Controls

Any of the 38,169 pregnancies that did not result in either an abortion, stillbirth, neonatal death, or infant death, or any malformation, for which the gravida did not have a "case pregnancy", for which the birth weight of the child was greater or equal to 2500 grams, and for which the IQ of the child was greater than 80 was eligible for selection as a "control pregnancy." There were 25,705 pregnancies that met these criteria.

An approximately two to one frequency matching of controls to cases was performed on the basis of weeks of gestation at time of entry into study, the number of the study pregnancy, and the type of occupational history form present. (Matching on the presence of occupational history form also implicitly

matches on year of entry into the CPP as the FHH-1 was used only through 1962, and all mother-child pairs with a SE-1 form filled out prior to 1963 were excluded). Two controls were matched to each case because matching with multiple controls is advantageous when the number of potential controls is large relative to the number of available cases, especially when "little" effort must be expended to obtain the necessary information on the controls. Also a 2:1 matching ratio fulfilled the time and cost constraints of the study.

There were 10,270 pregnancies selected as "controls" from the 25,705 eligible pregnancies. An exact two to one match was not obtained because of small frequencies in some of the matching categories.

3.2 Determination of Occupational Status

3.2.1 Creation of Occupational History Data File

3.2.1.1 Abstraction of Occupational History Information

Although information on occupational titles was available on the CPP Master Computer data files, due to the very broad categories used by the NINCDS this information was considered to be inadequate for the performance of the current project. Therefore, it was necessary to review the original CPP records on-site at NINCDS to abstract both maternal and paternal occupational titles and job descriptions, as originally recorded. Occupational titles and job descriptions were abstracted verbatim (see Appendix D for a copy of the data abstraction form). The items that were abstracted from the original CPP records along with the systematic procedure for their abstraction are also given in Appendix D. Copies of the original FHH-1 and SE-1 forms are presented in Appendix C. Available occupational history information other than job title and description were obtained directly from the CPP master computer data files.

To measure the quality of the data abstraction procedures, a random sample of 139 abstracted occupational histories were reviewed and compared to the original CPP records. There was complete concordance between the data abstracted and that on the original form.

At the writing of this report, information on 614 study pregnancies (cases and controls) had not been abstracted. The records on these pregnancies were off-site (away from NINCDS) and, thus, were not available to the investigators.

3.2.1.2 Description of the Occupational Dictionary and Coding Procedure

A modified version of the occupational dictionary and coding scheme developed by Hoar, Cole and Morrison (see Appendix F) was used in the present study to code occupational titles and job descriptions. This coding scheme classifies an individual according to the industry in which he/she is employed, and within that industry by the task which he/she performs. The modified version of the occupational dictionary contains 19 industrial categories. There are 450

possible industry specific occupational codes. The complete dictionary is presented in Appendix F.

In this method of coding, the industrial category is represented by the first two digits of a five digit code. The remaining three digits designate the task or occupation within that industry. The three digit task code is based on the occupational title number designated in the United States Dictionary of Occupational Titles (74). For the present study, certain modifications have been made.

The coding of occupational histories was performed at the University of Massachusetts/Amherst, Division of Public Health. The quality of the coding procedure was performed by reviewing and verifying a randomly selected sample of coded forms. This evaluation indicated that these data were being satisfactorily coded.

3.2.2 Defining Maternal Occupational Status

Each woman was classified at the time of the occupational interview as never having worked, having worked in the past but not currently employed, or employed at the time of the interview. The occupational histories along with the date that the mother was last employed (if she is no longer working), the length of time on her current or most recent job, the date of the interview in which the occupational information was collected, the date of birth or termination of the pregnancy, and the length of gestation at birth or termination of the pregnancy were used to determine the mother's exposure status.

For a woman who worked in the past, but was not currently employed at the time of the interview, the date of last employment and the length of time on that job was compared to the period of pregnancy (computed from the date of birth and the length of gestation) to determine if she worked during pregnancy, and, if so, during which trimesters. For a woman who was working at the time of the interview, the date of that interview and length of time on that job was compared to the period of pregnancy to determine when during the pregnancy she worked. (The occupational interview necessarily took place after conception. However, there was no fixed time during the study pregnancy that the interview took place. The point of gestation at which the interview took place was dependent on such factors as the length of gestation on admission to the study).

After determining the period of exposure for each woman, five exposure categories were created. The first category included the women who never worked or who were students at the time of the interview. The women who had worked at one time, but who had not worked within two months prior to the study pregnancy or during the study pregnancy up to the time of the interview made up the second category. Women in the third category had worked within the two months prior to their study pregnancy, but quit their jobs before conception, and did not work at any time during the pregnancy up to the time of interview. The fourth category consisted of the women who worked at any time during the first trimester of pregnancy. The fifth category was composed of women who were known to have been employed during the second and third trimesters, but whose first trimester exposure status was unknown. (Since the CPP occupational information contained dates worked for only the current or most recent occupation, any woman who started a new job during the second or third trimester will have no dates of

employment for her previous job, if any. Therefore, no information on the first trimester exposure status would be available).

Assuming that maternal exposure prior to conception would not adversely affect the fetus, the women who worked prior to two months before conception (category 2) were combined with the women who never worked (category 1) to comprise the "non-exposed" (non-employed) category. (Since there was no information on employment available after the interview date, it is possible that some of these women may have returned to work or started working after the interview date, and therefore, would not truly be non-exposed). The women who were known to have worked at some time during the first trimester (category 4) made up the "exposed" (employed) category. The women who worked during the two months prior to pregnancy but not during pregnancy (category 3) were excluded from analysis due to possible "carry over" effects of some maternal exposures, and also because of the approximate measure of length of gestation used to determine period of pregnancy (length of gestation was computed using the date of the last menstrual period). The women who worked in the second and third trimester, but had an unknown first trimester exposure (category 5) were excluded from further analysis so that the period of exposure would be known more precisely, and could be more readily defined.

Each woman who was defined as "exposed" was further grouped according to the industry and task in which she was employed during the study pregnancy.

The present study's attention was restricted to exploring the reproductive effects of first trimester occupation due to the time and cost constraints within which this study was to be performed. Also, it was recognized that teratogenic and other adverse outcomes of pregnancy develop most often during earlier gestation, when the developing fetus is "at greatest risk."

For the screening analysis performed in this study, an "inappropriate maternal exposure" refers to any maternal occupational exposure which was classified in either category 3 or category 5 above.

3.3 Data Analysis

3.3.1 An Overview: Epidemiologic Considerations

In undertaking an epidemiologic study of reproductive outcomes in relation to suspected risk factors, certain major issues related to non-experimental studies should be addressed - including the control of bias, measuring the associations, and assessing the role of chance.

3.3.1.1 Sources of Potential Bias

In epidemiologic studies, one of the principal concerns is possible bias. In the identification of statistical associations between occupation and reproductive outcome, consideration should be given to whether the increases in the observed relative risk estimates can be attributed to bias. In general, there are three forms of bias which are addressed in a study of this type.

Each form of bias can produce false associations between an occupational exposure and an adverse reproductive outcome, and each can obscure the true level of association.

"Observation" or "information" bias may arise in a cohort study when information on reproductive outcome is obtained or measured differently for children (or fetuses) of "exposed" and "non-exposed" women. (Although the present study follows a case-control format, the CPP data were originally collected in a cohort fashion, so that bias associated with cohort studies should be considered). The likelihood that "observation" bias exists in the present study is negligible, since data were collected prior to (and ignorant of) any specification of hypotheses involving occupation and reproductive outcome. In addition, data on occupation were gathered prior to termination of pregnancy.

A second form of bias, "selection" bias, may occur if subjects are identified or recruited for study on the basis of their exposure status. It appears unlikely that "selection" bias occurred in the identification and recruitment of the study cohort. There is no indication that women were recruited for the study on the basis of their occupation.

Thus, the single most relevant form of potential bias which must be considered, in the current study, is that of "confounding" bias. "Confounding" bias arises when some third factor, or set of factors, either is responsible for some indirect association between an exposure (occupation) and an adverse reproductive outcome, or conceals a direct association. There is a potential for confounding bias in epidemiologic studies. Confounding bias may arise from many sources, and its nature can be complex and subtle.

In the current study, control of selected potential confounding variables were controlled during the matched selection of controls to cases (see above) and, during data analysis. Analytic control of confounding effects can be accomplished by a variety of methods, these methods have in common the objective of achieving comparability between the various exposure groups (in a cohort study), or the categories of reproductive outcome (in a case-control study).

3.3.1.2 Measures of Association

In the study of risk factors (such as occupation) in relation to reproductive outcome, a useful measure of association is the point estimate of relative risk. The relative risk can be defined as the ratio of the rate of a particular reproductive outcome in "exposed" pregnancies to the rate of "non-exposed" pregnancies. Due to the "case-control" viewpoint being adopted in the proposed study, relative risk, as is traditional in case-control studies, will be estimated via relative odds (or odds ratios).

In non-experimental epidemiologic studies the possible existence of confounding bias must be considered in the evaluation of any association. Since it is never possible to rule out confounding bias with complete confidence, it is never possible

to measure with precision the effects of chance. For this reason the interpretation of tests of statistical significance in a non-experimental study must be carried out with extreme caution.

The limitations inherent in performing many tests of statistical significance should be stressed. It is well recognized that the actual "p values" rises significantly as the number of statistical tests increases. In the present study, therefore, statistical significance will be used as a general guide to help identify associations between parental occupation and reproductive outcomes which may warrant further study. For example, due to the large numbers of possible reproductive outcomes, and occupational categories, any statistical screening procedure used to detect meaningful associations will involve literally hundreds if not thousands of statistical tests of significance. Clearly a number of "statistically significant" associations are bound to arise by chance; without recourse to other data, there is no way to identify which associations might be explicable on this basis, and which may be "causal", if any.

The results of the screening analysis are given both in terms of crude (observed) odds ratios, and corresponding odds ratios adjusted for several concomitant variables (hospital, age, and race). Comparisons of these two measures also can help to assess whether a particular association potentially is meaningful.

3.3.2 Screening for Associations Between Maternal Occupation and Adverse Reproductive Outcome

Data analysis involved bivariate statistical methods. To identify possible associations between adverse reproductive outcomes and parental occupation, a traditional 2x2 contingency table format was employed. Crude measures of relative risk (odds ratio denoted as OR) were obtained to summarize each association. However, it is well recognized that a two dimensional statistical analysis is often inadequate for investigating complex associations such as occupational effects on the developing fetus. Thus, the procedure proposed by Mantel and Haenszel (75) was applied to control for certain potential confounders. This stage of analysis considered the possible influences of age, race, and hospital. The measures of associations obtained at this level of statistical analysis were age-race and hospital standardized relative risk estimates. Although frequency matching was employed in subject selection, the matching was not taken into account in the screening analysis.

A Chi-square test of statistical significance was performed when the expected number of "exposed" pregnancies within a particular outcome was greater than 2. Otherwise, a binomial approximation to the hypergeometric distribution was used to test for statistical significance. The screening procedure produced contingency tables for each adverse outcome and occupation. For each adverse reproductive outcome, a summary table was created that included the number of "exposed" pregnancies with the particular outcome in each occupational category, and the total number "exposed" in each occupational category, the unadjusted odds ratio, and the age-race and hospital standardized odds ratios for each occupational category and the results of the appropriate statistical tests (see Appendix J).

For each outcome group (category), the number of non-exposed (i.e., "non-employed") women for both the case and control series was constant. Thus, each 2x2 contingency table, within each malformation or other "adverse outcome" group uses the same number of "non-exposed" cases and "non-exposed" controls. Furthermore, for all outcomes, the number of controls who were "non-exposed" remained constant.

Each calculated single degree of freedom Chi-square statistic (presented in Appendix J) can be compared to the following critical values (of the Chi-square distribution) to determine the estimated "p-value": $X^2_{(1)} = 2.71$ ($p < 0.10$), $X^2_{(1)} = 3.84$ ($p < 0.05$), $X^2_{(1)} = 6.63$ ($p < 0.01$), $X^2_{(1)} = 10.8$ ($p < 0.001$).

For the purposes of the present report, an association is referred to as significantly elevated when the Chi-square test statistic or the binomial procedures indicates a probability (p-value) of less than or equal to 0.05. A marginal or borderline association refers to the situation where the Chi-square or binomial test indicates a p-value of less than or equal to 0.10, but greater than 0.05.

A total of 267 malformation categories and 3 categories of death were available for analysis in the present study. However, only those adverse outcome categories with more than five "exposed" pregnancies were included in the screening.

Certain occupational categories were also excluded during the screening. Any industry or occupational category with fewer than 15 "exposed" pregnancies was excluded from subsequent analysis. In addition, there were exclusions specific to each comparison of occupation and adverse outcome (that is each contingency table). If a comparison had fewer than one expected and two observed adverse outcomes for an occupation category, that comparison was excluded from the summary table for that particular outcome.

4.0 Results of Screening Maternal Occupational Exposure

4.1 Composition of Study Sample

There were 10,270 control pregnancies selected for inclusion in the present study, the distributions of maternal age and race, and hospital of birth among the control pregnancies is presented in tables 5 to 7.

Table 5

Distribution of Maternal Age for
the 10,270 Control Pregnancies

<u>Maternal age (Years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	75	*
15-19	2,074	20
20-24	3,655	36
25-29	2,273	22
30-39	2,006	20
<u>40 and older</u>	<u>187</u>	<u>2</u>
all ages	10,270	100

*Less than one percent.

Table 6

Distribution of Maternal Race Among
the 10,270 Control Pregnancies

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	5,042	49
Black	4,631	45
<u>Puerto Rican</u>	<u>597</u>	<u>6</u>
All races	10,270	100

Table 7

Distribution of Hospital of Birth Among
the 10,270 Control Pregnancies

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	2,383	23
BU	781	8
CH	542	5
CO	505	5
JH	766	7
VA	542	5
MN	663	6
NY	726	7
OR	620	6
PA	1,514	15
PR	530	5
TN	698	7
All hospitals	10,270	100

4.1.1 Exclusions from Screening Analysis

Although the original study sample consisted of 5,333 case pregnancies, the abortions were not included in the present analysis due to the quality of the abortion data. In particular, the pregnancies which terminated prior to 20 weeks gestation (abortions) were underrepresented in this study, since the majority of the pregnancies were registered when they were well beyond their 20th week of pregnancy. This reduced the number of case pregnancies to 4,674, and the total sample to 14,944 pregnancies.

Of the remaining 14,944 pregnancies, 1,906 pregnancies were excluded prior to the screening analysis. The reasons for these exclusions are described in section 3.2.2. There were 1,689 pregnancies excluded, since they did not meet the criteria for having a first trimester "exposure." Unknown occupation resulted in the exclusion of another 216 pregnancies. One additional pregnancy was excluded because the woman's occupation was included in an industrial category with fewer than 15 exposed women.

Certain exclusions were also made during the screening stage. Outcome categories with fewer than 6 "exposed" women were excluded during the screening analysis. However, this did not result in the exclusion of any additional pregnancies from the overall screening, because the adverse pregnancy outcome categories were not mutually exclusive. Thus, all pregnancy outcomes were included in the more general major malformation categories (e.g., any cardiovascular, musculoskeletal, etc. malformation).

After these exclusions, there was a total of 4,022 case pregnancies and 9,016 control pregnancies available for screening. The frequencies of the major outcome categories for both included and excluded pregnancies are presented in table 8. Fourteen percent of all case pregnancies were excluded from screening, while, 12 percent of the control pregnancies were likewise excluded. The frequencies of the included and excluded pregnancies for each outcome and major category is presented in Appendix G.

Table 8

Frequencies of the 14,944 Study Pregnancies for the Major Outcome Categories for Maternal Occupation Screen

<u>Outcome Category</u>	<u>Included in Screening</u>	<u>Excluded From Screening</u>	<u>Total</u>
Control Pregnancies	9,016	1,254	10,270
All case pregnancies	4,022	652	4,674
All deaths under one year	1,641	269	1,910
Stillbirth	666	97	763
Neonatal death	653	119	772
Infant death	322	53	375
All malformations*	2,747	439	3,186
Musculoskeletal	747	124	871
Eye/Ear	101	18	119
Respiratory	342	67	409
Gastrointestinal	828	131	959
Cardiovascular	347	61	408
Genitourinary	353	51	404
Tumors	143	15	158
Central Nervous System	222	40	262
Syndromes	141	29	170
Total	13,038	1,906	14,944

*Since the major malformations are not mutually exclusive, the category totals will not sum to the total malformations.

4.2 Distribution of Maternal Occupations

During the screening analysis, many of the related industry-specific occupational categories were combined due to the small numbers of exposed pregnancies in some categories. The resulting categories along with the occupations included in each category are presented in Appendix H. A total of

18 industrial and 104 industry-specific occupational categories were used to classify the occupations in the case and control series. The distribution of maternal occupations among all pregnancies included in the screening is presented in table 9.

Of the 13,038 pregnancies remaining after all of the exclusions described previously, the current occupation (if the woman is employed at the time of the interview) or the most recent occupation (if the woman was employed at some time in the past, but not at the time of the interview) was known for 10,838 (83%) of these pregnancies. An additional 1,838 (14%) of these women had never worked or were listed as students. Only 362 (3%) had an unknown current or most recent occupation.

Of the 10,838 women with known occupation, the most commonly reported industrial category that was used in the present study was the low chemical exposure industries with 3,758 (35%) of these women included in this category. The second and third most commonly reported industries were food and tobacco and textiles with 1,696 (16%), and 1,393 (13%) of the women with known occupation included, respectively.

The most frequent industry-specific occupations in the present screening analysis were office work in an industry with a low chemical exposure which employed 1,263 (12%) of the 10,838 women with known occupation. Domestic occupations and waitressing, which employed 1,187 (11%) and 792 (7%) of the women with known occupation respectively, were the second and third most common occupations for the women included in the present study. The frequency and percentages for all occupations and industries are presented in table 9.

Table 9

Distribution of Industries and Occupations Among
the Pregnancies Included in the Analysis of Maternal Exposure

<u>Industry and Occupational Category</u>	<u>Frequency</u>	<u>Percent</u>
Total pregnancies included	13,038	100
Total with known occupation	10,838	83
Never worked (students)	1,838	14
Unknown occupation	362	3
Agriculture, Forestry, Fishing	81	*†
Office work	21	*
Plant farming	32	*
Animal farming	10	*
Fishery and related occupations	11	*
Other farming and related work	12	*

*Less than 1%

†All subsequent percentages are based on the total number of women with known occupation (n=10,838).

Table 9 Continued

<u>Industry and Occupational Category</u>	<u>Frequency</u>	<u>Percent</u>
Construction	22	*
Office work	22	*
Paper and Wood	248	2
Office work	91	*
Production and processing	9	*
Paper working	68	*
Printing Occupation	17	*
Wood product fabrication	6	*
Material handling	57	*
Clay, Glass, Stone	34	*
Office work	8	*
Processing and production	7	*
Product fabrication	9	*
Material handling	10	*
Metal	107	1
Office work	31	*
Metal working and machining	18	*
Processing and production	45	*
Material handling	13	*
Machinery and Electrical	244	2
Office work	105	1
Metal working and machining	14	*
Metal products and fabrication	12	*
Electrical products fabrication	178	2
Other production	15	*
Material handling	20	*
Transportation	140	1
Office work	92	*
Stewardess	10	*
Motor vehicle manufacturing	24	*
Garage work, drivers	14	*
Food and Tobacco	1,696	16
Office work	73	*
Clerks and cashiers	125	1
Processing	111	1
Other Production	14	*
Domestic cooks	15	*
Waitress	792	7
Bartender	32	*
Cooks (Establishments)	107	1
Other food service occupations	234	2
Material handling	193	2

*Less than 1%.

Industry and Occupational Category	Frequency	Percent
Textiles	1,393	13
Office work	80	*
Sales	58	*
Processing	172	2
Textile Machining	95	*
Sewing	419	4
Other fabrication of textile products	65	*
Other production	45	*
Laundry	273	2
Other textile service occupations	31	*
Material handling	156	1
Chemicals, Drugs, Paints	66	*
Office work	27	*
Processing and production	22	*
Material handling	17	*
Rubber, Plastics	125	1
Office work	18	*
Processing	18	*
Machine trades	15	*
Rubber, plastic products fabrication	51	*
Material handling	23	*
Fuel	24	*
Office work	24	*
Leather	152	1
Office work	19	*
Sales	9	*
Leather products fabrication	94	*
Processing and production	16	*
Material handling	14	*
Medicine and Science	1,201	11
Laboratory occupations	70	*
Nurses	206	2
Dental assistants and technicians	28	*
X-ray technicians	17	*
Nurse's aides	332	3
Other medicine and health	32	*
Office work	168	2
Housekeepers	55	*
Hospital laundry	11	*
Hospital kitchen service	282	3
Entertainment	178	2
Dance, drama, music	40	*
Office work	15	*
Hairdressers	123	1

*Less than 1%.

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Table 9 continued

<u>Industry and Occupational Category</u>	<u>Frequency</u>	<u>Percent</u>
Miscellaneous Occupations	553	5
Office work	34	*
Art occupations	30	*
Photography occupations	16	*
Engraving	10	*
Fabrication of products of assorted materials	366	3
Book binders	16	*
Material handling	81	*
Unknown Industry	712	7
Office work	473	4
Switchboard operator	9	*
Sales	31	*
Stitching	72	*
Factory work	55	*
Laborer	34	*
Material handling	38	*
Low Exposure	3,758	35
Students	79	*
Teachers	276	2
Librarians	35	*
Managers and professionals	93	*
Office work	1,263	12
Switchboard operators	133	1
Sales	312	3
Domestic work	1,187	11
Personal services	54	*
Recreational attendants	28	*
Protective services	16	*
Building services	218	2
Material handling	64	*

4.3 Results of the Maternal Occupational Screening Analysis

Among the 9,016 controls available for screening, 3,487 had some maternal (first trimester) occupational exposure. The remaining 5,529 control pregnancies were considered non-exposed, and constituted the non-exposed control group which was utilized for each screening comparison in this report.

The major outcome categories for the screening analysis are listed in table 10 in the order in which they were analyzed.

Table 10

Major Adverse Reproductive Outcome Categories Screened
For Association with Mother's Occupation

<u>Adverse Reproductive Outcome</u>	<u>Number</u>
Stillbirths	666
Neonatal deaths	653
Infant deaths	322
Non-uniform malformations	949
Uniform malformations	2594
Musculoskeletal system malformations	747
Eye and ear system malformations	101
Respiratory system malformations	342
Gastrointestinal system malformations	828
Cardiovascular system malformations	347
Genitourinary system malformations	353
Central nervous system malformations	143
Tumors	222
Syndromes	141

4.3.1 Stillbirths

A total of 763 stillbirths were included in the 4,674 case pregnancies selected from the CPP cohort for the present report. Of these, only 666 were available for the screening analysis. The 97 stillbirths were excluded for the following reasons, all of which are due to inappropriate maternal occupational exposure: 80 were excluded because the mother did not have a known first trimester exposure and the mother did not meet the criteria to be included in the non-exposed category; 16 were excluded because maternal occupation was not known; and 1 was excluded because the maternal occupation was included in an industrial category with fewer than 15 exposed women. The distributions of maternal age and race, and hospital of birth are presented in tables 11 to 13 for those pregnancies which terminated in a stillbirth. The results of the screening for associations between maternal occupation and subsequent stillbirths are presented in Table A.1. in Appendix K.

Table 11

Distribution of Maternal Age Among the
763 Pregnancies that Terminated in a Stillbirth

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	9	1
15-19	122	16
20-24	218	29
25-29	172	23
30-39	209	27
40 and older	33	4
All ages	763	100

Table 12

Distribution of Maternal Race Among the
763 Pregnancies that Terminated in a Stillbirth

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	303	40
Black	396	52
<u>Puerto Rican</u>	<u>64</u>	<u>8</u>
All race	763	100

Table 13

Distribution of Hospital of Birth Among the 763
Pregnancies that Terminated in a Stillbirth

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	161	21
BU	38	5
CH	44	6
CO	30	4
JH	63	8
VA	54	7
MN	46	6
NY	63	8
OR	40	5
PA	147	19
PR	36	5
<u>TN</u>	<u>41</u>	<u>5</u>
All hospitals	763	100

Fifteen industrial categories are included in Table A.1 along with 48 industry-specific occupations. The most common industrial category among those pregnancies resulting in a stillbirth was that for the low exposure occupations. Domestic occupations was the most frequent occupation observed among the exposed mothers of stillborn children.

An elevated odds ratio was observed for textile processing occupations (OR = 3.1). This odds ratio was reduced only slightly when adjusted for age and race, and hospital of birth. Also, bartenders were noted to have significantly elevated odds ratios only after adjustment for age and race, and hospital of birth. However, the adjusted odds ratio did not differ greatly from the crude odds ratio and therefore these significant results were due to the use of the chi-square test with fewer than two expected pregnancies. In addition the number of women who worked as bartenders and experienced a stillbirth was very small (n=3).

4.3.2 Neonatal Death

Among the 4,174 cases selected for study, there were 772 neonatal deaths. However, 111 neonatal deaths were excluded for reasons related to the period of maternal exposures (mentioned above in section 3.2.2). An additional 8 deaths were excluded due to unknown occupation among the exposed women. The distributions of maternal age and race, and hospital of birth are presented in tables 14 to 16 for those pregnancies that resulted in a neonatal death. Results of the screening for associations between neonatal death and occupation are presented in Table A.2.

Table 14

Distribution of Maternal Age Among the 772
Pregnancies Resulting in a Neonatal Death

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	7	1
15-19	175	23
20-24	264	34
25-29	150	19
30-39	162	21
40 and older	14	2
All ages	772	100

Table 15

Distributions of Maternal Race Among the 772
Pregnancies Resulting in a Neonatal Death

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	287	37
Black	432	56
Puerto Rican	53	7
All race	772	100

Table 16

Distribution of Hospital of Birth Among the 772
Pregnancies Resulting in a Neonatal Death

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	136	18
BU	31	4
CH	42	5
CO	27	3
JH	58	8
VA	39	5
MN	28	4
NY	73	9
OR	52	7
PA	192	25
PR	43	6
TN	51	7
All hospitals	772	100

Fifteen industrial and 46 industry-specific occupational categories are included in table A.2. The most common industrial and occupational categories for exposed women whose pregnancies resulted in a neonatal death are the low chemical exposure industrial category and the domestic work category.

A positive association ($OR = 2.4$) was observed between laundry workers and neonatal death. Although the age-race and hospital adjusted odds ratios were slightly reduced in magnitude, they were still statistically significant. The hospital adjusted odds ratio ($OR = 2.2$) for electrical products fabrication occupations was also significantly elevated.

4.3.3 Infant Death

Of the 375 infants in the present sample who died during the first year of life, 332 were available for the screening analysis. Period of maternal exposure other than first trimester was responsible for 46 exclusions. Unknown occupation accounted for another 7 exclusions. The distributions of maternal age and race and hospital of birth are presented in tables 17 to 19 for those pregnancies that resulted in an infant death. Results of the screening for associations between infant death and maternal occupation are presented in table A.3.

Table 17

Distribution of Maternal Age Among the 375
Pregnancies Resulting in an Infant Death

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	3	1
15-19	101	27
20-24	164	44
25-29	63	17
30-39	31	8
40 and older	13	3
All ages	375	100

Table 18

Distribution of Maternal Race Among the 375
Pregnancies Resulting in an Infant Death

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	125	33
Black	225	60
Puerto Rican	25	7
All race	375	100

Table 19

Distribution of Hospital of Birth Among the 375
Pregnancies Resulting in an Infant Death

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	52	14
BU	5	1
CH	23	6
CO	8	2
JH	21	6
VA	25	7
MN	23	6
NY	39	10
OR	34	9
PA	88	23
PR	27	7
TN	30	8
All hospitals	375	100

Thirteen industrial categories and 20 industry-specific occupational categories were included in the screening for infant death. The most common industrial category for the exposed mothers of children who died during the first year of life was the low chemical exposure occupations, while domestic occupations were the most frequent occupations observed among these women.

A significantly elevated odds ratio (OR = 2.0) was observed for waitresses. This odds ratio was fairly constant when adjusted for age and race, and hospital of birth.

4.3.4 Any Congenital Malformation

There was a total of 3,186 children with malformations who were included as cases in the present study. A total of 7,770 malformations were present among these 3,186 malformed children. Only one malformation was present for 1054 (33%) of these children; 1418 (95%) had two malformations present, and 708 children (22%) had 3 or more malformations present (Table 20).

Table 20

Frequency of Malformations Among the
3,186 Malformed Children

<u>Number of Malformations</u>	<u>Number of Malformed Children</u>	<u>Percent</u>
1	1,054	33
2	1,418	45
3	234	6
4	206	6
5	59	2
6	47	1
7	35	1
8	31	1
9	24	1
10	17	1
<u>More than 10</u>	<u>61</u>	<u>2</u>
Total	3,186	100

Of these, 439 were excluded because of inappropriate maternal exposure which did not meet the criteria specified in section 3.2.2. Thus, the screening analysis included 2,747 malformed children. Although the potential problems that may arise from combining the non-uniform malformations (see Section 2.3) with the uniformly distributed malformations, were minimized by hospital standardization. These two sets of malformations were analyzed separately.

4.3.4.1 Uniform Malformations

Of the 2,747 children with any malformation, 2,594 had at least one uniform malformation present. Screening results for associations between uniform malformations and occupation are presented in table A.4. Seventeen industrial categories and 64 industry-specific occupational categories are included in this table. Again, the low chemical exposure occupations comprise the largest occupational category and domestic occupations are the most frequently reported occupations among the exposed mothers of children with uniform malformations.

Elevated crude odds ratios were observed for office work in the machinery and electrical industries (OR = 2.2), textile production workers, (OR = 2.5), office workers in the fuel industries (OR = 3.5), library workers (OR = 2.5), and domestic occupations (OR = 1.2). With the exception of the occupation domestics, odds ratios remained increased when standardized for age and race, and hospital. However, for domestics, the age-race odds ratio was no longer significantly increased.

4.3.4.2 Non-Uniform Malformations

Of the 2,747 children with any malformations 949 had at least one non-uniform malformation. The results of screening for associations between any non-uniform malformation and occupation are presented in table A.5.

Sixteen industrial categories and 56 industry-specific occupational categories are included in this table. The low exposure occupations are the most frequently observed among the exposed mothers of children with any non-uniform malformations, and domestic occupations are the most common occupations among these mothers.

Associations, which can be considered statistically borderline, were observed for art occupations (OR = 3.8) and hospital housekeepers (OR = 3.4). However, both of these associations are based on a small number of exposed mothers with malformed children ($n \leq 5$). The association between domestic occupations and the non-uniform malformations became significantly elevated (OR = 1.4) only after adjusting for hospital of birth.

4.3.5 Musculoskeletal System Malformation

Among the 3,186 children with any malformation included in the present study, 871 were diagnosed as having at least one musculoskeletal system (MS) malformation. Multiple malformations were present in 81 (9%) of the children. Of the affected children, polydactyly was the most common MS malformation occurring in 368 children. Syndactyly was also common being present in 119 children. Club foot, which showed variability in its hospital distribution, was diagnosed in 188 children. Table 21 lists the individual MS malformations.

Table 21

Frequency of Musculoskeletal System Malformations
Included and Excluded in Screening Analysis

<u>Malformation</u>	<u>Number Included</u>	<u>Number Excluded</u>	<u>Total</u>
Any musculoskeletal malformation	747	124	871
Polydactyly	310	58	368
Syndactyly	103	16	119
Congenital Dislocated hip	81	10	91
Absence of limb or part	28	2	48
Hypoplasia limb or part	40	8	48
Micronathia/hypoplastic jaw	18	2	20
Club foot*	159	29	188

*Non-uniformly distributed among CPP hospitals.

A complete description of the risk factors for the CPP MS malformations used in the present report has been published elsewhere (13). The distribution of children with MS malformations by maternal age and race, and hospital of birth are presented in tables 22 to 24.

Table 22

Distribution of Maternal Age Among the 871
Children with Musculoskeletal Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	14	2
15-19	181	21
20-24	313	36
25-29	191	22
30-39	153	18
<u>40 and older</u>	<u>19</u>	<u>2</u>
All ages	871	100

Table 23

Distribution of Maternal Race Among the 871
Children with Musculoskeletal Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	330	38
Black	503	58
Puerto Rican	38	4
All race	871	100

Table 24

Distribution of Hospital of Birth Among the 871
Children with Musculoskeletal Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	167	19
BU	54	6
CH	49	6
CO	63	7
JH	53	6
VA	57	6
MN	36	4
NY	43	5
OR	41	5
PA	200	23
PR	40	5
TN	68	8
All hospitals	871	100

Of the 871 children with MS malformations, 124 were excluded prior to the screening analysis for reasons related to maternal occupational exposure (see Section 3.2.2). The results of the screening on the remaining 747 children are presented in table A.6.

Fifteen industrial categories and 49 industry-specific occupational categories were present for this analysis. The low exposure industrial category was the most frequently reported industrial category by the exposed mothers of children with musculoskeletal malformations. Similarly, domestic occupations were the most frequent occupation observed among the exposed mothers of children with musculoskeletal malformations.

Significantly elevated odds ratios were observed for women who worked in material handling occupations for the textile industry (OR = 2.7), for hospital and medical office workers (OR = 2.0), for library workers (OR = 4.5), for domestic occupations (OR = 1.5), and for women in the low exposure personal service occupations (OR = 2.8). For each of these occupations the age-race and hospital standardized odds ratios were also significantly elevated with the exception of the domestic occupations which did have an elevated hospital standardized odds ratio, but no increase was seen when the odds ratio was age and race adjusted. The odds ratios for the library workers and personal service occupations were both based on small numbers of exposed mothers with affected children ($n \leq 5$).

In addition to the presence of any musculoskeletal malformation, 7 specific musculoskeletal malformations were reported in adequate numbers for the purpose of this screening analysis. These malformations, along with their frequencies, also are listed in table 21.

Polydactyly: Polydactyly was present in 368 children in the study sample. Fifty-eight of these children were excluded from the screening due to the lack of appropriate maternal exposure or occupational information as defined in Section 3.2.2. The screening results for the remaining 310 malformed children is presented in table A.7.

Table A.7 includes 13 industry and 28 industry-specific occupational categories. The low exposure industrial category and the domestic occupations were the most frequent industrial and occupational categories for the exposed mothers of children with polydactyly.

The unadjusted odds ratios for all mothers working in the food and tobacco industry (OR = 1.5), for cooks (OR = 3.8), for women working in material handling jobs in the textile industry (OR = 5.8), and for domestic workers (OR = 2.0) were all significantly elevated. However, only the textile material handlers showed any increased risk after controlling for age and race, and hospital. The observed association between cooks and polydactyly is based on a small number of exposed mothers with affected children ($n=5$).

Syndactyly: Syndactyly was reported in 119 of the study children. After exclusions for unknown or inappropriate maternal occupation or exposure, 103 children with syndactyly were available for the screening. The results of that screening analysis are presented in table A.8.

Seven industrial categories were included for this analysis along with 9 industry-specific occupational categories. The largest industrial category for the mothers of children with syndactyly was the low exposure occupations. Office workers in both the low exposure and unknown industrial categories were the most frequent occupations observed among the exposed mothers of children with syndactyly.

Elevated crude odds ratios were observed for all women in the unknown industry category (OR = 2.7) and for office workers in the unknown industrial category (OR = 3.4). These increases were consistent after adjustment for age-race and hospital. A borderline increase was observed for the miscellaneous occupational category (OR = 2.9). This association became statistically significant only after adjusting for age and race. However, this association was based on a small number (n=5) of exposed mothers with affected children.

Congenital Dislocated Hip: Congenital dislocated hip was reported in 91 of the children in the present study. Ten children were excluded from the screening analysis due to inappropriate or unknown maternal exposure. The results are presented for the 81 remaining children with congenital dislocated hip in table A.9.

Seven industrial and seven industry-specific occupational categories were included in this screening analysis. The low exposure industrial category and the low exposure office workers were the most frequently reported industrial and occupational categories among the mothers of the children with congenital dislocated hip.

Elevated crude odds ratios were observed for the medicine and science industrial category (OR = 2.8), and the hospital and medical office workers (OR = 7.8). These results were consistent for each of the adjusted odds ratios.

Borderline increases were also seen for the paper and wood industrial category (OR = 4.5). The odds ratios for nurse's aides became significantly elevated when adjusted for both age and race (OR = 5.5) and hospital (OR = 4.0). All the occupational associations observed for this malformation were based on small numbers of exposed mothers with affected children (n₄), with the exception of the medicine and science industry category.

Absence of Limb: Absence of a limb or part of a limb was noted in 30 study children. Two of these were excluded due to unknown occupation or inappropriate exposure, leaving 28 children for the screening analysis. The screening results are presented in table A.10. Among four industrial and two industry-specific occupational categories, the low exposure industrial category and domestic occupations were the most frequently reported by exposed mothers of children with the absence of a limb or part of a limb.

Only the age-race adjusted association between domestic workers and the malformed children was significantly elevated. However, this association was based on only 4 exposed mothers with affected children.

Hypoplasia of Limb: Hypoplasia of a limb or part of a limb was present for 48 study children. Eight of these children were excluded because of unknown or inappropriate maternal exposure or occupation. The screening results for the remaining 40 children are presented in table A.11.

Five industrial and three industry-specific occupational categories were available for this screening analysis. The low exposure industrial category and domestic workers again were the most frequently reported industrial and occupational categories.

No elevated odds ratios were observed for the occupations and industries included in table A.11.

Micrognathia/Hypoplastic Jaw: Micrognathia and/or hypoplastic jaw was reported in 20 children. Two children were excluded because of an inappropriate or unknown maternal exposure, leaving 18 children for the screening analysis. The results of this screening are presented in table A-12.

The low exposure industrial category and the teaching occupational category were the only categories available for this screening analysis. The teachers category demonstrated an elevated crude odds ratio (OR = 13.5). The standardized odds ratios were also elevated for the teachers. However, this association was based on only 3 affected children of the exposed mothers.

Clubfoot: Clubfoot was reported for 188 children in this present study. However, 29 of these children were excluded because of an inappropriate or unknown maternal occupation or exposure. The results of the screening on the remaining 159 malformed children are presented in table A.13.

Nine industrial categories are included in this screening analysis with the low exposure category being reported most frequently. Seventeen industry-specific occupational categories were included with domestic occupations being the most frequently reported occupation.

One borderline elevated crude odds ratio was observed for women in managerial positions in the low exposure industries. This association became significantly increased when adjusted for the age-race and hospital of birth. However, this association was based on only 3 exposed mothers with affected children.

4.3.6 Eye and/or Ear Malformations

Among the 3,186 malformed children included in the present study, 119 were diagnosed as having at least one eye and/or ear malformation. Multiple malformations were present in 13 (11%) of these children. Table 25 lists the individual eye and ear malformations that were used in this screening analysis.

Table 25

Frequency of Eye and/or Ear Malformations Included
and Excluded in the Screening Analysis

<u>Malformation</u>	<u>Children Included</u>	<u>Children Excluded</u>	<u>Total</u>
Any eye/ear malformation	101	18	119
Cataract	38	6	44
Pre-Auricular skin tag	30	6	36

A complete description of the risk factors for the CPP eye and ear malformations used in the present study has been published elsewhere (13). The distribution of children with eye and ear malformations by age and race of the mother, and by hospital of birth are indicated in tables 26 through 28.

Table 26

Distribution of Maternal Age Among the 119
Children with Eye and/or Ear Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	0	0
15-19	22	18
20-24	48	40
25-29	27	23
30-39	21	18
40 and older	1	1
All ages	119	100

Table 27

Distribution of Maternal Race Among the 119
Children with Eye and/or Ear Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	53	45
Black	54	45
Puerto Rican	12	10
All race	119	100

Table 28

Distribution of Hospital of Birth Among the 119
Children with Eye and/or Ear Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	35	29
BU	3	2
CH	6	5
CO	4	3
JH	1	1
VA	3	2
MN	9	8
NY	11	9
OR	4	3
PA	27	23
PR	2	2
TN	14	12
All hospitals	119	100

A total of 119 children with eye and/or ear malformations were included in the study sample. Of these, 101 were available for screening (Table 25). Appropriate maternal exposures were not available for 16 malformed children and occupation was unknown for an additional 2 children. Results of the screening for the children with any eye and/or ear malformations and maternal occupational exposure are presented in table A.14.

Eight industrial categories and 11 industry-specific occupational categories were included in this screening analysis. The low exposure industrial category included the largest number of exposed mothers of the malformed children. Likewise, the domestic occupations were the most commonly reported occupation among the exposed mothers of children with any eye and/or ear malformations.

No elevated odds ratios were observed for any occupation screened in the analysis of children with any eye and/or ear malformation.

In addition to the screening eye and/or ear malformations, two specific eye and ear malformations were reported in adequate numbers for the purpose of a more specific screening analysis. These malformations along with their frequencies are presented in table 25.

Cataract: Cataracts were noted in 44 children in the study sample. Six of these children were excluded from the screening analysis due to the lack of appropriate maternal exposure or occupational information. Screening results for the remaining 38 children are presented in table A.15.

The screening analysis for children cataracts included 5 industrial categories of which the textile industry was the most frequently reported among the exposed mothers of the children with cataracts. Only 3 occupational categories met the criteria for inclusion in this screening. Domestic occupations were the most frequently reported by the exposed mothers of children with cataracts.

No elevated odds ratios were observed for any industry or occupation screened in this analysis.

Pre-auricular skin tag: Of the 119 children with any eye and/or ear malformation 36 had a pre-auricular skin tag. Six of these children were excluded from the screening due to the lack of appropriate maternal exposure or occupational information. Screening results for the remaining 30 malformed children are presented in table A.16.

Only 4 industrial groups were included in this screening and none had more than 2 exposed mothers of children with pre-auricular skin tag. The domestic occupations was the only occupational category with any exposed mothers of malformed children (n=1).

No elevated odds ratios were observed for any industry or occupation screened in this analysis.

4.3.7 Respiratory System Malformations

Among the 3, 186 malformed children in the present sampe, 409 children were diagnosed as having at least one respiratory system (RS) malformation. Of these 409 children, 316 (77%) had multiple malformations. There were 188 with some cleft anomaly. Cleft gum only, a non-uniformly distributed malformation, was the most commonly diagnosed RS malformation being present in 100 children. Table 29 lists the individual RS malformations, as well as the combined malformation groups, that were used in this screening analysis.

Table 29

Frequency of Respiratory System Malformations Included in the Screening Analysis

<u>Malformation</u>	<u>Number Included</u>	<u>Number Excluded</u>	<u>Total</u>
Any respiratory malformation	342	67	409
Any cleft lip/palate/gum	150	39	188
Cleft lip only	21	3	24
Union cleft lip & co-existence lip and palate	41	7	48
Celft palate only	22	8	30
Cleft gum only*	87	23	110
Any malf. thoracic wall/cavity	94	14	108
Amlf. thoracic wall	16	2	18
Hypoplasia/agenesis lung	26	3	29
Malformed lung	21	4	25
Pectus excavatum*	79	12	91

*Non-uniformly distributed by CPP hospital.

A complete description of the risk factors for the CPP, RS malformations used in the present study is published elsewhere (13). The distribution of children with any respiratory system malformation by maternal age and race, and hospital of birth are presented in tables 30 through 32.

Table 30

Distribution of Maternal Age Among the 409 Children with Respiratory Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	5	1
15-19	77	19
20-24	146	36
25-29	84	20
30-39	82	20
40 and older	15	4
All ages	409	100

Table 31

Distribution of Maternal Race Among the 409
Children with Respiratory Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	119	49
Black	190	46
<u>Puerto Rican</u>	<u>20</u>	<u>5</u>
All race	409	100

Table 32

Distribution of Hospital of Brith Among the 409
Children with Respiratory Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	90	22
BU	45	11
CH	14	3
CO	30	7
JH	25	6
VA	47	12
MN	20	5
NY	20	5
OR	16	4
PA	67	16
PR	19	5
<u>TN</u>	<u>16</u>	<u>4</u>
All hospital	409	100

Of the 409 children with any RS malformations, 342 were included in the screening analysis (table 29). Sixty-three children had inadequate maternal exposure malformation (see Section 3.2.2) and 4 children had an unknown maternal occupation. The results of the screening for the 342 children with any respiratory malformation are presented in table A.17.

Thirteen industrial and 29 industry specific occupational categories met the criteria to be included in the screening analysis for any respiratory malformation. The industrial category with the largest number of exposed mothers of children with a respiratory malformation was the low exposure category. The most frequent occupation observed in this screening analysis for the exposed mothers of the malformed children was the group of domestic occupations.

No elevated odds ratios were observed for any industry or occupation included in this screening analysis.

In addition to the children reported to have any respiratory system malformation, ten specific respiratory malformation categories had adequate numbers of children for the purpose of this screening analysis. These malformation categories, along with their frequencies, are listed in table 29.

Cleft lip/palate/gum: Any cleft anomaly (lip, palate and/or gum) was diagnosed in 188 study children. However, 38 were excluded due to inappropriate or unknown maternal occupation and exposure leaving 150 children with this malformation available for analysis. The results for the children with any cleft are presented in table A.18.

Of the 150 children with any cleft anomaly, 21 had cleft lip only, 41 had either cleft lip only or co-existing cleft lip and palate, 22 had cleft palate only, and 87 had cleft gum only. The results of the screening analysis for these 4 categories are presented in tables A.19 through A.22.

Ten industrial categories met the inclusion criteria for the screening for cleft anomalies with the low exposure industries category containing the largest number of exposed mothers with malformed children. Domestic occupations were the most frequently reported occupations among the 17 included in this analysis.

A marginally elevated odds ratio was observed between any cleft anomaly and mothers working in the rubber and plastic industry (OR = 5.2). This was not substantially altered when age and race, and hospital were controlled. A significant positive association was observed for hairdressers and cleft anomalies only after adjustment for age and race (OR = 3.6), and hospital of birth (OR = 3.7). However, the adjusted odds ratios did not differ from the crude odds ratio. The significant result after adjustment is due to the use of the chi-square test of significance. Both the associations noted here are based on small numbers of exposed mothers with affected children (n=3).

No positive associations were observed for any of the other cleft categories included in this analysis.

Malformation Thoracic wall and/or cavity: Of the 409 children with some respiratory malformation, 108 had a malformation of the thoracic wall and/or cavity. Fourteen exclusions due to unknown or inappropriate maternal exposure or occupation left 94 malformed children for analysis. The results of this screening analysis are presented in table A.23.

Thoracic wall malformations were present in 16 of these 94 affected children. The results of the screening for thoracic wall malformations are presented in table A.24.

Seven industrial categories and eight industry-specific occupational categories met the criteria for inclusion in this screening analysis. The low exposure industrial category, and the low exposure office workers and domestic workers were the most frequently reported industry and occupations among the exposed mothers of the malformed children.

No significantly elevated crude odds ratios were observed for any industry or occupation included in the screening for children with any thoracic wall and/or cavity malformation. However, after adjustment, both the age-race standardized odds ratio (OR = 4.1) and the hospital standardized odds ratio for domestic occupations (OR = 3.1) were significantly elevated.

A similar positive association between thoracic wall malformations and domestic work was seen only after age and race (OR = 6.1) and hospital (OR = 3.6) adjustment. This association is based on only 3 exposed mothers with affected children.

Hypoplasia/agenesis of the lungs: Hypoplasia and/or agenesis of the lungs was reported in 29 children. Three were excluded from screening because of inappropriate maternal exposure or occupational information. The results for the remaining 26 children are presented in table A.25.

Four industrial categories met the criteria for inclusion in the screening analysis for hypoplasia and/or agenesis of the lung. The food and tobacco and low exposure industries both contained the largest numbers of exposed mothers (n=4) of children with hypoplasia and/or agenesis of the lungs. No occupational categories were reported with any exposed mothers of malformed children.

A significantly elevated odds ratio (OR = 3.1) was observed for the food and tobacco industry only after adjusting for age and race.

Malformed lungs: Although 25 children in this study were reported to have malformed lungs, four were excluded due to the lack of appropriate maternal exposure or occupational information. The results of the remaining 21 children are presented in table A.26.

Three industrial categories and two industry-specific occupational categories were included in this screening. The medicine and science industry was the most frequent industry reported for exposed mothers of children with malformed lungs. The low exposure office work and domestic work categories each had one exposed mother of a child with a lung malformation.

No elevated odds ratios were observed for any industry or occupation included in the screening analysis for children with lung malformations.

Pectus excavatum: Pectus excavatum was observed in 91 study children. Of these, 79 were included in the screening analysis after the exclusion of 12 children whose mothers had unknown or inappropriate exposure or occupational information. The results for the 79 children are presented in table A.27.

Seven industrial and five industry-specific occupational categories are included in table A.27. The low exposure industries category and the low exposure office work occupational category were the most frequent industry and occupational categories for the exposed mothers of the children with pectus excavatum.

No elevated odds ratios were observed for any industry or occupation included in the screening of children with pectus excavatum.

4.3.8 Gastrointestinal System Malformations

Among the 3,186 malformed children included in the present sample, 959 had at least one gastrointestinal (GI) malformation. Multiple GI malformations were present in 772 (81%) of these 959 children. Inguinal hernia was, by far, the most common GI malformation being reported in 674 children. Table 33 lists the GI malformations included in this report.

Table 33

Frequencies of Children with Gastrointestinal System
Malformations Included in the Screening Analysis

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any gastrointestinal malformation	828	131	959
Omphalocele	22	0	22
Anal atresia	19	7	26
Malrotation	23	2	25
Pyloric stenosis	79	13	92
Accessory spleen	19	2	21
Any hernia	627	100	727
Inguinal hernia*	580	94	674
Umbilical hernia	44	6	50

*Non-uniformly distributed by CPP hospital.

Risk factors for the CPP GI malformations used in the present study have been well described elsewhere (13). The distribution of GI malformations by maternal age and race, and hospital of birth for the present sample are presented in tables 34 to 36.

Table 34

Distribution of Maternal Age Among the 959
Children with Gastrointestinal System Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	5	*
15-19	233	24
20-24	363	38
25-29	179	19
30-39	164	17
40 and older	15	2
All ages	959	100

*Less than 1 percent

Table 35

Distribution of Maternal Race Among the 959
Children with Gastrointestinal System Malformations

<u>Maternal Age</u>	<u>Frequency</u>	<u>Percent</u>
White	443	46
Black	476	50
Puerto Rican	40	4
All race	959	100

Table 36

Distribution of Hospital of Birth Among the 959
Children with Gastrointestinal System Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	225	24
BU	58	6
CH	36	4
CO	50	5
JH	53	6
VA	66	7
MN	73	8
NY	62	6
OR	55	6
PA	205	21
PR	34	4
TN	42	4
All hospitals	959	100

Of these 959 children with GI malformations, 828 were included in the screening analysis. Inadequate maternal exposure information resulted in the exclusion of 131 malformed children from the screening analysis (see Section 3.2.2). Results of this screening are presented in table A.28.

Fifteen industrial and 54 industry-specific occupational categories fulfilled the criteria to be included in the screening analysis for any GI malformation. The industrial category that includes the largest number of exposed mothers of children with a GI malformation was the low exposure industries category. The most frequent occupation of the exposed mothers of the children with GI malformation (observed in this screening analysis) was the domestic occupations category.

There were no elevated unadjusted odds ratios for any GI malformation. Significant increases were observed for bartenders (OR = 3.7), hospital housekeepers (OR = 3.4), metal products fabrication (OR = 3.5), and domestic work (OR = 1.4) after adjusting the associations for hospital of birth. All these associations with the exception of domestic work, were based on fewer than four exposed mothers with malformed children.

In addition to the children reported to have any GI malformation, eight specific GI malformation categories had adequate numbers of children for the purpose of this screening analysis. These malformation categories, along with their frequencies, are listed in table 33.

Omphalocele: Omphalocele was reported in 22 study children. All 22 were included in the screening. Results of the screening are presented in table A.29.

Only three industrial categories, food and tobacco, medicine and science, and low exposure industries, and one occupational category, domestic occupations, were included in this analysis.

A marginally increased risk of omphalocele was observed for the domestic occupations (OR = 4.0). This association became significantly elevated after adjusting for hospital of birth (OR = 8.4). This association was based on only four exposed mothers of affected children.

Anal Atresia: Anal atresia was observed in 26 of the study children. Seven exclusions due to the lack of appropriate maternal exposure information left 19 children for the screening analysis. The results are presented in table A.30.

Only the low exposure industries and the domestic occupations met the inclusion criteria. Elevated odds ratios were observed for both the low exposure industries (OR = 3.5) and the domestic occupations (OR = 5.8). The odds ratios remained elevated when age-race, and hospital standardized.

Malrotation: Malrotation was noted for 25 study children. Twenty-three children were available for analysis after the exclusions for inappropriate maternal exposure. Results of the screening are presented in table A.31.

Four industrial and two industry specific occupational categories were included in the screening for malrotation. No industrial category had more than 2 exposed mothers of malformed children. Domestic occupations was the only occupational category with any exposed mothers of children with malrotation.

No elevated odds ratios were observed for any industry or occupation included in this screening of children with malrotation.

Pyloric Stenosis: Pyloric stenosis was observed for 92 of the children in the study sample. After excluding 13 children whose mothers had inappropriate exposure information, 79 children with pyloric stenosis were available for the screening analysis. The results are presented in table A.32.

Six industrial and five industry-specific occupational categories met the inclusion criteria. Low exposure industries and office work in the low exposure industries were the industrial and occupational categories with the largest number of exposed mothers of children with pyloric stenosis.

The low exposure industries (OR = 4.4) and office work in the low exposure industries (OR = 6.6) both exhibited elevated crude odds ratios. However, after adjustment for age, race, and hospital, the odds ratios were no longer significantly elevated.

Assessory Spleen: Assessory spleen was reported for 21 of the study children. Two of these malformed children were excluded from screening because of an inappropriate maternal exposure. Results of the screening on the remaining 19 children are presented in table A.33.

Only two industrial categories, food and tobacco and low exposure industries, and only the low exposure office work occupational category fulfilled the criteria for the screening analysis. None of these categories had an elevated odds ratios.

Any Hernia: Of the 959 children with any GI malformation, 727 had a hernia of some type. Of these children, 100 were excluded due to inappropriate maternal exposure. Results of the screening analysis on the remaining 627 children with any hernia are presented in table A.34.

Fifteen industrial categories and 46 industry-specific occupational categories are included in table A.34. Low exposure industries and domestic occupations are again the most frequently reported industrial and occupational categories for the exposed mothers of children with any hernia.

A marginally elevated odds ratio was seen for hospital housekeepers (OR = 4.2). Textile production workers and stitchers with no reported industry had significantly elevated odds ratios after age and race, and hospital adjustment. However, the adjusted odds ratios for these associations differed little from the crude association. The significant result was due to the use of the Chi-square test. All of those observed associations are based on small numbers of exposed mothers with affected children ($n \leq 5$).

Inguinal Hernia: Of the 727 children with any hernia, 674 had an inguinal hernia. There were 94 children excluded from screening due to inappropriate maternal exposure. Results for the remaining 580 malformed children are presented in table A.35.

Fifteen industrial and 44 industry-specific occupational categories are present in table A.35. The low exposure industries and domestic occupations were the most frequent industrial and occupational categories among the exposed mothers of the children with inguinal hernia.

Hospital housekeepers show an elevated odds ratio (OR = 4.5) which is consistent when adjusted for age, race and hospital. Stitchers for whom no industry was reported had a significant positive association only after age and race, and hospital adjustment. However, this significant result was due to the use of the chi-square statistic. Both of these associations are based on small numbers ($n=4$) of exposed mothers with affected children.

Umbilical hernia: Umbilical hernia was noted for 50 study children. After six exclusions for inappropriate maternal exposure, the screening analysis was performed on the remaining 44 children. The results are presented in table A.36.

Five industrial and three industry-specific occupational categories were included in table A.36. While the low exposure industries was again the most frequently reported industrial category, all three occupational categories (waitress, low exposure office work, and domestics) had three exposed mothers of children with umbilical hernias.

The textile industrial category exhibited an elevated odds ratio (OR = 2.7), but adjustment for both age and race, and hospital reduced the magnitude of the association.

4.3.9 Cardiovascular System Malformations

A full description of the cardiovascular system (CV) malformations in the CPP has been published elsewhere (76). As pointed out in section 2.3, the cardiovascular system malformations were ascertained in a somewhat different manner than were the other malformations. The overall effect was to give more complete and accurate identification of the cardiovascular malformations.

Among the 3,186 malformed children included in the present sample, 398 had cardiovascular malformations. A large array of anomalies constituted this group. Of the 398 children with cardiovascular malformations, 384 had multiple malformations. Ventricular septal defects were the most common malformation, occurring in 168 children. Table 37 lists the individual cardiovascular defects, as well as combinations, that were used in the screening analysis.

Table 37

Frequency of Children with Cardiovascular System Malformations
Included in the Screening Analysis

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any cardiovascular malformation	347	51	398
Any atrial septal defect	44	8	52
Atrial septal defect-secundum	31	7	38
Atrial septal defect-secundum, isolated	23	5	28
Atrial septal defect-secundum, multiple	8	2	10
Any atrial septal defect, isolated	31	6	37
Any atrial septal defect, multiple	13	2	15
Any ventricular septal defect	148	20	168
Ventricular septal defect (open)	111	15	126
Ventricular septal defect (open), isolated	63	11	74
Ventricular septal defect (open), multiple	55	5	60
Ventricular septal defect-spontaneously closing	30	4	34
Any ventricular septal defect (open or closing), isolated	93	15	107
Any ventricular septal defect (open or closing), multiple	55	6	61
Pulmonic valve malformation	62	11	73
Aortic ventricular canal	18	0	18
Aortic valve malformation	20	7	27
Pulmonic valvular or unspecified stenosis	46	10	56
Pulmonic valvular or unspecified stenosis, isolated	23	6	29
Pulmonic valvular or unspecified stenosis, multiple	23	4	27
Pulmonic valve malformation, isolated	28	6	34
Pulmonic valve malformation, multiple	34	5	39
Any malposition of great vessels (union)	26	3	29
Any malposition of great vessels, multiple	23	3	26
Ductus arteriosus persistens	43	2	45
Ductus arteriosus persistens, isolated	27	2	29
Any coarctation of aorta	33	2	35
Coarctation of aorta-preductal	24	1	25
Coarctation of aorta-preductal, multiple	16	0	16
Any coarctation of aorta, isolated	17	2	19
Any coarctation of aorta, multiple	16	0	16
Aortic and mitral valve atresia	10	3	13
Hypoplasia cordis	17	2	19
Conus arteriosus syndrome	40	4	44
Endocardial cushion defect	32	2	34
Hypoplastic left heart syndrome	21	3	24

Risk factors for the CPP cardiovascular malformations used in the present study have been well described elsewhere (76). The distribution of cardiovascular malformations by age and racial characteristics of the mother, and by hospital of birth are presented in tables 38 to 40.

Table 38

Distribution of Maternal Age Among the 398
Children with Cardiovascular System Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	3	1
15-19	68	17
20-24	128	32
25-29	93	23
30-39	89	22
40 and older	17	4
All ages	398	100

Table 39

Distribution of Maternal Race Among the 398
Children with Cardiovascular System Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	192	48
Black	179	45
Puerto Rican	27	7
All race	398	100

Table 40

Distribution of Hospital of Birth Among the 398
Children with Cardiovascular System Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	85	21
BU	27	7
CH	25	6
CO	21	5
JH	34	8
VA	23	6
MN	17	4
NY	30	8
OR	25	6
PA	63	16
PR	27	7
TN	19	5
All hospitals	398	100

Of the 398 children with cardiovascular malformations, 51 were excluded prior to the screening analysis because of an inappropriate maternal occupational exposure (see Section 3.2.2). The results for the remaining 347 malformed children are presented in table A.37.

Thirteen industrial and 31 industry-specific occupational categories fulfilled the inclusion criteria for the screening analysis. Among the exposed mothers of children with CV malformations, the low exposure industries category was the most common industrial category and the domestic occupations category was the most common occupational category.

Positive associations were noted between the children with cardiovascular defects and the following maternal occupational exposures: any work in the metal or related industries (OR = 4.1), bartending (OR = 6.9), and library work (OR = 6.9). Each of these associations was either unchanged or strengthened after adjusting for age and race, and hospital. All the associations noted here are based on a small number of exposed mothers with affected children ($n \leq 5$). Although the age-race and hospital adjusted odds ratios for the material handling trades in the low exposure industries were both significantly elevated, this result may only be due to the use of the Chi-square test of significance when the expected number of exposed mothers with affected children did not exceed two. The actual magnitude of the adjusted odds ratios was not larger than the crude odds ratio.

In addition to the presence of any cardiovascular malformations, 35 individual and combined cardiovascular defects had adequate numbers of malformed children to be included in the screening. Results for the individual cardiovascular defects, as well as the combinations are presented in tables A.38 through A.71.

Atrial septal defects: Any atrial septal defect was observed in 52 children in the study sample. Of these, 8 were excluded due to inappropriate maternal exposure information. The results for the remaining 44 children with any atrial septal defect are presented in table A.38.

Of the 52 children with any atrial septal defects, 37 had isolated defects and 15 had multiple defects. Secundum atrial septal defects were present in 38 children. Twenty-eight of these were isolated while 10 were multiple. The numbers of children excluded from each category are presented in table 37. The results of the screening analyses for these 5 categories of atrial septal defects are presented in tables A.39 through A.43.

Six industrial and four industry specific occupational categories fulfilled the inclusion criteria for the screening analysis for atrial septal defects. Among the mothers of the children with any atrial septal defect, the low exposure industries category and the domestic occupations were the most common industrial and occupational categories.

Positive associations were noted between any atrial septal defect and the maternal occupational exposure of any work in the metal industry (OR = 20.6). A marginal association was observed for sewing occupations in the textile industry (OR = 4.5). Neither of these associations were effected by adjustment for age and race, and hospital. These associations were based on only three exposed mothers with affected children.

Among the other categories of atrial septal defects, the following positive associations were observed: maternal exposure in the metal industry and secundum atrial septal defect (OR = 33.4), maternal exposure in the textile industry and any multiple atrial septal defect (OR = 9.8), and the sewing occupations in the textile industry and any multiple atrial septal defect (OR = 29.0). Adjustment for age and race, and hospital either had a negligible effect or increased the magnitude of the odds ratio for each of these associations. Every association noted for all categories of atrial septal defect are based on a small number of exposed mothers with affected children ($n \leq 5$). In addition, significant associations were noted for both multiple secundum atrial septal defects and any multiple atrial septal defects, and the low exposure industries after age and race, and hospital adjustment. These results are most likely due to the use of the Chi-square test when the expected number of exposed mothers with affected children was less than two, as the magnitude of the adjusted odds ratios was not substantially larger than the crude odds ratio for these associations.

Ventricular septal defect: The presence of any ventricular septal defect (VSD) was observed in 168 of the malformed children in the study sample. Twenty of these children were excluded from the screening analysis due to inappropriate maternal exposure information. The results for the remaining 148 children are presented in table A.44.

Of the 168 children with any VSD, 107 had an isolated VSD and 61 had multiple VSD; 126 had open VSD and 34 had a spontaneously closing VSD. There were 74 children with isolated open VSD and 60 with multiple open VSD. The number of children excluded from each category are presented in table 37. The results of the screening analyses for these 6 categories of ventricular septal defects are presented in tables A.45 through A.50.

Nine industrial and sixteen industry-specific occupational categories were included in the screening analyses for any ventricular septal defect. Among the mothers of children with this malformation, the low exposure industries category and the domestic occupations were the most common industrial and occupational categories.

A positive association was observed between children having any ventricular septal defect and exposed mothers employed in the material handling occupations of the textile industry (OR = 5.2). This association was unaffected by age-race and hospital standardization.

Among the other categories of VSD, one positive association is observed between a maternal exposure in the material handling trades of the textile industry and any isolated VSD (OR = 9.0). Another marginal association (OR = 4.8) is noted for spontaneously closing VSD and mothers with an unknown industrial exposure.

Pulmonic valve malformations: Pulmonic valve malformations (PVM) were noted in 73 children. Of these 62 were available for screening after excluding the children with inappropriate maternal exposure information. Results of this analysis are presented in table A.51.

Of the 73 children with PVM, 56 had pulmonic valvular or unspecified stenosis (PVS). Twenty-nine children had isolated PVS and 27 children had multiple PVS. Isolated PVM was present in 34 children while 39 had multiple PVM. The number of children excluded from each category for reasons related to maternal occupational exposure is presented in table 37. The results of the screening analyses for these five categories of PVM are presented in tables A.52 through A.56.

Six industrial and six industry-specific occupational categories were present for the screening of PVM. Among the mothers of children with PVM the low exposure industries was the most frequently reported industrial category and nurse's aide was the most frequently reported occupation.

An association was noted for children with multiple PVM and the occupation nurse's aides (OR = 6.3). This association was not substantially altered when adjusted for age and race (OR = 7.8) and hospital (OR = 6.2). This association was based on a small number of exposed mothers with affected children (n=3).

Atrioventricular canal defects: Eighteen children were observed to have atrioventricular canal defects. All eighteen were available for screening analysis. However, none of the industrial or industry-specific occupational categories fulfilled the inclusions criteria for the screening analysis.

Aortic valve malformations: Aortic valve malformations were observed for 27 study children. After excluding 7 of these children for reasons related to maternal occupational exposure, 20 children remained available for the screening analysis. The results of this screening are presented in table A.57.

Only the textile and low exposure industries categories fulfilled the inclusion criteria for the screening analysis. No industry-specific occupational categories were included. No associations were observed between the children having aortic valve malformations and the two maternal exposure categories included in the screening analysis.

Mitral valve malformation: Sixteen of the children with cardiovascular malformations had a mitral valve malformation. The exclusion of three children for reasons related to maternal occupational exposure left only 13 malformed children for analysis. Results of the screening for mitral valve malformations are presented in table A.58.

Only the low exposure industrial category and the domestic occupations category met the criteria for inclusion. Both of these categories demonstrated elevated odds ratios for mitral valve malformations. The association between the low exposure industries and mitral valve defects (OR = 4.5) increased when adjusted for age and race (OR = 6.7), and hospital (OR = 6.4). A more dramatic increase was seen for the association between the domestic occupations and mitral valve defects (OR = 7.8) when age-race (OR = 13.8) and hospital (OR = 22.5) standardized. It must again be cautioned that these associations are based on a small number of exposed mothers with affected children ($n \leq 5$).

Malposition of the great vessels: Any malposition of the great vessels (MGV) was reported for 29 children. The results for the 26 available malformed children remaining after the maternal occupational exposure exclusions are presented in table A.59.

Of the 29 children with MGV, 26 had multiple MGV. Again three children were excluded leaving 23 children for the screening analysis. The results of this analysis are presented in table A.60.

Only four industrial categories were included in the analysis of MGV. Only the low exposure office work and domestic occupations categories were included. No elevated odds ratios were observed for any industrial or occupational category included in this analysis.

Ductus Ateriosus Persistens: Forty-five of the children with cardiovascular malformations had ductus arteriosus persistens (DAP). Of these, two were excluded for reasons related to maternal occupational exposure. The remaining 43 children were included in the screening analysis. The results are presented in table A.61.

Of the 45 children with DAP, 29 had isolated DAP. Two were excluded, leaving 27 children for the screening analysis. The results are presented in table A.62.

Five industrial and three industry-specific occupational categories were included in the present screening analysis. The low exposure industries industrial category and the low exposure office work and domestic occupations categories were the most frequently reported industrial and occupational categories among the exposed mothers of children with DAP persistens.

No positive associations were seen for any industry or occupation included in this screening analysis and ductus arteriosus persistens.

Coarctation of the aorta: Any coarctation of the aorta (COA) was noted in 35 children. Two exclusions for reasons related to maternal exposure left 33 children for the screening analysis. Results of this analysis are presented in table A.63.

Of the 35 children with COA, 19 had isolated COA and 16 had multiple COA. Twenty-five children had preductal COA. All of the children with multiple COA also had preductal COA. The number of children excluded from each COA category for reasons related to maternal exposure are indicated in table 37. The results of the screening are presented in table A.64 through A.66.

Four industrial categories were present in the COA screening with the low exposure industrial category the most common among exposed mothers of children with this malformation. Only the low exposure office work and domestic occupations categories were included.

No positive associations were observed for industrial or occupational category included in the screening of COA.

Aortic/mitral valve atresia: Only thirteen children with cardiovascular malformations had aortic and mitral valve atresia. Three of these children were excluded for reasons related to maternal occupational exposure. The results for the remaining ten children are presented in table A.67.

The low exposure industries category was the only exposure category which fulfilled the industry criteria. The crude odds ratio for this category was not significantly elevated. However, this odds ratio did increase substantially and became marginally significant when age-race adjusted (OR = 5.4) and the hospital adjusted (OR = 4.5). Again, this association is based on only three exposed mothers with affected children.

Hypoplasia cordis: Hypoplasia cordis was noted in 19 children. After two were excluded for reasons related to maternal occupational exposure, 17 were available for analysis. The results are presented in table A.68.

Only the low exposure industries category fulfilled the criteria for inclusion in the screening analysis. There was no association between exposed mothers. This industrial category and children with hypoplasia cordis.

Conus arteriosus syndrome: The conus arteriosus syndrome was observed in 44 study children. Four children were excluded because of reasons related to maternal occupational exposure. The screening results for the remaining 40 children are presented in table A.69.

Five industrial and four industry-specific occupational categories are present. Among the exposed mothers of children with conus arteriosus syndrome, medicine and science, and nurse's aides are the most common industrial and occupational categories.

A positive association is observed between children with conus arteriosus syndrome and the maternal occupation of nurse's aides (OR = 7.4). A slight increase in this odds ratio is seen after adjusting for age and race (OR = 8.4) and hospital (OR = 8.1). This association is based on only four exposed mothers of children with conus arteriosus syndrome.

Endocardial Cushion defects: Thirty-four of the children with cardiovascular malformations had endocardial cushion defects. Of these, 32 were available for screening. The results are presented in table A.70.

Four industrial categories met the criteria for inclusion in the screening analysis. Among the exposed mothers of children with endocardial cushion defects, the low exposure industries were the most common. Only the low exposure office work and the domestic occupations categories were included in this analysis. No positive associations were noted for any occupational category included in this analysis and this malformation.

Hypoplastic left heart syndrome: Twenty-four children with cardiovascular malformations had hypoplastic left heart syndrome. Three of these children were excluded from screening because of reasons related to maternal occupational exposure. The results for the remaining 21 children are presented in table A.71.

The food and tobacco, textile, and low exposure industries were the only industrial categories to fulfill the inclusion criteria for screening analysis. Textile sewing occupations and domestic occupations were the only occupational categories included.

Positive associations were demonstrated between children with hypoplastic left heart syndrome, and all textile workers (OR = 4.8) and textile sewing occupations (OR = 10.5). Neither association was substantially affected by adjusting for age and race, and hospital. A significantly elevated odds ratio was also noted for domestic workers when adjusted for hospital of birth (OR = 7.2). As for all other associations between CV malformations and the various occupational categories, these associations are all based on small numbers of exposed mothers with affected children ($n \leq 5$).

4.3.10 Genitourinary System Malformations

Among the 3,186 malformed children included in the present sample, 404 were diagnosed as having at least one genitourinary system (G.U.) malformation. Of the 404 children with G.U. malformations, 312 had multiple malformations. Hypospadias was by far the most common malformation occurring in 184 children. Table 41 lists the individual G.U. malformations, as well as the combinations of malformations, that were used in the screening.

Table 41

Frequency of Children with Genitourinary System
Malformations Included in the Screening Analysis

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any genitourinary malformation	353	51	404
Malformations of the male genitalia	184	28	212
Hypospadias	162	22	184
Malformations of the female genitalia	30	5	35
Major malformations of the female genitalia	12	2	14
Minor malformations of the female genitalia	19	3	22
Obstructive uropathy	35	8	43
Stenotic ureter	19	6	25

Table 41 continued

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Hyproureter	15	3	18
Urethral obstruction*	58	8	66
Polycystic kidney	26	3	29

*Non-uniform malformation

A complete description of the risk factors for the CPP G.U. malformations used in the present study has been published elsewhere (13). The distribution of children with G.U. malformations by age and race of the mother, and by hospital of birth are presented in tables 42 through 44.

Table 42

Distribution of Maternal Age Among the 404
Children with Genitourinary System Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	1	*
18-19	88	22
20-24	151	37
25-29	82	20
30-39	75	19
<u>40 and older</u>	<u>7</u>	<u>2</u>
All ages	404	100

*Less than 1 percent.

Table 43

Distribution of Maternal Race Among the 404
Children with Genitourinary System Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	195	48
Black	190	47
<u>Puerto Rican</u>	<u>19</u>	<u>5</u>
All race	404	100

Table 44

Distribution of Hospital of Birth Among the 404
Children with Genitourinary System Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	104	26
BU	19	5
CH	16	4
CO	19	5
JH	11	3
VA	26	6
MN	24	6
NY	20	5
OR	25	6
PA	111	28
PR	18	5
TN	11	3
All hospitals	404	100

Of the 404 children with G.U. malformations, 51 were excluded prior to the screening analysis for reasons related to maternal occupational exposure (see Section 3.2.2). The results of the screening for the remaining 353 children are presented in table A.72.

Thirteen industrial and 30 industry specific occupational categories fulfilled the inclusion criteria for the screening analysis. Among the exposed mothers of children with G.U. malformations, the low exposure industries category and the domestic occupations category were the most common industrial and occupational categories.

Positive associations were noted between the children with G.U. malformations and the following maternal occupational exposures: any work with a known occupation, but unknown industry (OR = 2.1); any factory work in an unknown industry (OR = 10.5). These associations are not substantially affected by adjusting for age and race, and hospital. In addition, the hospital adjusted odds ratio for domestic occupations is significantly elevated (OR = 1.8).

In addition to the analysis of children with any G.U. malformation, screening analysis was also performed on ten individual and combined categories of G.U. malformations. The malformation categories along with their frequencies are listed in table 41. The results of the screening for these G.U. malformations are presented in tables A.73 through A.82.

Malformations of the male genitalia: This was the most common combined malformation category. Of the 404 children with drug G.U. malformation 212 had at least one malformation of the male genitalia. Of these 212 children, 184 had hypospadias. Twenty-eight and 21 children were excluded from screening for reasons related to maternal exposure for all malformations of the male genitalia and hypospadias, respectively. The results for the remaining 184 children with malformations of the male genitalia are presented in table A.73. The results for the remaining 162 children with hypospadias are presented in table A.74.

Nine industrial and 17 industry-specific occupational categories were included in the screening for malformations of the male genitalia. The low exposure industries category and the domestic occupations category were the most common industrial and occupational categories among the exposed mothers of children with malformations of the male genitalia.

Positive associations were noted between children with any malformation of the male genitalia and the following maternal occupational exposures: sewing in the textile industry (OR = 2.7); any work in an unknown industry (OR = 2.9); office work in an unknown industry (OR = 2.2); and factory work in an unknown industry (OR = 12.8). After adjustment for age and race, and hospital, the association between the malformation of the male genitalia and the office work in an unknown industry was no longer observed. The other three associations were not substantially affected by the adjustment. The association between factory work in an unknown industry and this malformation is based on only three exposed mothers of affected children.

Similar associations were seen between hypospadias and the same occupational and industrial categories, except that the category of factory work in an unknown industry did not meet the criteria for inclusion in this analysis.

In addition to the above associations, associations between hypospadias and domestic occupations was observed after age and race (OR = 2.0), and hospital (OR = 2.3) adjustment, and any malformation of the male genitalia and domestic occupations after adjustment for hospital (OR = 1.9).

Malformations of the female genitalia: Thirty-five children were reported to have malformations of the female genitalia. Of these 14 children had major malformations and 22 children had minor malformations. (These categories are not mutually exclusive). Five children (2 with major malformations and 3 with minor malformations) were excluded prior to the screening analysis for reasons related to maternal occupational exposure. The results for children with any malformation of the female genitalia, major and minor malformations of the female genitalia are presented in table A.75 through A.77, respectively.

A positive association was seen between any malformations of the female genitalia and domestic work (OR = 4.4). This association was substantially increased after adjusting for age and race (OR = 6.5) and hospital (OR = 10.8). A similar association was seen for minor malformations of the female genitalia and domestic occupations after age-race (OR = 7.4) and hospital (OR = 11.6)

adjustment. A positive association was also observed between any worker in the food and tobacco industry and major malformations of the female genitalia (OR = 8.4). All of these associations with malformations of the female genitalia were based on a small number of exposed mothers with affected children. ($n \leq 5$).

Obstructive uropathy: Obstructive uropathy was reported 43 study children. Twenty-five of these children had stenotic ureter while another 18 had hydro-ureter. Of the 43 with obstructive uropathy, 8 were excluded from screening. The screening results of the remaining 35 children with obstructive uropathy are presented in table A.78. Similar results for 19 children with stenotic ureter and 15 with hydroureter are presented in tables A.79 and A.80.

Only the food and tobacco, textiles, medicine and science, and low exposure industrial categories were included in the screening of obstructive uropathy. Office work in low exposure industries and domestic work are the only occupational categories included.

No positive associations are seen for any of the categories of obstructive uropathy and the industries and occupations included in this analysis.

Urethral obstruction: One of the non-uniform malformations (see Section 2.3) included in this screening is urethral obstruction. It was noted in 66 children, 8 of whom were excluded because of maternal exposure. The results for the remaining 58 are presented in table A.81.

Six industrial and four industry-specific occupational categories were included in the screening of urethral obstruction. Low exposure industries and domestic occupations were the most common industrial and occupational categories among the exposed mothers of children with this malformation.

No positive associations were observed between children with urethral obstruction and any of the maternal occupational exposures included in this analysis.

Polycystic kidney: The last G.U. malformation that was included in the screening analysis was polycystic kidney. Twenty-nine children were observed to have this malformation. Three of these children were excluded prior to screening for reasons related to maternal occupational exposure. Results of the analysis are presented in table A.82.

Only the food and tobacco, and low exposure industries, and office work in the low exposure industries and domestic work fulfilled the criteria for exclusion in the screening. No positive associations were observed for these maternal exposure categories.

4.3.11 Tumors

Among the 3,186 malformed children included in the study sample, 158 were diagnosed as having at least one tumor. Of these 158 pregnancies, 156 had two or more tumors. Most of the tumors (n=133) were benign. Only 23 children with malignant tumors were identified. (Two children had mixed tumors). Children with cysts (except dermoid) made up the largest category of benign tumors with 39. Table 45 lists the tumor categories included in this analysis.

Table 45

Frequency of Children with Tumors Included
in the Screening Analysis

<u>Tumor</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any benign/malignant tumor	143	15	158
Any malignant tumor	21	2	23
Any benign tumor	120	13	133
Any cyst (except dermoid)	36	3	39
Hairy Nevus	20	1	21
Other benign	21	3	24

A complete description of the risk factors associated with the CPP children with tumors used in the present study has been published elsewhere (13). The distribution of the children with tumors by maternal age and race, and hospital of birth are presented in tables 46, 47, and 48.

Table 46

Distribution of Maternal Age Among the 158
Children with Tumors

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	1	1
15-19	30	19
20-24	60	38
25-29	40	25
30-39	24	15
40 and older	3	2
All ages	158	100

Table 47

Distribution of Maternal Race Among the 158
Children with Tumors

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	85	54
Black	63	40
<u>Puerto Rican</u>	<u>10</u>	<u>6</u>
All race	158	100

Table 48

Distribution of Hospital of Birth Among the 158
Children with Tumors

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	45	28
BU	12	8
CH	6	4
CO	8	5
JH	18	11
VA	8	5
MN	14	9
NY	11	7
OR	8	5
PA	19	12
PR	5	3
<u>TN</u>	<u>4</u>	<u>3</u>
All hospitals	158	100

Of the 158 children with tumors, 15 were excluded prior to the screening analysis for reasons related to maternal occupational exposure (see Section 3.2.2). The results of the screening for the remaining 143 are presented in Table A.83.

Of the 158 children with tumors, 23 had malignant and 133 had benign tumors (2 children had mixed tumors). Of the children with benign tumors, 39 children had cysts (except dermoid) and 21 had hairy nevus. The number of excluded children in each tumor category are listed in table 45. The results of the screening are presented in tables A.84 through A.88.

Nine industrial and 15 industry specific occupational categories were included in the screening of children with tumors. The low exposure industries and the low exposure office work categories were the most common industrial and occupational categories among the exposed mothers of children with tumors.

The only positive crude association seen among the tumor categories was between children with hairy nevus and maternal exposure to any occupation in the textile industry (OR = 4.8). This odds ratio was consistent when adjusted for age and race, and hospital. A significantly elevated hospital adjusted odds ratio (OR = 6.5) was seen for the low exposure office work category. However, neither the crude nor the age-race adjusted odds ratios were significantly elevated. Both of these associations were based on less than five exposed mothers of affected children.

4.3.12 Central Nervous System Malformations

Among the 3,186 malformed children included in this present study, 262 were diagnosed as having central nervous system (CNS) malformations. All of the CNS malformations were multiple. Microcephaly and hydrocephaly were the most commonly recorded CNS malformations with 74 children with each malformation. Table 49 lists the CNS malformations that were included in this screening analysis along with their frequencies.

Table 49

Frequency of Children with Central Nervous System Malformation
Included in the Screening Analysis

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any CNS malformation	222	40	262
Any brain malformation	200	38	238
Anencephaly	22	4	26
Hydrocephaly	62	12	74
Microcephaly	63	11	74
Craniosynostosis	23	3	26
Any spinal malformation	49	8	57
Craniospinal Fusion Defects	43	10	53
Meningomyelocele	29	7	36

The risk factors for the CPP CNS malformations used in the present study have been well documented elsewhere (13). The distribution of CNS malformations by maternal age and race, and hospital of birth are presented in tables 50 to 52.

Table 50

Distribution of Maternal Age Among the 262
Children with Center Nervous System Malformations

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	2	1
15-19	54	21
20-24	97	37
25-29	52	20
30-39	50	19
40 and older	7	3
All ages	262	100

Table 51

Distribution of Maternal Race Among the 262 Children
With Center Nervous System Malformations

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	128	49
Black	108	41
Puerto Rican	26	10
All race	262	100

Table 52

Distribution of Hospital Birth Among the 262 Children
with Central Nervous System Malformations

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	66	25
BU	13	5
CH	24	9
CO	11	4
JH	24	9
VA	15	6
MN	13	5
NY	20	8
OR	15	6
PA	40	15
PR	12	5
IN	9	3
All hospitals	262	100

Of the 262 children with CNS malformations, 40 were excluded prior to screening for reasons related to maternal occupational exposure (see Section 3.2.2). The results for the remaining 222 children with CNS malformations are presented in table A.89.

Ten industrial and 20 industry specific occupational categories were included in the screening of children with CNS malformations. Among the exposed mothers of the children with CNS malformations, the low exposure industrial category and the office work category in the low exposure industry were most frequently reported industrial and occupational categories.

One positive association was noted between children with CNS malformations and maternal occupational exposure in the rubber and plastics industry only after age-race (OR = 3.5) and hospital (OR = 3.6) adjustment.

Brain malformation: Any brain malformation was reported in 238 children. After the exclusion of 38 children for reasons related to maternal exposure, 200 children with brain malformations were available for screening. The results are presented in table A.90.

Of the 238 children with any brain malformation, 56 had anencephaly, 74 had hydrocephaly, 74 had microcephaly and 26 had craniosynostosis. Table 49 lists the number of each of these grain malformations that were excluded from screening. The results of the screening analysis for these four brain malformations are presented in tables A.91 and A.94.

The same industrial and industry-specific occupational categories are included for all brain malformations as were for all CNS malforations.

As with any CNS malformation the only positive association for any brain malformation was an association with the rubber and plastic industry after age-race and hospital adjustment. This result was most likely due to the use of the chi-square test with less than two malformed children expected among the exposed mothers. The adjusted odds ratios did not differ substantially from the crude odds ratio (which was not significantly elevated). Ancephaly demonstrated associations with both the maternal exposures to medicine and science after age and race adjustment (OR = 4.4) and low exposure office work after adjusting for hospital of birth (OR = 4.6). The other brain malformations did not demonstrate any elevated odds ratios for the industries and occupations used in this screening. All associations noted for the brain malformations were based on only three exposed mothers of affected children.

Spinal malformations: Any spinal malformation was diagnosed in 57 children. Of these, 49 had appropriate maternal exposures and were included in the screening analysis. The results are presented in table A.95.

Thirty-six of the children with any spinal malformation had meningomyelocele. Screening was performed on 29 of these children who had appropriate maternal exposures. Results are presented in table A.96.

The screening of children with any spinal malformations included only five industrial and three occupational categories. No positive associations were seen for the spinal malformations and the industries and occupations included in this analysis.

Craniospinal Fusion defects: Craniospinal fusion defects include a mixture of both spinal and brain malformations. (Actually only 2 children with any brain malformation were included in this category). There were 53 children in this combined malformation category. After 10 children were excluded for reasons related to maternal occupational exposure, 43 children remained for the screening analysis.

As for the screening of children with spinal malformations, five industrial and three occupational categories were present. No positive associations were observed for these industries and occupations (Table A.97).

4.3.13 Syndromes

Among the 3,186 children with malformations in this study, 170 were diagnosed as having syndrome malformations. Seventy of these children had multiple syndromes. The specific defects included in the present analysis are shown in table 53. Over one third of the children with syndromes had Down syndrome. Another 26 children had abnormalities of the adrenal gland.

Table 53

Frequency of Children with Syndromes Included
in the Screening Analysis

<u>Syndrome</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any syndrome	141	29	170
Any chromosomal abnormalities	57	9	66
Down syndrome - mongolism	50	8	58
Adrenal atrophy or hypoplasia	21	5	26

The risk factors associated with these syndromes in the CPP are well described elsewhere (13). The distributions of children with syndromes by maternal age and race, and hospital of birth are presented in tables 54 to 56.

Table 54

Distribution of Maternal Age Among the 170
Children with Syndromes

<u>Maternal Age (years)</u>	<u>Frequency</u>	<u>Percent</u>
Less than 15	2	1
15-19	33	20
20-24	55	32
25-29	24	14
30-39	40	24
40 and older	16	9
All ages	170	100

Table 55

Distribution of Maternal Race Among the 170
Children with Syndromes

<u>Maternal Race</u>	<u>Frequency</u>	<u>Percent</u>
White	88	52
Black	72	42
Puerto Rican	10	6
All race	170	100

Table 56

Distribution of Hospital of Birth Among the 170
Children with Syndromes

<u>Hospital of Birth</u>	<u>Frequency</u>	<u>Percent</u>
BO	48	28
BU	6	4
CH	7	4
CO	10	6
JH	17	10
VA	12	7
MN	12	7
NY	6	4
OR	11	6
PA	27	6
PR	6	4
TN	8	5
All hospitals	170	100

Of the 170 children with any syndrome, 29 were excluded for reasons related to maternal occupational exposure. The screening results for the remaining 141 children are presented in table A.98.

Chromosomal abnormalities are present in 66 of the children with syndromes. Of these, Down syndrome is the most frequent affecting 58 children. The number of excluded children with these syndromes and with abnormalities of the adrenal gland are listed in table 53. The results of the screening for children with these syndromes are presented in tables A.99 through A.101.

Ten industrial and 16 industry-specific occupational categories were included for the screening of children with syndromes. Among exposed mothers of children with syndrome malformations, the low exposure industrial category and the domestic occupations categories were the most common industrial and occupational categories.

Marginal positive associations were observed for any syndrome and any occupation in the rubber and/or plastic industry ($OR = 5.1$). This association was not greatly affected by adjusting for age and race, and hospital. This association was based on only three exposed mothers of affected children. Although a significant association was noted between n adrenal hypoplasia or atrophy and any medicine and/or science occupation after age-race and hospital adjustment, this most likely was the result of using the chi-square test when fewer than two affected children are expected among the exposed mothers. The crude and adjusted odds ratios did not differ substantially.

4.3.14 Summary of Maternal Occupational Screening Results

This section provides a summary list of those associations meeting the following selected criteria: (1) increased crude (observed) odds ratio, (2) adjusted odds ratio whose related Chi-square statistic is "significant" at $p < 0.05$ and (3) an "intersecting" cell (i.e., the number of cases who were "exposed") with a frequency greater than 5.

The purpose of the following list is to present, in summary form, those associations between an industry or occupation and an adverse reproductive outcome which are based on some of the larger sample sizes in the study.

Thus, depending on the criteria established by an investigator, this list represents associations which may warrant further evaluation.

Summary of the Statistically Significant ($p < 0.05$)
Observed Associations Between Maternal Occupational Exposure
and the Various Adverse Reproductive Outcomes for which there were
more than 5 Observations in the Exposure Category and the
Statistically Significant ($p < 0.05$) Adjusted Odds Ratio
(Age-Race and Hospital)

<u>Industry-Occupation</u>	<u>Reproductive Outcome</u>	<u>OR</u>	<u>Number of affected obser- vations in the "exposed" category</u>
Fuel industry office work	Any uniform malformation	3.5	6
Textile material handling	Any musculoskeletal malf.	2.7	8
Sewing occupations	Hypospadias	2.7	6
Textile material handling	Polydactyly	5.8	7
Sewing occupations	Malform. male genitalia	2.7	7
Low Exposure industries	Anal atresia	3.5	7
Textile Production	Uniform malformations	2.5	8
Low Exposure Industries	Polycystic kidney	3.2	8
Library work	Uniform malformations	2.5	8
Textile processing	Stillbirth	3.1	10
Medicine and Science Industry	Congenital dislocated hip	2.8	10
Hospital office work	Any musculoskeletal malform.	2.0	10
Machinery and electrical office work	Uniform malformations	2.2	13
Laundry work	Neonatal death	2.4	14
Waitressing	Infant death	2.0	19
Domestic work	Uniform malformation	1.2	151

5.0 Methods for Screening Paternal Occupational Exposures

All methods used to analyze the paternal occupational exposures are identical to those for the maternal exposures (see section 3.3) with the exception of the differences noted in this section.

5.1 Defining Paternal Occupational Exposures

For the purposes of the present study the occupation of interest was that occupation in which the father of the baby had been employed for the longest period of time. Length of employment was not used in this analysis because this information was not available for the earlier CPP occupational history form (FHH-1).

The nature of the paternal occupation was used to determine exposure status. The office work category in any industry, and certain occupations in the low chemical exposure industrial category were combined to create the "non-exposed" category. As in the maternal screening analysis, this "non-exposed" group remained constant within each case and control series, for each outcome category. (All occupational categories used to create the non-exposed group are indicated in Appendix J).

5.2 Analysis of Paternal Occupational Data

As with the maternal exposures, the procedure proposed by Mantel and Haenszel (75) was applied to control the potential confounding effects of hospital of birth, age and race. For this analysis, paternal age was used. However, due to a sizeable amount of missing information on paternal race, maternal race was used in the screening of paternal occupations. Pregnancies were excluded from the screening of paternal occupation if paternal occupation was unknown, if paternal age was unknown, or if paternal age was greater than 55.

In the screening of paternal occupational exposure, as in the maternal screening analysis, associations between pregnancy outcome and occupation were reported if the appropriate tests of significant indicated a "p-value" of less than or equal to 0.05. However, no "marginal" associations were reported for paternal occupations (see section 3.3.2).

6.0 Results - Screening Paternal Occupational Exposure

6.1 Composition of Study Sample: Exclusions from Screening Analysis

There were 14,544 pregnancies available for analysis of these 4,558 were excluded from the screening phase. These exclusions were due to unknown paternal occupation which resulted in the exclusion of 3371 pregnancies. An additional 1,155 pregnancies were excluded due to paternal age of over 55 years, unknown paternal age accounted for an additional 32 exclusions.

6.2 Distribution of Paternal Occupations Among the 14,944 Pregnancies

Due to the small number of pregnancies with certain paternal occupations, many of the industry-specific occupational categories were combined, leaving 19 industrial and 143 industry-specific occupational categories to classify the paternal occupations in the present screening analysis. These categories along with the occupations included in each category are listed in Appendix J. Of the 14,944 pregnancies in the sample, 11,542 (77%) had some known occupation, while 3,371 (23%) had unknown occupation. There were also 31 pregnancies (less than 1%) for which the father never worked (Table 57).

Among the 19 industrial categories, the low chemical exposure industrial category was the most commonly reported for the fathers. There were 2,411 (21%) of the 11,542 pregnancies with known paternal occupation in this category. The transportation industry and the food and tobacco industry were the second and third most frequent industries with 1728 (15%) and 1,453 (13%), respectively. Of the 143 industry-specific occupational categories used in the present study, only 28 categories included at least one percent of the total with known occupation. The largest industry-specific occupational category was the protective service category which included 861 (7%) of the pregnancies with known paternal occupation. The second and third largest categories were the drivers in the transportation industry and construction workers, which included 643 (6%) and 453 (4%) of the pregnancies, with known paternal occupation, respectively.

Table 57

Frequency of Paternal Occupations Among the 14,944
Pregnancies Included in the Present Study

<u>Industry-Occupation</u>	<u>Frequency</u>	<u>Percent</u>
Total	14,944	100
Total with known occupation	11,542	77
Unknown occupation	3,371	23
Never worked	31	*

*Less than one percent.

Table 57 Continued

<u>Industry-Occupation</u>	<u>Frequency</u>	<u>Percent</u>
Agriculture, Forestry, Fishing	422	4+
Office work	18	*
Plant farming	81	*
Animal farming	21	*
Other farming and related work	177	2
Veterinarians and animal care	24	*
Logging and forestry occupations	18	*
Fishing and fishery related work	46	*
Material handling	37	*
Mining	12	*
Construction	1,162	10
Office work	64	*
Painters, plasterers	179	2
Glass, clay, stone related work	32	*
Masons	83	*
Carpenters	144	1
Roofers	55	*
Metal structural work	29	*
Electricians	26	*
Plumbers	54	*
Paners	43	*
Construction, NOS	453	4
Paper and Wood	575	5
Office work	55	*
Paper and wood processing	56	*
Paper working	58	*
Printers	124	1
Wood machining	29	*
Wood product fabrication	74	*
Material handling	179	2
Glass, Clay, Stone	108	*
Office work	11	*
Processing	24	*
Machining and fabrication	32	*
Material handling	41	*
Metal	698	6
Office work	46	*
Processing	111	*
Ore refining	23	*
Metal machining	103	*
Metal working	82	*
Structural work	60	*
Metal product fabrication	66	*
Other production	110	*
Material handling	97	*

*Less than one percent.

+All subsequent percentages are based on the total number of men with a known occupation (n=11,542).

<u>Industry-Occupation</u>	<u>Frequency</u>	<u>Percent</u>
Machinery and Electrical	541	5
Engineers	47	*
Office work	39	*
Sales	19	*
Metal working and machining	65	*
Machine mechanics	34	*
Electrical products fabrication	138	1
Other production, NOS	55	*
Linemen and service men	74	*
Material handling	50	*
Transportation Industry	1,728	15
Office work	77	*
Radio, radar work	61	*
Sales	33	*
Personal services	29	*
Metal working and machining	58	*
Engine mechanics	309	3
Service station work	175	2
Autobody work	36	*
Drivers	643	6
Railroad personnel	63	*
Motor vehicle manufacturing	111	*
Material handling	133	1
Food and Tobacco	1,453	13
Managers and clerks	128	1
Office work	43	*
Sales	61	*
Cooks	187	2
Waiters	108	*
Bartenders	43	*
Meat cutters	28	*
Food preparation and service work	208	2
Butcher	70	*
Bakers	73	*
Other food processing	178	2
Material handling	326	3
Textile	560	5
Office work	42	*
Processing	138	1
Textile Machining	31	*
Product fabrication	88	*
Laundering	108	*
Material handling	153	1

*Less than one percent.

<u>Industry-Occupation</u>	<u>Frequency</u>	<u>Percent</u>
Chemicals, Drugs, and Paints	190	2
Chemistry occupations	51	*
Chemistry educators	4	*
Office work	32	*
Chemical processing	54	*
Material handling	49	*
Rubber, Plastics, Synthetics	171	1
Processing	56	*
Office work	9	*
Machining	20	*
Product fabrication	58	*
Material handling	28	*
Fuel	120	1
Office work	17	*
Processing	27	*
Material handling	29	*
Utilities production	47	*
Leather	133	1
Office work	26	*
Processing	12	*
Product fabrication	76	*
Material handling	19	*
Medicine and Science	393	3
Office work	14	*
Physicians	15	*
Dentists	12	*
Pharmacists	15	*
Nurses, Attendants	114	1
Other medical work, NOS	26	*
Laboratory work	28	*
Other science occupations, NOS	13	*
Psychology occupations	7	*
Dieticians and assistants	6	*
Morticians	12	*
Hospital laundry, cleaning	55	*
Other hospital service	76	*
Entertainment and Recreation	138	1
Drama, dance, music	48	*
Office work	4	*
Barbering and related work	54	*
Other entertainment related work	32	*

*Less than one percent.

<u>Industry-Occupation</u>	<u>Frequency</u>	<u>Percent</u>
Miscellaneous Occupations (Art and Products of Assorted Materials)	259	2
Artists	14	*
Photography	31	*
Other art related work, NOS	23	*
Office work	8	*
Fabrication of products of assorted materials	137	1
Material handling	46	*
Unknown Industry	468	4
Engineers	33	*
Office work	111	*
Laborers	102	*
Factory work	83	*
Material handling	139	1
Few Chemical Exposures	2,411	21
Architects and draftsmen	52	*
Science occupations	30	*
Students	155	1
Educators	157	1
Lawyers	25	*
Clergy	23	*
Accountants	74	*
Other professional and technical work, NOS	69	*
Office work	208	2
Mail carriers	39	*
Sales	120	1
Personal services	106	*
Food and lodging services	12	*
Recreational attendants	31	*
Protective Services	861	7
Building services	296	3
Material handling	134	1
Utilities distribution	19	*

6.3 Results of Paternal Occupational Screening Analysis

6.3.1 Stillbirths

There were 763 stillbirths in the study sample; 494 were included in the paternal screening analysis. Two hundred and sixty-nine pregnancies resulting in a stillbirth were excluded on the basis of the reasons mentioned above. Results of this screening analysis are presented in table B.1.

*Less than one percent.

A significantly elevated (crude and adjusted) odds ratio for stillbirth was observed for textile machining occupations (OR = 4.3).

6.3.2 Neonatal Deaths

The sample selected from the CPP cohort contained 772 neonatal deaths. A total of 288 of these cases were excluded from the analysis. Screening analysis is presented in table B.2.

The construction trades occupations had an elevated odds ratio for neonatal death (OR = 1.7). Adjustment for age and race and for hospital resulted in little change in the magnitude of the ratio. The division of "other construction" within the construction category had an increased odds ratio (OR = 1.9). When adjusted for age and race, and hospital, this ratio was somewhat decreased. The neonatal death odds ratio for pregnancies fathered by electricians (OR = 2.8) increased in magnitude and was significant when adjusted for age and race (OR = 3.4), and for hospital (OR = 3.6). This ratio is based on only 3 neonatal deaths.

The material handling occupations in agriculture, forestry, and fishing had an elevated odds ratio (OR = 4.9). When adjusted for age and race, and hospital, the ratio changed little. These odds ratios are calculated on 5 deaths.

Fathers employed in personal services in the transportation industry showed a significant association for having children who died in the neonatal period (OR = 4.7). Adjustment did not greatly affect the odds ratio. The odds ratios are based on 4 neonatal deaths.

6.3.3 Infant Death

There were a total of 375 infant deaths in the sample selected from the CPP cohort. Among these, 211 infant deaths were included in the screening. Results of this analysis are presented in table B.3.

Fathers employed in the agriculture, forestry, fishing occupations category displayed a significant association for infant death (OR = 2.7). This odds ratio was not affected when adjusted for age and race, and hospital.

Paper working occupations were highly associated with infant death (OR = 6.7), even after adjustment for age and race, and hospital. The odds ratio is based on a small number of events, however, only 4 infant deaths occurred in this category.

The odds ratio for infant death in the children of radio and radar operators was elevated, although not statistically significant. Significance was achieved when standardization for age and race (OR = 5.2) and for hospital (OR = 3.3) was performed. However, these calculations are based on 3 deaths.

6.3.4 Any Malformations

There were 3,186 pregnancies in the study sample with any malformation. A total of 2,170 of the cases met the inclusion criteria for the analysis. The screening analysis was divided into two parts: a screen for non-uniformly distributed defects, and a screen for uniformly distributed defects. The difficulties involved with combining the two types of malformation distribution in a single analysis were discussed in Section 2.3.

6.3.4.1 Uniform Malformations

Of the 2,170 children who were born with any malformation, 838 had at least one uniformly distributed malformation. Results of the screening analysis for associations between uniform malformations and paternal occupation are presented in table B.4.

For this group of malformations, there was no significantly associated paternal occupation category.

6.3.4.2 Non-Uniform Malformations

Of the 2,170 children who were born with any malformation, 306 had at least one non-uniformly distributed malformation. Results of the screening analysis for associations between non-uniform malformations and paternal occupation are presented in table B.5.

Significantly elevated crude (OR = 2.8) and adjusted odds ratios for non-uniform malformation were observed in children of men employed in structural work in the metal industry.

Pharmacists' children had a significant association with non-uniform malformations only after age-race and hospital adjustment (OR = 3.6). These calculations are based on only 3 cases.

6.3.5 Musculoskeletal System Malformations

There were 871 children in the study sample who were born with any musculoskeletal system malformation. A total of 579 cases met the inclusion criteria and were eligible for analysis. Results of the screening analysis are presented in table B.6.

A total of 7 specific musculoskeletal malformation categories were reported in adequate numbers for the purpose of this screening analysis. The outcomes of each of the analyses will be presented in the following subsections.

Polydactyly:

There were 368 cases of polydactyly in the study sample, 200 were eligible for the analysis. The results of the screening analysis are presented in table B.7.

Absence of All or Part of Limb:

There were 30 children in the study sample born with part or all of a limb missing. A total of 24 were eligible for the analysis. The results of the screening analysis are presented in table B.8. No significant associations between any industry or occupation and this malformation were observed.

Hypoplasia of All or Part of Limb:

There were 48 children in the study sample born with hypoplastic of all or part of a limb. A total of 35 were eligible for analysis. The results of the screening analysis are presented in table B.9. No significant associations between any industry or occupation and this malformation were observed.

Syndactyly:

There were 119 children in the study sample born with syndactyly, of which a total of 95 were eligible for analysis. The results of the screening are presented in table B.10. No significant associations for syndactyly were noted in the screened occupations.

Congenital Dislocation of Hip:

There were 91 children in the study sample born with congenital dislocation of the hip, of which a total of 73 were eligible for analysis. The results of the screening analysis are presented in table B.11. No significant associations between this malformation and paternal occupation were noted.

Micrognathia/Hypognathous Jaw:

There were 20 children in the sample born with micrognathia or hypognathous jaw. A total of 13 were eligible for analysis. The results of the screening analysis are presented in table B.12. No significant associations for this malformation category were noted in the screened occupations.

Clubfoot:

There were 188 children in the study sample born with clubfoot; a total of 136 cases were eligible for the analysis. The results of the screening analysis are presented in table B.13. No significant associations for this malformation group were noted in the screened occupations.

6.3.6 Any Eye and/or Ear Malformation

There were 119 children in the study sample born with any eye and/or ear malformation. A total of 87 cases were eligible for the analysis. The results of the screening analysis are presented in table B.14.

The odds ratio for eye and/or ear defects in children of men in machinery and electrical industry occupations was virtually unchanged after age-race and hospital adjustment (OR = 2.5). The other production category of this industry also had a significantly elevated odds ratio (OR = 8.4); but was based on only 3 cases.

There were 2 specific eye and/or ear malformations which were reported in adequate numbers for the purpose of this screening analysis. The outcomes of each of the analyses will be presented in the following subsections.

Cataract:

There were 44 children in the study sample born with cataract. A total of 35 cases were deemed eligible for the analysis. The results of the screening analysis are presented in table B.15. No significant associations between paternal occupation and cataract in the offspring were observed.

Pre-Auricular Skin Tag:

There were 36 children in the study sample born with pre-auricular skin tag. A total of 28 were deemed eligible for the analysis. The results of the screening analysis are presented in table B.16. No significant associations between pre-auricular skin tag and paternal occupation were observed.

6.3.7 Respiratory System Malformations

There were 409 children in the study sample born with any respiratory malformation. A total of 288 were deemed eligible for the analysis. The results of the screening analysis are presented in table B.17.

The "other construction" occupations category had a significantly elevated crude odds ratio (OR = 1.9) which was virtually unaffected by adjustment.

The odds ratio for autobody work, based on only 3 cases, became significant on age-race adjustment (OR = 3.5) and hospital adjustment (OR = 7.4).

There were 10 specific respiratory malformations which were reported in adequate numbers for the purpose of this screening analysis. The outcomes of each of the analyses will be presented in the following subsections.

Any Malformation of Thoracic Wall and/or Cavity:

There were 108 children in the study sample born with any malformation of the thoracic wall and/or cavity. A total of 90 cases were considered eligible for analysis. The results of the screening analysis are presented in table B.18.

The crude odds ratio for thoracic wall and/or cavity defects in children of men in the "other construction" category became statistically significant when controlled for age-race (OR = 3.0), and hospital (OR = 2.7).

Thoracic Wall Malformation:

There were 18 children in the study sample born with malformation of the thoracic wall. A total of 12 were eligible for the analysis. The results of the screening analysis are presented in table B.19. No significant associations between paternal occupation and this malformation were observed.

Cleft Lip/Palate and/or Gum:

There were 188 children in the study sample born with cleft lip, palate, and/or gum. A total of 119 were eligible for the analysis. The results of the screening analysis are presented in table B.20.

The construction industry occupations inclusive had a significantly elevated crude odds ratio for cleft lip/palate/gum in the offspring (OR = 2.4). The association was not altered by age-race or hospital adjustment.

A significant positive association between paternal employment in the food and tobacco industry and a cleft defect in offspring was observed unadjusted and adjusted odds ratios. This elevated odds ratio was also present in 3 of the specific food and tobacco job classifications, however each was based on 6 or fewer cases.

Two job classifications within the textile industry were associated with cleft lip/palate and/or gum defect, however, each was based on 4 or fewer cases.

Hypoplasia and/or Agenesis of the Lungs:

There were 29 children in the study sample born with hypoplasia and/or agenesis of the lungs. A total of 22 were deemed eligible for the analysis. The results of the screening analysis are presented in table B.21.

The leather industry, and leather processing and production occupations in particular, had significantly elevated crude and adjusted odds ratios. However, there was a small number of cases in these occupation categories.

Malformation of the Lungs:

There were 25 children in the study sample born with malformed lungs. A total of 15 were eligible and included in the analysis. The results of the screening analysis are presented in table B.22. No significant associations between paternal occupation and malformation of the lungs in the offspring were observed.

6.3.8 Gastrointestinal System Malformations

There were 959 children in the study sample with any gastrointestinal malformation. A total of 647 were considered eligible for analysis. The results of the screening analysis are presented in table B.28.

An elevated crude odds ratio for GI malformations, based on 4 cases, was observed in the children of pharmacists (OR = 5.5). The association was not substantially affected by adjustment.

There were 8 specific GI malformations which were reported in adequate numbers for the purpose of this screening analysis. The outcomes of each of the analyses will be presented in the following subsections.

Omphalocele:

There were 22 children in the study sample born with omphalocele. A total of 12 were included in the analysis. The results of the screening analysis are presented in table B.29. No association between either of the two industries included in the analysis and the malformation was noted.

Anal Atresia:

There were 26 children in the study sample born with anal atresia. A total of 17 were deemed eligible for analysis. The results of the screening are presented in table B.30.

An elevated crude odds ratio for anal atresia was noted in children of men in the textile industry (OR = 11.6). Age-race and hospital standardization increased the odds ratio. However, the association is based on only 3 cases.

Malrotation:

There were 25 children in the study sample born with malrotation. A total of 16 were included in the analysis. The results of the screening analysis are presented in table B.31. No significant positive associations were noted between any occupation and malrotation in employees' children.

Inguinal Hernia:

There were 674 children in the study sample born with inguinal hernia. A total of 446 were considered eligible for analysis. The results of the screening analysis are presented in table B.32.

An elevated crude odds ratio for inguinal hernia, based on 4 cases, was observed in children of men in material handling occupations in agriculture, forestry, and fishing. Standardization for age-race (OR = 3.1) and hospital (OR = 3.4) yielded significant results.

Pectus Excavatum:

There were 91 children in the study sample born with pectus excavatum. A total of 79 cases were eligible for the analysis. The results of the screening analysis are presented in table B.23.

The "other construction" category was observed to have a significantly elevated odds ratio for pectus excavatum in employees' children after controlling for age and race (OR = 3.5), and hospital (OR = 3.3).

Any Malformation of Thoracic Wall and/or Cavity:

There were 108 children in the study sample born with any malformation of the thoracic wall and/or cavity. A total of 90 cases were considered eligible for analysis. The results of the screening analysis are presented in table B.18.

The crude odds ratio for thoracic wall and/or cavity defects in children of men in the "other construction" category became statistically significant when controlled for age-race (OR = 3.0), and hospital (OR = 2.7).

Cleft Lip Only:

There were 24 children in the study sample born with cleft lip. A total of 21 cases were eligible for the analysis. The results of the screening analysis are presented in table B.24. No significant associations between any of the industries and cleft lip in employees' children was observed.

Co-Existent Cleft Lip and Palate:

There were 48 children in the study sample born with cleft lip and palate. A total of 39 were considered eligible for analysis. The results of the screening analysis are presented in table B.25.

Elevated age-race (OR = 7.6) and hospital (OR = 8.2) adjusted odds ratios for co-existent cleft lip and palate were observed in the children of men employed in material handling work in the food and tobacco industry. However, the association is based on only 3 cases.

Cleft Palate Only:

There were 30 children in the study sample born with cleft palate. A total of 22 were included in the analysis. The results of the screening analysis are presented in table B.26.

A significantly elevated crude odds ratio for cleft palate was observed in children of men employed in the construction industry (OR = 4.7). This association increases lightly when controlling for age-race (OR = 5.9), and hospital (OR = 5.6). However, these estimates are based on 5 cases.

Cleft Gum Only:

There were 110 children in the study sample born with cleft gum only. A total of 58 cases were eligible for the analysis. The results of the analyses are presented in table B.27. No significant associations between cleft gum and paternal occupation were noted.

Children of pavers were noted to have a significant positive association for inguinal hernia only after adjustment for age-race (OR = 3.0), and hospital (OR = 3.0). However, these odds ratios are based on 4 cases.

Children of men employed in structural work in the metal industry (OR = 3.3), and as cooks (OR = 2.2) had elevated crude odds ratios for inguinal hernia that were not substantially affected by age-race, or hospital adjustment.

Pyloric Stenosis:

There were 92 children in the study sample born with pyloric stenosis. A total of 74 were considered eligible for analysis. The results of the screening analysis are presented in table B.33. All of the associations noted in this category were based on 5 or fewer cases.

Children of carpenters were observed to have a significantly elevated odds ratios for pyloric stenosis only after adjustment for age-race (OR = 3.8) and for hospital (OR = 4.4). A marginally significant crude odds ratio in offspring of men in metal working and machining occupations because significant when standardized for age-race (OR = 6.7), and hospital (OR = 3.3).

Accessory Spleen:

There were 21 children in the study sample born with an accessory spleen. A total of 16 cases were included in the analysis. The results of the screening analysis are presented in table B.34. No significant associations for accessory spleen were observed in offspring of men in the occupations included in the screening analysis.

Umbilical Hernia:

There were 50 children in the study sample born with an umbilical hernia. A total of 33 cases were considered eligible and included in the analysis. The results of the screening analysis are presented in table B.35. No significant associations for umbilical hernia were observed in the offspring of men in the occupations included in the screening analysis.

Any Hernia:

There were 727 children in the study sample born with any hernia. A total of 480 cases were deemed eligible for analysis. The results of the screening analysis are presented in table B.36.

Children of men in forestry and logging occupations had a marginally significant elevated crude odds ratio based on only 3 cases, for any hernia (OR = 4.4). The odds ratio increased slightly and became significant when age-race and hospital standardized.

Significantly elevated crude and adjusted odds ratios for any hernia were observed in children of pavers (OR = 3.7) and in the offspring of men in structural work in the metal industry (OR = 3.1). The association for the pavers' children is based on 5 cases.

6.3.9 Cardiovascular System Malformations

There were 398 children in the study sample born with any cardiovascular malformation. A total of 273 met the eligibility criteria for inclusion in the analysis. Table 58 lists the individual cardiovascular system malformations used in screening paternal employment history. The results of the screening analysis for only cardiovascular defect are presented in table B.37.

Table 58

Frequency of Children with Cardiovascular System Malformations
Included in the Paternal Occupation Screening Analysis

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any cardiovascular malformation	273	125	398
Any atrial septal defect	38	14	52
Atrial septal defect-secundum	27	11	38
Atrial septal defect-secundum, isolated	18	10	28
Atrial septal defect-secundum, multiple	9	1	10
Any atrial septal defect, isolated	25	12	37
Any atrial septal defect, multiple	13	2	15
Any ventricular septal defect	127	41	168
Ventricular septal defect (open)	97	29	126
Ventricular septal defect (open), isolated	55	19	74
Ventricular septal defect (open), multiple	47	13	60
Ventricular septal defect-spontaneously closing	25	9	34
Any ventricular septal defect (open or closing), isolated	79	28	107
Any ventricular septal defect (open or closing), multiple	48	13	61
Atrioventricular canal	12	6	18
Aortic valve malformation	18	9	27
Pulmonic valve malformation	48	25	73
Pulmonic valvular or unspecified stenosis	39	17	56
Pulmonic valvular or unspecified stenosis, isolated	16	13	29
Pulmonic valvular or unspecified, stenosis, multiple	23	4	27
Pulmonic valve malformation, isolated	17	17	34
Pulmonic valve malformation, multiple	31	8	39
Any malposition of great vessels (union)	18	11	29
Any malposition of great vessels, multiple			
Ductus arteriosus persistens	28	17	45
Ductus arteriosus persistens, isolated	18	11	29
Any coarctation of aorta	25	10	35

Table 58 Continued

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Coarctation of aorta-preductal	18	7	25
Coarctation of aorta-preductal, multiple	12	4	16
Any coarctation of aorta, isolated	13	6	19
Any coarctation of aorta, multiple	12	4	16
Aortic and mitral valve atresia	9	4	13
Hypoplasia cordis	13	6	19
Conus arteriosus syndrome	33	11	44
Endocardial cushion defect	25	9	34
Hypoplastic left heart syndrome	17	7	24
Mitral valve malformation	12	4	16

A marginally significant elevated crude odds ratio for any cardiovascular defect, based on 3 cases, was observed in the children of electricians (OR = 4.1). The association became significant when controlled for age-race (OR = 3.6) and hospital (OR = 3.8).

A significant positive association for cardiovascular defect was observed in the children of men in chemistry occupations only after age-race and hospital adjustment (OR = 3.0). This association is based on 4 cases.

There were 35 specific cardiovascular malformations which were reported in adequate numbers for the purpose of this screening analysis. The outcomes of the separate analyses will be covered in the following subsections.

Atrial Septal Defects:

There were 52 children in the study sample born with any atrial septal defect. A total of 38 cases were eligible for the analysis. These 38 cases were also classified into five subsets (not mutually exclusive) of particular atrial septal defects: atrial septal defect secundum; atrial septal defect secundum, isolated; atrial septal defect secundum, multiple; any atrial septal defect, isolated; any atrial septal defect, multiple. The results of these 6 screening analyses are presented in tables B.38 - B.43. No positive associations for atrial septal defects were noted in the industries and occupations that were screened.

Ventricular Septal Defects:

There were 168 children in the study sample born with any ventricular septal defect. A total of 127 cases met the criteria for inclusion in the analysis. These 127 cases were also classified into 6 subsets (not mutually exclusive) of particular ventricular septal defects: open; open, isolated; open, multiple; spontaneously closing; open or closing, isolated; open or closing, multiple. The results of these 7 screening analyses are presented in tables B.44

There were 3 cases of ventricular septal defects in children of men employed in chemistry occupations. A marginally significant elevated crude odds ratio for any ventricular septal defect was noted. Standardization for age-race and for hospital yielded significant associations (OR = 4.6). Significant crude (OR = 5.7) and adjusted odds ratios were also calculated for open ventricular septal defect.

Significant crude (OR = 5.8) and adjusted odds ratios for any ventricular septal defect, based on 3 cases, were noted in bartenders' children. Elevated odds ratios for isolated open or closing defects were also observed in this group (OR = 9.5).

Atrioventricular Canal Defect:

There were 18 children in the study sample born with atrio-ventricular canal defects. A total of 12 cases were eligible for the analysis. The results of the screening analysis are presented in table B.51. No positive associations were noted for atrioventricular canal defects in the children of men employed in the screened industries.

Aortic Valve Malformation:

There were 27 children in the study sample born with aortic valve malformation. A total of 18 cases were eligible for the analysis. The results of the screening analysis are presented in table B.52. No significant associations between paternal occupation and aortic valve malformations were observed.

Pulmonic Valve Malformation:

There were 73 children in the study sample born with pulmonic valve malformation. A total of 48 cases met the criteria for inclusion in the analysis. These 48 cases were also classified into 5 subsets (not mutually exclusive) of defects isolated, multiple and inclusive pulmonic valvular or unspecified stenosis, isolated and multiple pulmonic valve malformation. The results of the 6 screening analyses are presented in tables B.53 - B.58. No consistent significant associations for pulmonic valve malformations were observed in any occupational category.

Mitral Valve Malformation:

There were 16 children in the study sample born with mitral valve malformation. A total of 12 cases were eligible for the analysis. The results of the screening analysis are presented in table B.59. No significant associations between paternal occupation and mitral valve malformation were noted.

Malposition of the Great Vessels:

There were 29 children in the study sample born with malposition of the great vessels. A total of 17 cases were eligible for the analysis. All of these cases were multiple malpositions of the vessels. The results of the screening analysis are presented in table B.60. No significant positive associations between any paternal occupation and malposition of the great vessels were noted.

Ductus Arteriosus Persistens:

There were 45 children in the study sample with ductus arteriosus persistens. A total of 28 cases met the criteria for inclusion in the analysis. Of the 28 cases, 18 were classified as isolated ductus arteriosus persistens; a separate screening was run on this specific defect. The results of the two analyses are presented in tables B.61 and B.62. No significant associations between ductus arteriosus persistens and paternal occupation were observed.

Coarctation of the Aorta:

There were 35 children in the study sample born with coarctation of the aorta. A total of 25 cases were eligible for the analysis. These 25 cases were also classified into 3 subsets (not mutually exclusive) of coarctation of the aorta: multiple; preductal; and multiple preductal. The results of the 4 screening analyses are presented in tables B.63 - B.66. No significant associations between coarctation of the aorta and paternal occupation were noted.

Aortic and Mitral Valve Atresia:

There were 13 children in the study sample born with aortic and mitral valve atresia. A total of 9 cases were eligible for the analysis. The results of the screening analysis are presented in table B.67. No significant association between aortic and mitral valve atresia and paternal occupation were noted.

Hypoplasia Cordis:

There were 19 children in the study sample born with hypoplasia cordis. A total of 13 cases met the eligibility criteria for the analysis. The results of the screening analysis are presented in table B.68. No significant association was found for hypoplasia cordis in the children of men employed in either of the industries included in this screen.

Conus Arteriosus Syndrome:

There were 44 children in the study sample born with conus arteriosus syndrome. A total of 33 cases were eligible for the analysis. The results of the screening analysis are presented in table B.69. No significant associations between conus arteriosus syndrome and paternal occupation were observed.

Endocardial Cushion Defect:

There were 34 children in the study sample born with endocardial cushion defect. A total of 25 of the cases were eligible for the analysis. The results of the screening analysis are presented in table B.70. No significant association between paternal occupation and endocardial cushion defect was noted.

Hypoplastic Left Heart Syndrome:

There were 24 children in the sample born with hypoplastic left heart syndrome. A total of 17 cases met the criteria for inclusion in the analysis. The results of the screening analysis are presented in table B.71. No significant associations between paternal occupation in one of the screened industries and hypoplastic left heart syndrome were observed.

Genitourinary System Malformations:

There were 404 children in the study sample born with any genitourinary malformation. A total of 276 cases met the eligibility criteria for the analysis. Table 59 lists the individual genitourinary system malformations used in screening paternal employment history. The results of the screening analysis are presented in table B.72.

Table 59

Inclusions and Exclusions of Cases with Genitourinary
System Malformations

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any genitourinary malformation	276	128	404
Urethral obstruction	42	24	66
Polycystic kidney	21	8	29
Stenotic ureter	18	7	25
Malformation, male genitalia	142	69	211
Hypospadias	124	60	184
Malformation, female genitalia	27	8	35
Malformation, female genitalia, minor	15	7	22
Hydroureter	15	3	18
Obstructive uropathy	32	11	43

A significantly elevated crude odds ratio for any genitourinary defect was noted in children whose fathers worked as cooks (OR = 3.5). Adjustment for age-race and for hospital did not materially affect the association. There were 9 specific genitourinary defects which were reported in adequate numbers for the purpose of this screening analysis. The outcomes of these analyses are presented in the following subsections.

Urethral Obstruction:

There were 66 children in the study sample born with urethral obstruction. A total of 42 cases were eligible for the analysis. The results of the screening analysis are presented in table B.73.

A significant association for urethral obstruction, based on 3 cases, was observed in carpenters' children when standardized for age and race (OR = 3.8) and for hospital (OR = 6.5).

Polycystic Kidney:

There were 29 children in the study sample born with polycystic kidney. A total of 21 cases met the criteria for inclusion in the analysis. The results of the screening analysis are presented in table B.74. No significant associations between polycystic kidney and paternal occupation were noted.

Stenotic Ureter:

There were 25 children in the study sample born with stenotic ureter. A total of 18 cases were eligible for the analysis. The results of the screening analyses are presented in table B.75. No significant associations between stenotic ureter and paternal occupation were noted.

Male Genitalia Malformations:

There were 211 children in the study sample born with malformations of the male genitalia. A total of 142 cases were eligible for the analysis. The results of the screening analysis are presented in table 3.76.

Significantly elevated crude (OR = 2.1) and adjusted odds ratios for defects of the male genitalia were observed in the children of men employed in the paper and wood industry. A positive association was also noted in printers' children, although the calculations are based on only 5 cases (OR = 3.9).

Children of men in materials handling work in the metal industry were observed to have significantly elevated age-race adjusted (OR = 5.5) and hospital standardized (OR = 5.1) odds ratios for defects of the male genitalia. The association is based on 3 cases.

The results of the screening analysis for hypospadias are presented in the next subsection.

Hypospadias:

There were 184 children in the study sample born with hypospadias. A total of 124 cases were eligible for the analysis. The results of the screening analysis are presented in table 3.77.

Significantly elevated age-race (OR = 5.6) and hospital (OR = 5.1) adjusted odds ratios for hypospadias were observed in the sons of men employed in material handling occupations in the metal industry. These calculations are based on 3 cases.

Significantly elevated crude (OR = 4.1) and adjusted odds ratios for hypospadias were noted in cooks' children.

Significant crude (OR = 2.4) and adjusted odds ratios for hypospadias were noted in sons of men employed in unknown industry.

Female Genitalia Malformations:

There were 35 children in the study sample born with malformation of the female genitalia. A total of 27 cases met the criteria for inclusion in the analysis. There were 15 cases that were also classified as minor malformations. The results of the 2 screening analyses are presented in tables B.78 - 3. 79.

Children of fathers in the medicine and science industry had elevated age-race and hospital adjusted odds ratios for defects of the female genitalia (OR = 7.3; 10.8, respectively). These calculations were based on only 3 cases.

Hydroureter:

There were 18 children in the study sample born with hydroureter. A total of 15 cases were eligible for the analysis. The results of the screening analysis are presented in table B.80.

No significant association between hydroureter and either of the screened industries was noted.

Obstructive Uropathy:

There were 43 children in the study sample born with obstructive uropathy. A total of 32 cases met the criteria for inclusion in the analysis. The results of the screening analysis are presented in table B.81.

A significantly elevated odds ratio for obstructive uropathy, based on 4 cases, was noted in children of men in the agriculture, forestry, and fishing industry when the odds ratio was standardized for age-race (OR = 5.8) and hospital (OR = 4.2).

Significantly elevated odds ratios for obstructive uropathy were observed in the offspring of engine mechanics, only when age-race (OR = 5.0) and hospital (OR = 4.6) adjusted. This association was based on only 3 cases.

6.3.11 Benign or Malignant Tumors

There were 158 children in the study sample born with any benign or malignant tumor. A total of 116 cases were eligible for the analysis. The results of the screening analysis are presented in table B.82. No significant positive associations for any benign or malignant tumor were found in the children in any paternal occupation classification.

There were adequate numbers of 5 specific type of tumors in the sample for the purpose of the screening analysis. The outcomes of these separate analyses are reported in the following subsections.

Any Malignant Tumors:

There were 23 children in the study sample born with any malignant tumor. A total of 19 cases were eligible for the analysis. The results of the screening analysis are presented in table B.83. No significant positive associations between paternal occupation and malignant tumors were noted.

Any Benign Tumors:

There were 133 children in the study sample born with any benign tumor. A total of 95 cases were eligible for the analyses. The results of the screening analysis are presented in table B.84. No significant association between any benign tumors and any paternal occupation were observed.

Any Cyst:

There were 39 children in the study sample born with any cyst. A total of 24 cases met the criteria for inclusion in the analysis. The results of the screening analysis are presented in table B.85. No associations between any cyst and paternal occupation were noted.

Hairy Nevus:

There were 21 children in the study sample born with hairy nevus. A total of 15 cases were eligible for the analysis. The results of the screening analysis are presented in table B.86. No positive associations between hairy nevus and paternal occupation were noted.

Other Benign Tumors:

There were 24 children in the study sample born with other benign tumors. A total of 21 cases met the criteria for inclusion in the analysis. The results of the screening analysis are presented in table B.87. No associations between other benign tumors and paternal occupation were noted.

6.3.12 Central Nervous System Malformations

There were 262 children in the study sample born with any CNS malformation. A total of 184 cases were considered eligible for the analysis. The results of the screening analysis are presented in table B.88.

There was a significant association for CNS defects in children of material handlers in the machinery and electrical industry which was not reduced after adjustment (OR = 5.7). However, the association was based on only 4 cases.

Significant age-race and hospital adjusted odds ratios for CNS defects were noted in offspring of men employed in product fabrication work in the textile industry (OR = 3.5; 3.0, respectively). However, this association is based on only 4 cases.

Elevated crude and adjusted odds ratios for children of men employed in the leather industry (OR = 4.2), and in leather processing and production (OR = 5.0) were also observed.

There were 9 specific central nervous system defects which were reported in adequate numbers for the purpose of the screening analysis. The results of these separate screenings will be presented in the following subsections. Table 60 lists the cases of CNS malformations included in and excluded from the analysis.

Table 60
Inclusions and Exclusions of Cases with Central
Nervous System Malformations

<u>Malformation</u>	<u>Included</u>	<u>Excluded</u>	<u>Total</u>
Any central nervous system malformation	184	78	262
Any brain malformation	169	69	238
Any hydrocephaly	49	27	76
Microcephaly	53	23	76
Anencephaly	22	4	26
Any spinal malformation	39	18	57
Meningomyelocele	24	12	36
Craniospinal fusion defects	37	16	53
Craniosynostosis	16	10	26

Brain Malformations:

There were 238 children in the study sample born with any brain malformation. A total of 169 cases were deemed eligible and included in the analysis. The 169 cases were further classified into 3 specific categories of brain defects: any hydrocephaly, anencephaly, and microcephaly. The results of the 4 screening analyses are presented in tables B.89 - B.92.

Children of men in the agriculture, forestry and fishing industry had significantly elevated crude and adjusted odds ratios for any brain malformation (OR = 2.5). A significant association, based on 5 cases, was also noted for any hydrocephaly in this group (OR = 8.5).

Elevated crude and adjusted odds ratios for any brain malformation were observed in the offspring of men in forestry and logging work (OR = 16.8). These odds ratios are based on only 3 cases.

A significant association with any brain defect, based on 3 cases, was observed in children of men employed as material handlers in the machinery and electrical industry (OR = 5.6). The crude odds ratio for anencephaly in children of men in the machinery and electrical industry occupations became significant when adjusted for age-race (OR = 5.5) and for hospital (OR = 6.6). This association was also based on 3 cases.

An elevated crude ratio (OR = 5.9) for any hydrocephaly in children of men in the transportation industry retained its significance after adjustment for age-race (OR = 6.2) and hospital (OR = 3.6). Elevated odds ratios for any brain malformation were observed in children of men employed in service stations (OR = 3.3). Elevated odds ratios for any hydrocephaly were also observed in this group, however, the associations are based on only 3 cases (OR = 10.9). Material handling occupations in the transportation industry were associated with any brain malformation in the offspring (OR = 3.8), but this association was based on 5 cases. The same group also had elevated odds ratios for any hydrocephaly, however, the associations were based on 3 cases (OR = 15.2).

Elevated crude and adjusted odds ratios for any brain defect, based on 4 cases, were observed in the children of men employed in product fabrication in the textile industry (OR = 4.8).

A significant association is observed for any brain malformation in children of men in leather processing and production. Elevated crude (OR = 32.4) and age-race adjusted (OR = 42.9) odds ratios for anencephaly were also observed for leather workers; however, standardization for hospital reduced the odds ratios to 2.7. The association with anencephaly was based on 3 cases which occurred in both of the leather industry categories.

A marginally significant elevated odds ratio for any brain defect was observed in the children of nurses and attendants. This association, based on 4 cases, became significant when standardized for age-race (OR = 3.1) and for hospital (OR = 3.0).

A marginally significant association with any brain malformation, based on 3 cases, was noted in children of men employed in factory work in unknown industry. Standardization for age-race and for hospital yielded significant results (OR = 4.1).

Significantly elevated crude and adjusted odds ratios for anencephaly, based on 5 cases, were observed in offspring of men employed in the construction industry (OR = 4.7).

Spinal Malformations:

There were 57 children in the study sample born with any spinal malformation. A total of 39 cases were eligible for the analysis. Of the 39 cases, 24 were classified as meningomycele; an additional screening for this particular defect was performed. The results of the 2 screening analyses are presented in tables B.93 - B.94. No significant positive associations were found for any spinal malformation or for meningomycele in any of the paternal occupations which were screened.

Craniospinal Fusion Defects:

There were 52 children in the study sample born with craniospinal fusion defects. A total of 37 cases were eligible for the analysis. The results of the screening analysis are presented in table B.95. No consistently significant positive association between craniospinal fusion defects and paternal occupation was observed.

Craniosynostosis:

There were 26 children in the study sample born with craniosynostosis. A total of 16 cases were eligible for the analysis. The results of the screening analysis are presented in table B.96. No associations between paternal occupation and craniosynostosis were observed.

6.3.13 Syndromes

There were 170 children in the study sample born with any syndrome. A total of 125 cases were eligible for analysis. The results of the screening analysis are presented in table B.97.

Children of painters and plasterers had a significantly elevated crude odds ratio for any syndrome (OR = 4.8). The association remained elevated after adjustment for age-race (OR = 4.4), and for hospital (OR = 3.7).

An elevated crude odds ratio for any syndrome was noted in children of men employed in the fuel industry (OR = 4.2). Standardization for age-race (OR = 3.1) and for hospital (OR = 3.2) yielded significant results. The calculations, however, were based on only 4 cases. Similar results were noted in children of men in utilities production work (OR = 7.8). However, there were only 3 cases in this fuel industry occupation category.

There were 3 specific syndromes which were reported in adequate numbers for the purpose of the screening analysis. The results of these 3 additional screening analyses are presented in the following subsection.

Chromosomal Syndromes:

There were 66 children in the study sample born with any chromosomal syndrome. A total of 47 cases were deemed eligible for the analysis. The results of the screening analysis are presented in table B.98. No significant associations between paternal occupation and any chromosomal syndrome were observed.

There were 58 children in the study sample born with Down's Syndrome. A total of 40 cases were eligible for the analysis. The results of the screening analysis are presented in table B.99. No association between Down's Syndrome and paternal occupation was noted.

Hypoplasia/Atrophy of Adrenal Glands Syndrome

There were 26 children in the study sample born with adrenal hypoplasia and/or atrophy syndrome. A total of 22 cases were considered eligible for the analysis. The results of the screening analysis are presented in table B.100.

Elevated adjusted odds ratios for adrenal hypoplasia/atrophy were observed in children of men employed in the machinery and electrical industry (OR = 10.9). However, these calculations were based on 3 cases.

6.3.14 Summary of Paternal Occupational Screening Results

As in section 4.3.14 this section is intended to provide the reader with a list of those associations having: (1) an increased crude (observed) odds ratio, (2) an adjusted odds ratio whose related Chi-square statistic is "significant" at $p < 0.05$, and (3) an "intersecting" cell (i.e., the number of cases who were "exposed") with a frequency greater than 5.

The purpose of the following list is to present, in summary form, those associations between a paternal occupation or industry and an adverse reproductive outcome which are based on some of the larger sample sizes in the study.

As in 4.3.14, these associations are among those which may deserve further consideration and more detailed study.

Summary of the Statistically Significant ($p < 0.05$) Observed Associations Between Paternal Occupational Exposure and the Various Adverse Reproductive Outcomes for which there were more than 5 Observations in the Exposure Category and the Statistically Significant ($p < 0.05$) Adjusted Odds Ratios (Age-Race and Hospital).

<u>Industry-Occupation</u>	<u>Reproductive Outcome</u>	<u>OR</u>	<u>Number of Affected Observation in the "exposed" category</u>
Construction	Neonatal death	1.7	59
Other construction, NOS	Neonatal death	1.9	26
Agriculture, Forestry, Fishery	Infant death	2.7	12
Machinery and Electrical industry	Any eye/ear malform.	2.5	9
Other construction, NOS	Any respiratory malf.	1.9	17
Construction	Cleft lip/palate/gum	2.3	16
Food and tobacco material handling	Cleft lip/palate/gum	3.0	6
Food and tobacco	Cleft lip/palate/gum	2.4	21
Metal structural work	Inguinal hernia	3.3	6
Cooks	Inguinal hernia	2.2	14
Metal structural work	Any hernia	3.1	6
Cooks	Any genitourinary malf.	3.5	13
Paper and wood	Malf. of the male genitalia	2.1	11
Cooks	Malf. of the male genitalia	5.0	9
Leather processing and production	Any CNS malformation	5.0	6
Transportation industry	Hydrocephaly	5.9	15
Agriculture, forestry, fishery	Any brain	2.5	10
Service station work	Any brain	3.3	6
Leather processing and production	Any brain	6.5	6
Metal structural work	Non-uniform malform.	2.8	9

7.0 Discussion

The present study was designed and undertaken to systematically review a large data base containing information on a range of parental occupations and pregnancy outcomes. In particular, a primary goal was to identify and quantify associations between parental occupation during pregnancy and adverse reproductive outcomes. The information used for this purpose was the CPP of the NINCDS, a large-scale, multi-institutional cohort (prospective) epidemiologic study designed in the early 1950's, and implemented in the late 1950's until 1972 (when active data collection ceased).

Although the original NINCDS plans did not intend specifically to study parental occupation in relation to pregnancy outcome, relevant data on the employment history of the mothers and fathers were routinely collected. The present report is based on the work histories abstracted from the original CPP data collection forms.

Due to the time and cost constraints of the present study, it was deemed appropriate to adopt a case-control epidemiologic study design. Accordingly, the case series was identified on the basis of a pre-determined and appropriate definition of an "adverse" reproductive outcome. Although this "outcome" group could have been more broadly defined, the approach adopted in the present study was to concentrate on the more specific and "important" adverse outcomes of pregnancy. Therefore, within the limits of the CPP data base, and the time frame for completing the study, it was decided to review events such as mortality (e.g., infant, neonatal, and stillbirth) and selected "well-defined" physical congenital anomalies. A comparable control series was identified and "frequency matched" on roughly a 2:1 basis. In all, the statistical screening analysis was based on 4,022 "case" pregnancies and 9,016 "control" pregnancies.

The current project represented a unique opportunity to screen the "exposures" of the workplace for both parents in relation to unfavorable outcomes of pregnancy. It was recognized, however, that the current study would have limited capability of intensively studying the epidemiology of "poor" pregnancy outcome, particularly as it relates to parental occupation. The reasons for this were several-fold. First,

the original intent of the CPP project did not encompass the intensive study of either maternal or paternal occupation during pregnancy, and pregnancy outcome. Thus, the CPP midway through the data collection phase of the study changed the form on which employment history was being collected. Also, the specificity of the employment histories was not sufficiently precise to effectively undertake the detailed study of the "adverse" effects on pregnancy due to the risks related to the parents' workplace. This can be seen in the construction of the interview forms. For example, employment status was ascertained at a single point (time) in pregnancy, and any subsequent change in employment status was not available to the study. Thus, the present study was restricted to documenting the effects of first trimester "exposures" on pregnancy outcome.

It should be emphasized that concerns over the possible influences of information and selection bias for all practical purposes, should be minimal since employment histories were gathered prior to the pregnancy's termination, and study registration appeared not to be on the basis of employment status.

A second limitation was that due to relatively low incidence (rates) of many outcomes considered "adverse" in the present study, the eventual numbers of "exposed" with a particular "adverse" outcome was small. These small sample sizes affected the nature of the screening analysis. Although plans originally included a second more intensive screening stage involving multivariate statistical procedures, given the relatively small size of the frequencies observed in many of the "intersecting" cells of the 2x2 contingency tables it was decided to present only the first stage's screening results.

A third consideration in interpreting the results of the present study is the nature of the original interview and the resulting classification system for the paternal occupations. Given the information collected, the coding procedure assigned many jobs to broadly defined categories, which often did not enable a more specific evaluation of the workplace (and its "exposures"). A further analysis based on the more specific types of employment would have encountered the problem mentioned above - namely, diminishing sample sizes (due to further cross-classification).

Among the other considerations that should be taken into account in evaluating the results of the present study is the role of chance. The statistics provided in the Results (Appendix K) include both observed (crude) and adjusted point estimates of the odds ratio, and the corresponding (Chi-square) test statistics. These statistics provide

the minimal information needed to measure the strength of an association, and to assess the role of chance in "explaining" the observed level of the association. Thus, this information can be used to achieve the major goal of the project - to generate hypotheses which can be explored further by other investigators, using other resources.

It is recognized, however, that an hypothesis testing approach does not provide (explicitly) indications of the variability associated with each point estimate of the odds ratio. Also, as implied in the methods section, the issue of "multiple comparisons" (leading to "inflated" α levels) arises within the format of studies such as the present one. Thus, for example, the Chi-square test statistics (and associated "p-values") should be considered only as general indicators of the "true" level of statistical significance. An approach to the interpretation of the Chi-square test statistics (in the present report) is to use a very small "p-value" (e.g., $p < 0.001$) to avoid the difficulties resulting from performing many significance tests on the same body of data. This approach helps to minimize the risk of inappropriately declaring "statistical significance".

One strategy for gaining insight into the issue of the sampling variability about a particular odds ratio is to employ interval estimation. For any association of particular interest, it is suggested that a test-based procedure be used to compute the desired confidence interval (77).

Among the criteria commonly used to assess the validity of an association suspected as being "causal" is that the gathered evidence should be consistent with that previously documented - with respect to biologic credibility, (e.g., in laboratory and animal studies), and the results of other epidemiologic studies. Unfortunately, as seen in the accompanying literature review, there exists relatively little previous work identifying occupational or other work-related risks to the viability of the fetus or offspring.

The intention of this report is to provide the medical and public health communities with information with which they can further study the potentially harmful effects of work-related exposures on reproductive outcome. Rather than emphasizing and discussing any specific set of results or associations from the present screening analyses, it has been left to the reader to judge and identify those relationships between work history and adverse reproductive outcomes deserving extended study.

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APPENDIX A: Distribution of Cases by Institution

Appendix A

Summary of Case Selection by Institution

Institution	Registration		Number of Cases	
	From	To	In Sampling Frame	Selected Case Study
BO	1/02/59	12/31/65	13,137	13,137
BU	10/07/60	12/31/65	2,964	2,964
CH	3/15/60	12/31/65	18,890	2,590
CO	1/16/59	4/30/63	9,852	2,235
JH	1/06/59	12/31/64	8,573	3,774
VA	1/02/59	12/31/65	4,660	3,250
MN	1/20/59	12/31/65	3,468	3,275
NY	2/02/59	12/31/65	27,380	4,709
OR	3/02/59	12/31/65	6,327	3,255
PA	1/05/59	12/31/65	10,457	10,315
PR	3/02/60	12/31/65	6,300	2,851
TN	10/16/59	12/31/65	20,552	3,553
TOTAL	1/02/59	12/31/65	132,560	55,908

APPENDIX B: List of CPP Data Collection Forms

CPP Data Collection Forms

<u>Abbreviation</u>	<u>Form</u>
AR-1	Obstetrical Administrative Record
OB-2	Reproductive History
OB-3	History Since Last Menstrual Period
OB-4	Gynecological History
OB-5	Recent Medical History
OB-6	Past Medical History
OB-7	Infectious Disease and System Review
OB-8	Repeat Prenatal History (completed at each visit, and on admission for delivery)
OB-32	Labor Room Record
OB-33	Delivery Room Events
OB-40	Prenatal Record (optional form)
OB-42	Post Medical History
OB-43	Initial Prenatal History
OB-44	Prenatal Observations (completed at each visit)
OB-45	Laboratory Record
OB-46	Physicians Clinic Record
OB-47	Summary of Antepartum Hospitalization
OB-50	Admission History
OB-51	Admission Examination, Part I
OB-52	Admission Examination, Part II
OB-53	Delivery Report (Succeeded earlier Delivery Report, OB-34_
OB-56	Obstetric Summary
OB-57	Anesthetic Agents
OB-58	Summary of Puerperium
OB-60	Obstetric Diagnostic Summary
PATH-1	Placental Examination-Gross
PATH-2	Placental Examination-Microscopic
PATH-3	Autopsy Protocol (for stillbirths, neonatal, and infant deaths)
PED-1	Delivery Room Observation of the Neonate
PED-4	Report of Fetal or Infant Death
PED-11	One-Year Neurological Examination
FHH-1	Family Health History
SE-1	SE-1 Socioeconomic Interview (Succeeded FHH-1)

APPENDIX C: CPP Occupational Data Forms

FAMILY HEALTH HISTORY

PART I

1. Patient Identification

4. Religion

☐ P ☐ RC ☐ J ☐ Other [Specify]

5. Race: ☐ W ☐ N ☐ Or. 6. Phone

☐ Other [Specify]

7. Date 8. Interviewer

9. 2nd Appt. Date Time

10. Worksheet Received On

A. BIRTHPLACE AND EDUCATION

11. Place of Birth

INSIDE CONTINENTAL U.S.

a. (CITY OR COUNTY) (STATE)

b. CHECK ONE

- ☐ Urban (2500 pop. and over)
☐ Rural Non-Farm (less than 2500 pop.)
☐ Rural Farm

OUTSIDE CONTINENTAL U.S.

c. (CITY) (COUNTRY)

d. CHECK ONE

- ☐ Urban (2500 pop. and over)
☐ Rural Non-Farm (less than 2500 pop.)
☐ Rural Farm

e. When did you first come to the U.S.?

(MONTH) (YEAR)

f. Have you lived in this country ever since?

- ☐ Yes
☐ No: How long were you away?

12. How far did you go in school? [Circle biggest grade completed] 0 1 2 3 4 5 6 7 8 9 10 11 12

13. How old were you then?

[If less than 12th grade, ask]

a. How did it happen that you didn't go on?

- ☐ Went to work
☐ Got married
☐ Got pregnant
☐ Tired of school
☐ Ungraded class
☐ Other [Specify]

[If 12th grade, ask]

b. Did you have any schooling beyond that?

- ☐ No
☐ Yes, college and/or professional school
☐ Yes, all others

FAMILY HEALTH HISTORY

PART I (Continued)

15. Did you ever have to stay out of school for any length of time?

☐ No ☐ Yes [Probe for amount of time missed, reason, age, and grade.]

AMOUNT OF TIME MISSED (MONTHS)	REASONS	AGE	GRADE
1.			
2.			
3.			

TOTAL MONTHS MISSED _____

16. Were there any subjects that gave you trouble in school? [Specify which] _____

17. Did you have to repeat a grade at any time? ☐ No [If yes, probe for age, grade, reason] _____18. Did you ever go to any special school or any special class in school? ☐ No [If yes, probe for age, grade, reason] _____

B. GRAVIDA'S EMPLOYMENT

19. Do you have a job now?

☐ Yes

a. What kind of work do you do? _____

b. Type of business _____

c. Number of hours worked:

_____ hours per ☐ day ☐ week ☐ month

d. How long have you had this job? _____

☐ No☐ Never worked, housewife only.

e. What was your previous occupation? _____

f. Type of business _____

g. Number of hours worked:

_____ hours per ☐ day ☐ week ☐ month

h. When did you quit? _____ (MONTH) (YEAR)

i. How long did you have that job? _____

-125-

FAMILY HEALTH HISTORY

PART I (Continued)

21. What other kinds of work have you done? [Probe for description of work, type of business, and approximate dates worked] ☐ None
0

KIND OF WORK	TYPE OF BUSINESS	APPROXIMATE DATES WORKED
1.		
2.		
3.		

C. MARITAL HISTORY

22. Are you at present married, separated, divorced, widowed or single?

☐ Married ☐ Separated ☐ Divorced ☐ Widowed ☐ Single
2 6 8 4 1

23. Have you ever been married (before)? ☐ No ☐ Yes
0 1

24. Marriages and children

FROM (YEAR)	TO (YEAR)	TYPE OF TERMINATION	NUMBER OF CHILDREN		
			NOW ALIVE	WHO DIED	BORN DEAD
1.					
2.					
3.					
4.					

D. HUSBAND

25. Are you now living with your husband? [With baby's father if other than married]

☐ Yes ☒ No [Skip to question 31]
x

26. What is his name? _____

27. Date of birth? _____

28. How far did he go in school? [Circle highest grade completed] 0 1 2 3 4 5 6 7 8 9 10 11 12

-126-

FAMILY HEALTH HISTORY
PART I (Continued)

30. Is he employed at present?

☐ Yes

a. What kind of work does he do? _____

b. Type of business _____

c. How long has he had this job? _____

☐ No

d. How long has he been out of work? _____

e. Reason for unemployment: [*Probe for seasonal work, temporary lay-offs, etc.*] _____

f. What kind of work did he do on his last job? _____

g. Type of business _____

h. How long did he have that job? _____

31. What other kinds of work has he done? [*Probe for description of work, type of business, and approximate dates worked*] ☐ None

KIND OF WORK	TYPE OF BUSINESS	APPROXIMATE DATES WORKED
1.		
2.		
3.		

32. In the last 5 years about how many jobs has he had? _____

33. How much time has he spent unemployed in the last 5 years? _____

34. Who is the main wage-earner (breadwinner) in your household? _____

[If main wage-earner is other than husband or baby's father, ask]

32. What is his/her occupation? What type of business is that? _____

THANK GRAVIDA FOR COOPERATION. GIVE AND EXPLAIN WORKSHEET, ESPECIALLY SECTION ON FATHER OF BABY, NOT HUSBAND.

APPOINTMENT FOR SECOND INTERVIEW _____

COLR-3015-1
4-63
(41)

SOCIO-ECONOMIC INTERVIEW

25. PATIENT IDENTIFICATION

SECTION D

GRAVIDA'S WORK HISTORY

Now I'd like to talk to you about the kinds of jobs you've had.

REPEAT PREGNANCY - ABRIDGED FORM
R-3. HAVE YOU CHANGED JOBS OR STARTED TO WORK SINCE

DATE FROM ITEM 2A

☐ NO (skip to Item 31) ☐ YES (do Section D)

26. DO YOU HAVE A JOB NOW?

☐ YES (complete 26, omit 27)

☐ NO (omit rest of 26, ask 27)

A. HOW MANY HOURS PER WEEK DO YOU WORK?

HRS/WK

B. HOW LONG HAVE YOU HAD THIS JOB?

YRS MOS WKS

C. WHAT KIND OF WORK DO YOU DO ON THIS JOB?

27. HAVE YOU EVER HAD A JOB?

☐ YES (complete rest of 27)

☐ NO (skip to 31)

A. HOW MANY HOURS PER WEEK DID YOU WORK ON YOUR LAST JOB?

HRS/WK

B. HOW LONG DID YOU HAVE THIS JOB?

YRS MOS WKS

C. WHAT KIND OF WORK DID YOU DO ON THIS JOB?

D. WHEN DID YOU STOP WORKING?

MO. YEAR

28. HOW MANY OTHER KINDS OF WORK HAVE YOU DONE?

☐ ONE OR MORE (specify number in box. Omit A.)

☐ NONE (ask A.)

A. HOW MANY JOBS HAVE YOU HAD?

☐ ONE (ask Item 30)

☐ SEVERAL (ask Item 29 B)

29. A. WHAT KIND OF WORK DID YOU DO FOR THE LONGEST PERIOD OF TIME?

B. FOR HOW LONG DID YOU DO THIS KIND OF WORK?

YRS MOS WKS

30. OCCUPATIONAL HAZARDS

QUESTION	NO		YES		DESCRIBE WORK SITUATION	APPROXIMATELY HOW LONG? (In Months)
	0	1	0	1		
A. HAVE YOU EVER WORKED WITH X-RAY OR FLUOROSCOPE EQUIPMENT OR BEEN EXPOSED TO X-RAYS IN YOUR WORK?						
B. HAVE YOU EVER WORKED WITH OTHER RADIATION SUCH AS RADIOACTIVE ELEMENTS OR ISOTOPES?						
C. HAVE YOU EVER WORKED WITH TOBACCO DUST OR LEAF OR HANDLED TOBACCO?						
D. HAVE YOU EVER WORKED WITH STEAM OR VERY HIGH HEAT WHERE SPECIAL CARE HAD TO BE TAKEN?						
E. HAVE YOU EVER WORKED WITH CHEMICALS, THEIR DUSTS, GASES OR FUMES IN A JOB SITUATION?						
F. HAVE YOU EVER HAD TO LIFT HEAVY WEIGHTS ON ANY OF YOUR JOBS?						
G. HAVE YOU EVER HAD TO HANDLE ANY LIVE OR DEAD ANIMALS OR BIRDS ON ANY OF YOUR JOBS?						

31. HAVE YOU EVER CARED FOR, HANDLED, PLAYED WITH OR WORKED AROUND FARM ANIMALS, SUCH AS CHICKENS, DUCKS, GESE, COWS, PIGS, HORSES, DONKEYS, MULES, SHEEP OR GOATS, ETC.? (circle which)

A. ☐ YES ☐ NO (omit B and C)

B. HOW OFTEN?

☐ INCIDENTALLY

☐ FREQUENTLY

☐ OTHER

C. WHEN WAS THE LAST TIME THAT YOU DID THIS?

MO. YEAR

COL R-3015-1
4-53
(4)

SOCIO-ECONOMIC INTERVIEW

41. PATIENT IDENTIFICATION

42. Note: COLLECT DATA EITHER FOR HUSBAND OR FOR FATHER OF THE BABY AS THE CASE MAY BE.

for HUSBAND if: 1. He is a member of the household (item 23), or
2. He is reported as temporarily away (item 24) and no other member of the household is reported as the father of the baby (item 40).

for FATHER OF THE BABY for all other cases.

DATA REPORTED FOR: ☐ HUSBAND ☐ FATHER OF THE BABY

SECTION F

EDUCATION, BIRTHPLACE OF HUSBAND OR FATHER OF THE BABY

Now I'm going to ask a few things about your husband.
(The Father of this Baby as checked above)

REPEAT PREGNANCY - ABRIDGED FORM

† R-5. COMPARE MAN IN ITEM 9B WITH MAN IN ITEMS 23, 24 and 40:
☐ SAME MAN (ask R-6) ☐ NOT SAME MAN (complete this page)

† R-6. HAS HE ATTENDED SCHOOL SINCE _____ (INSERT DATE FROM 9A)
☐ NO (omit section F) ☐ YES (complete this page)

43. A. WHAT IS THE HIGHEST GRADE OF REGULAR SCHOOL THAT HE HAS COMPLETED? (circle one)

NONE	ELEMENTARY SCHOOL								JUNIOR HIGH			HIGH SCHOOL			ACADEMIC COLLEGE				GRADUATE OR PROFESSIONAL SCHOOL	
00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	some 17	degree 18		

B. DID HE PASS (GRADUATE FROM) THIS GRADE (SCHOOL)?

☐ YES ☐ NO

C. HAS HE HAD ANY OTHER SCHOOLING?

☐ NO
☐ YES

SPECIFY KIND AND AMOUNT OF SCHOOLING

D. WAS THE LAST REGULAR SCHOOL HE ATTENDED OUTSIDE UNITED STATES?

☐ NO
☐ YES

SPECIFY CITY AND COUNTRY

E. IS HE AT PRESENT GOING TO SCHOOL?

☐ NO
☐ YES

SPECIFY KIND OF SCHOOL

44. IN WHAT CITY OR TOWN WAS HIS FAMILY LIVING WHEN HE WAS BORN?

CITY (OR COUNTY) AND STATE OR COUNTRY

SECTION G

WORK HISTORY OF HUSBAND OR FATHER OF THE BABY

45. IS HE NOW WORKING? ☐ YES (ask rest of 45; omit 46) ☐ NO (omit rest of 45; ask 46)

A. HOW LONG HAS HE BEEN ON THIS JOB? _____ YRS _____ MOS _____ WKS

B. WHAT KIND OF WORK IS HE DOING?

46. HAS HE EVER WORKED? ☐ YES ☐ NO (omit rest of page)

A. HOW LONG WAS HE ON HIS LAST JOB? _____ YRS _____ MOS _____ WKS

B. WHAT KIND OF WORK WAS HE DOING?

C. HOW LONG HAS HE BEEN OUT OF WORK? _____ YRS _____ MOS _____ WKS

D. WHY IS HE UNEMPLOYED?

(SPECIFY SEASONAL, STRIKE, ILLNESS, INJURY, ETC.)

47. A. WHAT KIND OF WORK HAS HE DONE FOR THE LONGEST TIME?

B. FOR HOW LONG DID HE DO THIS WORK? _____ YRS _____ MOS _____ WKS FROM _____ MO _____ YR TO _____ MO _____ YR

48. A. HOW MUCH TIME HAS HE SPENT UNEMPLOYED IN THE PAST YEAR? _____ WKS

B. HOW MANY JOBS HAS HE HAD IN THE PAST YEAR? _____

APPENDIX D: Occupation Data Form and Abstracting System

-130-
Occupational Health Surveillance of Reproductive Outcomes
School of Public Health
University of Massachusetts/Amherst

Sequence No.

Patient I.D.

1	

3				

	0
8	

GRAVIDA'S WORK HISTORY

1. Current or Most Recent Occupation:
(SE1 - 26C or 27C/FHH1 - 19a or 19e)

10	

12			

2. What kind of work did you do for the longest time?
(SE1 - 29A/FHH1 - 19i or 21)

15	

17			

3. Occupational Hazards
(SE1 - 30)

EXPOSED
0 = no
1 = yes
blank = unk.

WORK SITUATION

MONTHS

A. X-ray

20

21			

B. Radiation

24

25			

C. Tobacco

28

29			

D. High Heat

32

33			

E. Chemicals

36

37			

F. Weights

40

41			

G. Animals

44

45			

WORK HISTORY OF FOB

4. Current or Most Recent Occupation
(SE1 - 45B or 46/FHH1 - 30a or 30f)

48	

50			

5. What kind of work has he done for the longest time?
(SE1 - 47A/FHH1 - 30h or 31)

53	

55			

Procedure for Data Abstraction

Occupational Health Surveillance of Reproductive Outcomes
School of Public Health
University of Massachusetts/Amherst

I. FHH-1 Form Present

- A. Locate Section B (Gravida's Employment) on page 2 FHH-1. If question 19 (Do you have a job now?) is answered:

1. "Yes": abstract the information from question 19a and 19b of the FHH-1 form to line 1 (Current or Most Recent Occupation - Gravida) of the "Occupational Health Surveillance" data collection form.

Proceed to question 21 (What other kinds of work have you done) page 3, FHH-1.

- a. If question 21 is answered "None", then "Same as 1" is written on line 2 (What kind of work did you do for the longest time?) of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

- b. If question 21 has one or more kinds of work listed, then the length of time on each job is computed from question 21 (approximate dates worked) and question 19d (How long have you had this job?).

- i. If the length of time indicated in question 19d is longer than any computed for question 21, then "Same as 1" is written on line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

- ii. Otherwise, the occupation listed in question 21 with the longest time of employment is abstracted from question 21 to line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

- iii. In the event of ties for longest length of employment, the most recent occupation with the longest length of employment is abstracted to line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

- iv. If question 19d or question 21 (approximate dates worked) is not completed, write "unknown" on line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

2. "No": abstract the information from question 19e and 19f of the FHH-1 form to line 1 of the data collection form.

Proceed to question 21 (What other kinds of work have you done?), page 3, FHH-1.

- a. If question 21 is answered "None", then "Same as 1" is written on line 2 (What kind of work did you do for the longest time?) of the data collection form.

Proceed to question 30, Section D on page 4 of the FHH-1 form.

- b. If question 21 has one or more kinds of work listed, then the length of time on each job is computed from question 21 (approximate dates worked) and question 19i (How long did you have that job?).

- i. If the length of time indicated in question 19i is longer than any computed for question 21, then "Same as 1" is written on line 2 of the data collection form.

Proceed to question 30, Section D on page 4 of the FHH-1 form.

- ii. Otherwise, the occupation listed in question 21 with the longest time of employment is abstracted from question 21 to line 2 of the data collection form.

Proceed to question 30, Section D on page 4 of the FHH-1 form.

- iii. In the event of ties for the longest length of employment, the most recent occupation with the longest length of employment is abstracted to line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

- iv. If question 19i or question 21 (approximate dates worked) is not completed, write "Unknown" on line 2 of the data collection form.

Proceed to question 30, Section D on page 4 of the FHH-1 form.

3. "Never Worked": write "Never worked" on line 1 and line 2 of the data collection form.

Proceed to Section D, question 30 on page 4 of the FHH-1 form.

4. If none of the above are indicated for question 19, write "unknown" on line 1 and line 2 of the data collection form.

Proceed to question 30, Section D on page 4 of the FHH-1 form.

3. Locate question 30, Section D (Husband) on page 4 of FHH-1. If question 30 (Is he employed at present?) is answered:

1. "Yes": abstract the information from question 30a and 30b of the FHH-1 form to line 4 (Current or Most Recent Occupation - Husband or Father of Baby) of the "Occupational Health Surveillance" data collection form. (Line 3 of the data collection form is left blank for FHH-1 forms).

Proceed to question 31 (What other kind of work has he done?) page 4, FHH-1 form.

- a. If question 31 is answered "None", then "Same as 4" is written on line 5 (What kind of work has he done for the longest time?) of the data collection form. Abstract is complete.
- b. If question 31 has one or more kinds of work listed, then the length of time on each job is computed from question 31 (approximate dates worked) and question 30c (How long has he had this job?).
 - i. If the length of time indicated in question 30c is longer than any computed for 31, then "same as 4" is written on line 5 of the data collection form. Abstract is complete.
 - ii. Otherwise, the occupation listed in question 31 with the longest time of employment is abstracted from question 31 to line 5 of the data collection form. Abstract is complete.
 - iii. In the event of ties for longest length of employment, the most recent occupation with the longest length of employment is abstracted to line 5 of the data collection form. Abstraction complete.
 - iv. If question 30c or question 31 (approximate dates worked) is not completed, write "unknown" on line 5 of the data collection form. Abstraction complete.

2. "No": abstract the information from question 30f and 30g of the FHH-1 form to line 4 (Current or Most Recent Occupation - Husband or Father of Baby) of the data collection form. (Line 3 of the data collection form is left blank for FHH-1 forms).

Proceed to question 31 (What other kind of work has he done?) page 4, FHH-1.

- a. If question 31 is answered "none", then "same as 4" is written on line 5 (What kind of work has he done for the longest time?) of the data collection form. Abstraction complete.

- b. If question 31 has one or more kinds of work listed, then the length of time on each job is computed from question 31 (approximate dates worked) and question 30h (How long did he have that job?).
 - i. If the length of time indicated in question 30h is longer than any computed for 31, then "same as 4" is written on line 5 of the data collection form. Abstraction complete.
 - ii. Otherwise, the occupation listed in question 31 with the longest time of employment is abstracted from question 31 to line 5 of the data collection form. Abstraction complete.
 - iii. In the event of ties for the longest length of employment, the most recent occupation with the longest length of employment is abstracted to line 5 of the data collection form. Abstraction complete.
 - iv. If question 30h or question 31 (approximate dates worked) is not completed, write "unknown" on line 5 of the data collection form. Abstraction complete.
3. If none of the above are indicated for question 30, write "unknown" on line 4 and line 5 of the data collection form. Abstraction complete.

II. SE-1 Form Present

- A. Locate Section D (Gravida's Work History) on page 3 of the SE-1 form. If question 26 is answered:
 1. "Yes": abstract the information from question 26c of the SE-1 form to line 1 (Current or Most Recent Occupation - Gravida) of the "Occupational Health Surveillance" data collection form.

Proceed to question 28A (How many kinds of jobs have you had?)

If question 28A is answered:

 - a. "one": then write "same as 1" on line 2 (What kind of work did you do for the longest time?) of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.
 - b. "several": then compare the occupation in question 29 to that in question 26c.
 - i. If they are the same write "same as 1" on line 2 of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.

- ii. If they are different, abstract the information from question 29 to line 2 of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.

- 2. "No": proceed to question 27.

If question 27 is answered

- a. "Yes": abstract the information from question 27c of the SE-1 form to line 1 (Current or Most Recent Occupation - Gravida) of the data collection form.

Proceed to 28A (How many kinds of jobs have you had?)

If question 28A is answered:

- i. "one": then write "same as 1" on line 2 (what kind of work did you do for the longest time?) of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.

- ii. "several": then compare the occupations in question 29 to that in question 27c.

- (a.) If they are the same write "same as 1" on line 2 of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.

- (b.) If they are different, abstract the information from question 29 to line 2 of the data collection form.

Proceed to question 30 on page 3 of the SE-1 form.

- b. "No": write "Never worked" on line 1 and line 2 of the data collection form.

Proceed to Section G on page 5 of the SE-1 form.

- 3. If questions 26 and/or 27 are not completely answered, write "unknown" on line 1 and line 2 of the data collection form.

- B. Locate question 30 (Occupational Hazards) on page 3 of the SE-1 form.

- 1. For question 30A

- a. Abstract all available information from the SE-1 form to line 3A of the data collection form.

- b. If no information is available, leave line 3A blank.

2. Repeat for questions 30B through 30G of the SE-1 form and lines 3B through 3G of the data collection form.

Proceed to Section G on page 5 of the SE-1 form.

- C. Locate question 45 in Section G (Work History of the Husband or Father of the Baby) on page 5 of the SE-1 form.

If question 45 (Is he now working?) is answered:

1. "Yes": abstract the information from question 45B (What kind of work is he doing?) to line 4 (Current or Most Recent Occupation - Husband or Father of Baby) of the data collection form.

Proceed to question 47A.

- a. If the answer to question 47A is the same as question 45B then write "same as 4" on line 5 of the data collection form. Abstraction complete.
 - b. If the answer to question 47A is different than the answer to question 45B, abstract the information from 47A to line 5 of the data collection form. Abstraction complete.
 - c. If there is no information for question 47A write "unknown" on line 5 of the data collection form. Abstraction complete.
2. "No": proceed to question 46.

- a. If question 46 is answered "yes", then abstract the information from question 46B to line 4 of the data collection form.

Proceed to question 47A

- i. If the answer to question 47A is the same as question 46B then write "same as 4" on line 4 of the data collection form. Abstraction complete.
 - ii. If the answer to question 47A is different from question 46B, then abstract the information from 47A to line 5 of the data collection form. Abstraction complete.
 - iii. If there is no information for question 47A write "unknown" on line 5 of the data collection form. Abstraction complete.
- b. If the question to question 46 is "no", write "never worked" on line 4 and line 5 of the data collection form. Abstraction complete.
3. If there is no information for question 45 or 46 then write "unknown" on line 4 and line 5 of the data abstraction form. Abstraction complete.

APPENDIX E: List of Malformations and Codes

List of Malformations and Codes

100	Any Musculoskeletal Malformation
101	Polydactyly
102	Absence limb or part
103	Hypoplasia limb or part
104	Syndactyly
105	Arthrogryposis
106	Anomalies of vertebrae
108	Hemivertebrae
110	Congenital dislocation hip
112	Hemimelia/phocomelia
113	Muscle absence/atrophy/hypo.
114	Absence/atrophy/hypo. pectoralis
115	Absence/atrophy/hypo. rectus abd.
117	Micrognathia/hypo. jaw
125	Misc. foot abnormality
*126	Clubfoot
132	Anomalies ribs/sternum
134	Abnormal face/skull
135	Abnormal implantation/deformed toes
*136	Abnormal hands/fingers
139	Webbed neck
149	Other musculoskeletal
150	Some muscle absence/atrophy/hypo.
200	Any Eye and/or Ear Malformation
201	Anophthalmia/Microphthalmia
202	Coloboma
203	Cataract
204	Glaucoma/Buphthalmos
205	Corneal Opacity
210	Other Eye
225	Absent/Abnormal External Meatus
226	Pre-Auricular Skin Tag
300	Any Respiratory Malformation
301	Laryngeal/tracheal malacia
302	Malfs. epiglottis/larynx/bronchi
303	Malfs. thoracic wall
304	Malfs. diaphragm
305	Diaphragmatic hernia
306	Cleft lip/palate gum
307	Hypoplasia/agenesis lung
308	Bilobed lung
313	Choanal atresia
319	Hiatal hernia
322	Malf. lung
323	Anomalies teeth
324	Other respiratory
*325	Pectus excavatum

*Non-uniform Malformation

327	Any malf. thoracic wall/cavity
350	Cleft lip only
351	Co-existence cleft lip and palate
352	Union cleft lip & co-existence cleft lip and palate
353	Cleft palate only
*354	Cleft gum only
355	Some epiglottis/bronchi malformations
400	Any Gastrointestinal Malformation
401	Omphalocele
402	Anal atresia
404	TE fistula
405	Malrotation
407	Hirschsprungs Disease
408	Duodenal atresia
409	Other gastrointestinal
*410	Inguinal hernia
411	Other hernia
412	Anomalies of pancreas
413	Anomalies of liver
414	Anomalies of gallbladder
415	Pyloric stenosis
416	Meckel's diverticulum
417	Atresia/agenesis colon
418	Atresia/hypoplasia small intestine
419	Anomalous shaped/lobation liver
421	Biliary atresia
422	Atrophy/hypoplasia intestine
423	Accessory spleen
424	Umbilical hernia
425	Any hernia
426	Asplenia
427	Anomalies pancreas/gallbladder
500	Any Cardiovascular Malformation
501	Any atrial septal defect (sec. or pr.)
502	Any ventricular septal defect (open or closing)
503	Atrioventricular canal
504	Aortic valve malformation (sten. or atr.)
505	Pulmonic valve malf. (valv, or unsp. or periph. or atr.)
506	Mitral valve malformation
507	Tricuspid valve malformation
508	Any malposition of great vessels (union)
509	Transposition of great arteries
510	Anomalous venous drainage
511	Abnormalities of coronary arteries, isolated
512	Ductus arteriosus persistens
513	Any coarctation of aorta (pre. or post.)
514	Truncus arteriosus
515	Vascular ring
516	Coarctation of aorta - preductal

*Non-uniform Malformation

517 Coarctation of aorta - postductal
518 Abnormalities of coronary arteries
519 Endocardial fibroelastosis
520 Endomyocardial fibrosis
521 Single atrium
522 Single ventricle
523 Tetralogy of Fallot
524 Aortic and mitral valve atresia
525 Ventricular septal defect and pulmonic stenosis (VSD open
or closing and PS or PPS)
526 Abnormalities of coronary arteries, multiple
527 Truncus arteriosus, isolated
528 Truncus arteriosus, multiple
529 Single ventricle, isolated
530 Single ventricle, multiple
531 Atrial septal defect - secundum
532 Atrial septal defect - secundum, isolated
533 Atrial septal defect - secundum, multiple
534 Atrial septal defect - primum
535 Atrial septal defect - primum, isolated
536 Atrial septal defect - primum, multiple
537 Any atrial septal defect (sec. or pr.), isolated
538 Any atrial septal defect (sec. or pr.), multiple
539 Ventricular septal defect (open)
540 Ventricular septal defect (open), isolated
541 Ventricular septal defect (open), multiple
542 Ventricular septal defect - spontaneously closing
543 Any ventricular septal defect (open or closing), isolated
544 Any ventricular septal defect (open or closing), multiple
545 Atrioventricular canal, isolated
546 Atrioventricular canal, multiple
547 Aortic stenosis
548 Aortic stenosis, isolated
549 Aortic stenosis, multiple
550 Vascular ring, isolated
551 Vascular ring, multiple
552 Hypoplasia left ventricle
553 Left vena cava
554 Wolff - Parkinson - White Syndrome
555 Anomalous right subclavian artery
556 Hypoplasia left atrium
557 Hypoplasia cordis
558 Endocardial Disease (union)
559 Aortic insufficiency
560 Conus arteriosus syndrome
561 Endocardial cushion defect
562 Aortic valve malformation (sten. or atr.), isolated
563 Aortic valve malformation (sten. or atr.), multiple
564 Pulmonic valvular or unspecified stenosis
565 Pulmonic valvular or unspecified stenosis, isolated
566 Pulmonic valvular or unspecified stenosis, multiple
567 Peripheral pulmonic stenosis
568 Peripheral pulmonic stenosis, isolated
569 Peripheral pulmonic stenosis, multiple

572	Pulmonary atresia
573	Pulmonary atresia, isolated
574	Pulmonary atresia, multiple
575	Tricuspid valve malformation, isolated
576	Pulmonic valve malformation, isolated
577	Pulmonic valve malformation, multiple
578	Mitral insufficiency
579	Tricuspid valve malformation, multiple
580	Rare single malformation
581	Hypoplastic left heart syndrome
584	Transposition of great arteries, isolated
584	Transposition of great arteries, multiple
586	Double outlet of right ventricle
587	Double outlet right ventricle, isolated
588	Double outlet right ventricle, multiple
589	Hypoplasia pulmonary artery
590	Any malposition of great vessels, isolated
591	Any malposition of great vessels, multiple
592	Ductus arteriosus persistens, isolated
593	Ductus arteriosus persistens, multiple
594	Coarctation of aorta - preductal, isolated
595	Coarctation of aorta - preductal, multiple
598	Any coarctation of aorta (pre. or post.), isolated
599	Any coarctation of aorta (pre. or post.), multiple
600	Any Genitourinary Malformation
601	Hypospadias
*602	Urethral obstruction
604	Polycystic kidney
605	Single kidney
606	Hypoplastic kidney
607	Horseshoe kidney
608	Other kidney
609	Double ureter
610	Absent ureter
611	Stenotic ureter
612	Hypoplasia penis
613	Abnormal testes
616	Malformed uterus/tubes
617	Abnormal ovary
619	Malfs. male genitalia
621	Recto-fistula
622	Malfs. female genitalia
623	Malposition/ectopic kidney
624	Double collecting system
625	Mullerian malfusion
626	Malfs. bladder/ureter
627	Hydronephrosis
628	Hydroureter
629	Obstructive uropathy
630	Ambiguous genitalia
631	Hydrocele
632	Malfs. male genitalia - minor
633	Malfs. female genitalia - major
634	Malfs. female genitalia - minor
635	Some uterine malformations
636	Some double collecting malformations

*Non-uniform Malformation

700	Any Benign/Malignant Tumor
702	Any Mixed Tumors
703	Any Malignant Tumore
706	Wilms Tumor
707	Leukemias
708	CNS Tumors
709	Other Malignant Tumors
710	Any Benign Tumors
711	Papillomas/Polyps
712	Dermoid Cysts
713	Any Cyst (Except Dermoid)
714	Hemangioma/Granuloma
715	Hairy Nevus
716	Other Benign
717	Lymphangioma
800	Any CNS Malformation
801	Anencephaly
803	Encephalocele
804	Meningomyelocele
805	Spina Bifida without CNS Involvement
806	Spina Bifida with Meningomyelocele
807	Absent Corpus Callosum
808	Hydrocephaly
810	Microcephaly
811	Hypoplasia/Atrophy Brain
812	Misc. Brain Abnormality
813	Malformed Medulla
814	Craniosynostosis
815	Macrocephaly
816	Absence Olfactory Nerve/Arrhinecephaly
818	Cerebral Hypoplasia
820	Porencephaly/Hydrancephaly
821	Anomalies Pituitary
822	Rachischisis/Cranioschisis
823	Misc. Sinus Tract
824	Arnold Chiaro/Dandy Walker
825	Atrophy/Hypoplasia Optic Nerve
826	Craniospinal Fusion Defects
827	Any Hydrocephaly
828	Any Cranial Nerve
829	Any Brain Malformation
830	Any Spinal Malformation
900	Any Syndrome
902	Mongolism - Downs
903	Situs inversus/dextrocardia
909	Hypertrophy/enlarged adrenal
912	Hypoplasia/atrophy adrenal
913	Anomalies thyroid
914	Other adrenal
915	Adrenogenital
918	Pierre Robin
920	Achondroplasia

935	Caffey's
936	Albinism
937	Inborn errors metabolism
938	Other syndromes
939	Turners
940	Other trisomies
941	Any chromosomal
942	Klinefelters syndrome

APPENDIX F: Industry-Occupation Coding Dictionary

Adapted from (Hoar, S., Cole, P.T., Morrison, A.)

Occupational Code

Industry

<u>Name</u>	<u>Code Number</u>
Agriculture, forestry, fishing	01
Mining	02
Construction	03
Processors, producers, and users of products made from	
Paper and wood	04
Glass, clay, and stone	05
Metal	06
Machinery and electrical equipment	07
Ship building, motor vehicles, aircraft and other transportation methods	08
Food and tobacco	09
Textiles	10
Chemicals, drugs, and paints	11
Rubber, plastics, and synthetics	12
Fuel	13
Leather	14
Medicine and science	15
Entertainment and recreation	16
Art: products of assorted material	17
Unknown industry (with known occupation)	98
Occupations with few chemical exposures	99
(Business, law, communications, sales, etc.)	

Occupational Code

Agriculture, Forestry, Fishing - 01

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Agricultural engineering occupations	01	- 013
Marine engineering occupations	01	- 014
Agricultural science occupations	01	- 040
Managers and officials	01	- 180
Office work, non-managerial, non-professional (eg. secretary, draftsman)	01	- 209
Sales: Horticultural and nursery products	01	- 260
Sales: Agricultural products	01	- 261
Sales: Farming equipment and supplies	01	- 277
Grain farming	01	- 401
Cotton farming	01	- 402
Cotton ginning and compressing	01	- 461
Vegetable farming	01	- 403
Fruit and nut farming	01	- 404
Tobacco farming	01	- 405
Plant farming, NOS (eg. gardener)	01	- 409
Dairy farming	01	- 411
Poultry farming	01	- 412
Livestock farming	01	- 413
Animal farming, NOS	01	- 419
Animal care and husbandry	01	- 466
Veterinarians	01	- 073
Miscellaneous farming and related occupations; farmer, NOS .	01	- 429
Blight and pest control	01	- 465
Agricultural service occupations	01	- 469
Forestry occupations	01	- 449
Logging occupations	01	- 949
Fishing, whaling	01	- 435
Marine life cultivation	01	- 439
Hunting, trapping, and guide occupations	01	- 459
Packaging and Materials handling occupations	01	- 929

Occupational Code

Mining - 02

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>Occupation</u>
Mining engineers	02	- 010
Geology occupations	02	- 024
Managers and officials	02	- 181
Office work, non-managerial, non-professional (eg. secretary, draftsman)	02	- 209
Production clerks	02	- 229
Sales: Mining equipment and supplies	02	- 276
Boring, drilling, cutting occupations	02	- 930
Blasting occupations	02	- 931
Loading and conveying occupations	02	- 932
Crushing occupations	02	- 933
Screening and related occupations	02	- 934
Extraction of minerals, NOS	02	- 939
Packaging and materials handling occupations	02	- 929

Occupational Code

Construction - 03

<u>Occupation</u>	<u>Code Number</u> <u>Industry - Occupation</u>	
Civil engineers	03	- 005
Vocational educators	03	- 097
Managers and officials	03	- 182
Office work, non-managerial, non-professional (eg. secretary, draftsman)	03	- 209
Production clerks	03	- 229
Sales: Construction equipment and supplies	03	- 276
Painters (art work)	03	- 144
Painters (benchwork)	03	- 749
Painters, plasterers, waterproofers, cementers	03	- 849
Sculptors (artwork)	03	- 148
Glass, clay, and stone machining occupations	03	- 679
Glass, clay, and stone fabrication and repair	03	- 779
Brick and stone masons	03	- 861
Wood machining occupations	03	- 669
Wood fabrication and repair	03	- 769
Carpenters	03	- 860
Metal fabrications (structural work)	03	- 809
Welders and flame cutters	03	- 819
Electricians	03	- 829
Plumbers and gas and steam fitters	03	- 862
Asbestos and insulation workers	03	- 863
Roofers	03	- 866
Excavating, paving, and grading occupations	03	- 859
Surveyors	03	- 018
Construction occupations, NOS (laborer, NOS)	03	- 899

Occupational Code

Paper and Wood - 04

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Industrial engineer	04	- 012
Managers, officials, professionals	04	- 183
Office work, non-managerial, non-professional (eg. secretary, draftsman)	04	- 209
Production Clerks	04	- 229
Sales: Paper products (eg. newspaper people) Wood products (eg. furniture)	04	- 265
Paper processing: Grinding, beating, mixing	04	- 530
Paper processing: Cooking, drying	04	- 532
Paper processing: Screening, washing, cooling, bleaching.	04	- 533
Paper processing: Calendering, sizing, coating.	04	- 534
Paper processing: Forming	04	- 535
Paper processing, NOS	04	- 539
Paper working occupations (eg. cutting, folding, serving).	04	- 649
Printing occupations (see Art, Industry = 17)	04	- 659
Wood processing: Mixing	04	- 560
Wood processing: Preserving	04	- 561
Wood processing: Saturating, coating	04	- 562
Wood processing: Drying, seasoning	04	- 563
Wood processing: NOS	04	- 569
Wood machining occupations (eg. wood cutter)	04	- 669
Wood product fabrication and repair	04	- 769
Carpenters	04	- 860
Logging occupations	04	- 949
Packaging and materials handling occupations	04	- 929

Occupational Code

Glass, Clay, and Stone - 05

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry - Occupation</u>	
Ceramic engineer	05	- 006
Industrial engineer	05	- 012
Managers and officials	05	- 183
Office work, non-managerial, non-professional (eg. secretary, draftsman)	05	- 209
Production clerks	05	- 229
Sales: Glass, clay, and stone products	05	- 271
Processing: Crushing, grinding, mixing	05	- 570
Processing: Separating	05	- 571
Processing: Melting	05	- 572
Processing: Baking, drying, heat treating	05	- 573
Processing: Impregnating, coating, glazing	05	- 574
Processing: Forming	05	- 575
Processing, NOS	05	- 579
Glass, clay, and stone machining occupations	05	- 679
Glass, clay, and stone products fabrication and repair . .	05	- 779
Sculptors	05	- 146
Art occupation, NOS	05	- 149
Brick and stone mason, tile setters	05	- 861
Glass setters, glaziers	05	- 865
Packaging and materials handling occupations	05	- 929

Occupational Code

Metal - 06

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>Occupation</u>
Metallurgist	06	- 011
Industrial engineer	06	- 012
Managers and officials	06	- 183
Office work, non-managerial, non-professional (eg. secretary, draftsman)	06	- 209
Production clerks	06	- 229
Sales: Metal and metal products	06	- 273
Ore refining: Mixing	06	- 310
Ore refining: Separating, filtering	06	- 311
Ore refining: Melting	06	- 312
Ore refining: Roasting	06	- 313
Ore refining: Pouring, casting	06	- 314
Ore refining: Crushing, grinding	06	- 315
Ore refining: Molders and coremakers	06	- 318
Ore refining, NOS	06	- 319
Metal processing: Electroplating	06	- 500
Metal processing: Dip plating	06	- 501
Metal processing: Melting, pouring, casting	06	- 502
Metal processing: Pickling, cleansing, degreasing	06	- 503
Metal processing: Heat-treating	06	- 504
Metal processing: Metal spraying, coating	06	- 505
Metal processing, NOS (eg. blacksmith)	06	- 509
Metal machining	06	- 609
Metal working	06	- 619
Metal products fabrication, assembly and repair	06	- 709
Structural work	06	- 809
Welders, flame cutters	06	- 819
Packaging and materials handling occupations	06	- 929

Occupational Code

Machinery - 07

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Electrical engineer	07	- 003
Industrial engineer	07	- 012
Managers and officials	07	- 183
Office work, non-managerial, non-professional (eg. secretary, draftsman)	07	- 209
Production clerks	07	- 229
Sales: Industrial equipment	07	- 276
Sales: Electrical equipment	07	- 278
Sales: Business and commercial machines	07	- 281
Metal processing	07	- 509
Metal machining	07	- 609
Metal working	07	- 619
Mechanics and machinery repair	07	- 639
Metal products fabrication, assembly and repair, NOS	07	- 709
Electrical equipment assembly and repair	07	- 729
Strippers, painters of electrical products	07	- 749
Structural work assembling, installing and repairing electrical equipment (eg. linemen, servicemen, tel. & tel., & power)	07	- 829
Packaging and materials handling occupations	07	- 929

Occupational Code

Shipbuilding, Motor Vehicles, Aircraft, and Other
Transportation Methods - 08

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Aeronautical engineer	08	- 002
Mechanical engineer	08	- 007
Radio Operators, air traffic controllers	08	- 193
Managers and officials	08	- 184
Office work, non-managerial, non-professional (eg. secretary, draftsman)	08	- 209
Production clerks	08	- 229
Sales: Transportation equipment	08	- 280
Stewardess, personal services	08	- 359
Metal processing (eg. blacksmith, electroplater)	08	- 509
Metal machining (eg. riveter)	08	- 609
Metal working (eg. welder, shipfitter)	08	- 619
Electrical equipment assembly and repair (eg. radar technicians)	08	- 729
Engine mechanics and repair	08	- 625
Gas station attendant, garage services	08	- 915
Painters, auto body work	08	- 849
Shipbuilding, motor vehicle manufacturing occupations, NOS (eg. rigger, helper, layout)	08	- 999
Boilermakers, locomotive, fireman, engineer, switchmen . .	08	- 905
Drivers, chauffeur, truckers, and pilots	08	- 900
Packaging and materials handling occupations	08	- 929

Occupational Code

Food and Tobacco - 09

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Wholesale and retail industry managers & clerks	09	- 185
Service industry managers	09	- 187
Office work, non-managerial, non-professional (eg. secretary)	09	- 209
Production clerks (in factories, plants)	09	- 229
Sales: Horticultural and nursery products	09	- 260
Sales: Agricultural products	09	- 261
Sales: Foodstuffs, beverages, and tobacco	09	- 262
Sales: Hotel and restaurant equipment and supplies	09	- 275
Food Research.	09	- 012
Processing: Mixing, compounding, blending, kneading, and shaping	09	- 520
Processing: Separating, crushing, milling, chopping, and grinding	09	- 521
Processing: Culturing, melting, fermenting, distilling, saturating, pickling and aging	09	- 522
Processing: Heating, rendering, melting, drying, cooling, freezing	09	- 523
Processing: Coating, icing and decorating	09	- 524
Processing: Slaughtering, breaking and curing	09	- 525
Processing: Cooking and baking	09	- 526
Processing, NOS	09	- 529
Cooks (domestic)	09	- 305
Cooks and chefs (establishment)	09	- 313
Hostesses, stewards, waiters, and waitresses	09	- 310
Bartenders	09	- 312
Meat cutters, excluding those in slaughtering houses	09	- 316
Preparation and service occupations, NOS	09	- 319
Packaging and materials handling occupations	09	- 929

Occupational Code

Textiles - 10

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Industrial and Mechanical engineers	10	- 012
Managers and officials	10	- 183
Office work, non-managerial, non-professional (eg. secretary)	10	- 209
Production clerks	10	- 229
Sales: Textiles and textile products, clothes models . . .	10	- 263
Processing: Shaping, blocking, stretching, and tentering .	10	- 580
Processing: Separating, filtering, and drying (eg. spinners)	10	- 581
Processing: Washing, steaming, and saturating (eg. dyers)	10	- 582
Processing: Ironing, pressing, glazing, staking, calendering, and embossing	10	- 583
Processing: Mercerizing, coating, and laminating	10	- 584
Processing: Singeing, cutting, shearing, shaving, and napping	10	- 585
Processing: Filtering and fulling	10	- 586
Processing: Brushing and shrinking	10	- 587
Processing, NOS	10	- 589
Machine and equipment mechanics and repair	10	- 628
Model makers, patternmakers (machine trades)	10	- 693
Upholstering, fabrication and repair of mattresses and bedspreads	10	- 780
Fur working occupations	10	- 783
Hat, cap and glove fabrication and repair	10	- 784
Sewers, embroiderers, knitters, seamstresses, and tailors. .	10	- 789
Laundrying, domestic	10	- 302
Laundrying, dry cleaning, pressing	10	- 363
Dyeing	10	- 364
Apparel and furnishings service occupations, NOS	10	- 369
Packaging and materials handling occupations	10	- 929

Occupational Code

Chemicals, Drugs, and Paints - 11

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Chemical engineer	11	- 008
Chemistry occupations	11	- 022
Chemistry college and university educators	11	- 090
Chemistry secondary school educators	11	- 091
Managers and officials	11	- 183
Office work, non-managerial, non-professional (eg. secretary)	11	- 209
Production clerks	11	- 229
Sales: Chemicals, drugs, and paints	11	- 266
Processing: Mixing and blending	11	- 550
Processing: Filtering, straining, and separating	11	- 551
Processing: Distilling	11	- 552
Processing: Heating, baking, drying, seasoning, melting and heat treating	11	- 553
Processing: Coating, calendering, laminating and finishing	11	- 554
Processing: Grinding and crushing	11	- 555
Processing: Casting and molding	11	- 556
Processing: Extruding	11	- 557
Processing: Reacting	11	- 558
Processing, NOS	11	- 559
Painters	11	- 849
Packaging and materials handling occupations	11	- 929

Occupational Code

Rubber, Plastics, and Synthetics - 12

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>Occupation</u>
Chemical engineer	12	- 008
Industrial engineer.	12	- 012
Chemistry occupations.	12	- 022
Managers and officials	12	- 183
Office work, non-managerial, non-professional (eg. secretary)	12	- 209
Production clerks.	12	- 229
Sales: Plastic products	12	- 268
Sales: Rubber products	12	- 270
Processing: Mixing and blending	12	- 550
Processing: Filtering, straining, and separating	12	- 551
Processing: Distilling	12	- 552
Processing: Heating, baking, drying, seasoning, melting, and heat treating	12	- 553
Processing: Coating, calendering, laminating, and finishing	12	- 554
Processing: Grinding and crushing	12	- 555
Processing: Casting and molding	12	- 556
Processing: Extracting	12	- 557
Processing: Reacting	12	- 558
Processing, NOS	12	- 559
Metal Machinist	12	- 609
Rubber, plastics, and synthetics machining	12	- 690
Tire, tube, and tread fabrication and repair (benchwork)	12	- 750
Laying out and cutting rubber, plastics and synthetics	12	- 751
Fitting, shaping, cementing, finishing (benchwork)	12	- 752
Rubber and plastic footwear fabrication and repair	12	- 753
Rubber, plastic, and synthetic product fabrication and repair, NOS	12	- 759
Packaging and materials handling occupations	12	- 929

Occupational Code

Fuel - 13

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Chemical engineer	13	- 008
Industrial engineer	13	- 012
Chemistry occupation	13	- 022
Geology occupations	13	- 024
Managers and officials	13	- 183
Office work, non-managerial, non-professional (eg. secretary)	13	- 209
Production clerks	13	- 229
Sales: Fuel and petroleum products	13	- 267
Extraction: Boring, drilling, and cutting	13	- 930
Extraction: Blasting	13	- 931
Extraction: Loading and conveying	13	- 932
Extraction: Crushing	13	- 933
Extraction: Screening	13	- 934
Extraction, NOS	13	- 939
Processing: Mixing and blending	13	- 540
Processing: Filtering, straining, and separating	13	- 541
Processing: Distilling, subliming, and carbonizing	13	- 542
Processing: Drying, heating, and melting	13	- 543
Processing: Grinding and crushing	13	- 544
Processing: Reacting	13	- 546
Processing, NOS	13	- 549
Boilermakers, utilities production and distribution occupations	13	- 959
Packaging and materials handling occupations	13	- 929
Nuclear engineering, mechanics and repair	13	- 631

Occupational Code

Leather - 14

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Engineer	14	- 019
Managers and officials	14	- 183
Office work, non-managerial, non-professional (eg. secretary)	14	- 209
Production clerks	14	- 229
Sales: Leather and leather products	14	- 264
Processing: Shaping, blocking, stretching, and tentering	14	- 580
Processing: Separating, filtering, and drying	14	- 581
Processing: Washing, steaming, and saturating (tanning) .	14	- 582
Processing: Ironing, pressing, glazing, staking, calendering, and embossing	14	- 583
Processing: Mercerizing, coating, and laminating	14	- 584
Processing: Singeing, cutting, shearing, shavings, and napping	14	- 585
Processing: Felting and fulling	14	- 586
Processing: Brushing and shrinking	14	- 587
Processing, NOS	14	- 589
Dyeing service occupations	14	- 364
Shoe, belts and luggage fabrication and repair	14	- 365
Boot blacks, shoe shine occupations	14	- 366
Apparel service occupations, NOS	14	- 369
Packaging and materials handling occupations	14	- 929

Occupational Code

Medicine and Science - 15

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Nuclear engineer	15	- 015
Chemistry occupation	15	- 022
Mathematics and physical sciences occupations	15	- 029
Biology occupations	15	- 041
Psychology occupations	15	- 045
Life sciences occupations, NOS	15	- 049
Physicians and surgeons	15	- 070
Osteopaths	15	- 071
Dentists	15	- 072
Dental Technicians and Assistants	15	- 078
Veterinarians	15	- 073
Animal care, NOS	15	- 356
Pharmacists	15	- 074
Registered nurses	15	- 075
Nurses and practical nurses	15	- 354
Nurse aids	15	- 307
Dietitians and dietetic aids	15	- 077
Embalmers, Morticians	15	- 338
X-Ray technicians	15	- 199
Medical and health occupations, NOS	15	- 079
Attendants at hospitals, morgues and related health services	15	- 355
Hospital laundering occupations	15	- 361
Hospital (nursing home) housekeepers	15	- 321
Porters, cleaners, and janitors	15	- 382
Service managers and officials	15	- 187
Service occupations, NOS	15	- 389
Public administration managers and officials	15	- 188
Sales & Purchasing: Chemicals and drugs	15	- 266
Sales & Purchasing: Medical and dental equipment and supplies	15	- 282
Office work, non-managerial, non-professional (eg. secretary)	15	- 209

Occupational Code

Entertainment and Recreation - 16

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Dramatics occupations	16	- 150
Theatrical make-up occupations	16	- 333
Dancing occupations	16	- 151
Music occupations	16	- 152
Radio operators	16	- 193
Sound recording, transcribing, and reproduction occupations	16	- 194
Athletes and other sports occupations	16	- 153
Entertainment and recreational occupations, NOS	16	- 159
Masseurs and related occupations	16	- 334
Bath attendants	16	- 335
Barbering, cosmetology, and related service occupations	16	- 339
Managers, officials, professionals	16	- 189
Office work, non-managerial, non-professional (eg. secretary)	16	- 209

Occupational Code

Miscellaneous Occupations:
Art; and Products of Assorted Materials - 17

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Art education occupations	17	- 099
Museum curators	17	- 109
Commercial artists	17	- 141
Designers	17	- 142
Paper processing	17	- 539
Paper working (folding, cutting, sewing, fastening)	17	- 649
Printing	17	- 659
Wood processing	17	- 569
Wood machining	17	- 669
Wood products fabrication and repair	17	- 769
Ceramic engineer	17	- 006
Sculptor	17	- 148
Glass, clay, and stone processing	17	- 579
Glass, clay, stone, and sand products, fabrication and repair	17	- 779
Metallurgy engineer	17	- 011
Metal processing	17	- 509
Metal machining and metal working (eg. jewelry engravers)	17	- 619
Metal products fabrication and repair	17	- 709
Textile and leather processing	17	- 589
Textile and leather machining	17	- 689
Textile and leather products fabrication and repair	17	- 789
Painters (art)	17	- 144
Painters (benchwork)(eg. sign painter)	17	- 749
Artwork occupations, NOS - brush, spray or pen	17	- 970
Rubber, plastics, synthetic, chemicals processing	17	- 559
Rubber, plastic, synthetics products fabrication and repair	17	- 759
Photography occupations	17	- 143
Darkroom occupations	17	- 976
Photographic equipment and supplies fabrication and repair	17	- 714
Photo engravers	17	- 971
Lithographers	17	- 972
Hard compositors, typesetters	17	- 973
Electrotypers	17	- 974
Stenotypers	17	- 975
Book binders	17	- 977
Graphic art occupations, NOS (eg. draftsmen)	17	- 979
Fabrication and repair of products of assorted materials (jewelry, sporting goods, etc.)	17	- 739
Fabrication and repair, NOS.	17	- 799
Art occupations, NOS	17	- 149
Managers, officials, professionals	17	- 199
Office work, non-managerial, non-professional (eg. secretary)	17	- 209
Packaging and materials handling occupations	17	- 929

Occupational Code

Unknown Industry - 98

<u>Occupation</u>	<u>Code Number</u>	
	<u>Industry</u>	<u>- Occupation</u>
Engineers, lab techs	98	- 019
Professionals	98	- 199
Managers and officials	98	- 189
Secretary and other office work	98	- 209
Bookkeeping, cashiers	98	- 219
Clerical work	98	- 249
Switchboard operator	98	- 235
Sales	98	- 269
Stitcher	98	- 699
Benchworking occupations	98	- 799
Packaging and material handling	98	- 929
Laborer, odd jobs	98	- 899

Occupational Code

Few Chemical Exposures
(Business, Law, Communications, Sales, Etc.) - 99

<u>Occupation</u>	<u>Code Number</u>	<u>Industry - Occupation</u>
Architects and draftsmen	99 - 001	
Mathematical science occupations	99 - 020	
Astronomy occupations	99 - 021	
Meteorology occupations	99 - 025	
Psychology occupations	99 - 045	
Social science occupations	99 - 059	
Students	99 - 098	
Educational occupations	99 - 099	
Museum, library, and archival occupations	99 - 109	
Judges, lawyers	99 - 119	
Clergy, religious occupations	99 - 129	
Writers	99 - 139	
Accountants, auditors, and other administrative specialists	99 - 169	
Managers and officials	99 - 189	
Professional, technical, and managerial occupations, NOS	99 - 199	
Secretaries, stenographers, typists, and filing occupations	99 - 209	
Bookkeepers, cashiers, tellers	99 - 219	
Factory work, NOS	99 - 229	
Messengers, mail carriers	99 - 239	
Clerical occupations, NOS (Note: office work, not saleswork)	99 - 249	
Telephone operator	99 - 235	
Sales: Services	99 - 259	
Sales: Commodities	99 - 269	
Homemaker, domestic services (eg. babysitters)	99 - 309	
Food preparation occupations	99 - 319	
Lodging services	99 - 329	
Amusement and recreational attendants (eg. camp counselors)	99 - 349	
Personal services occupations, NOS (eg. parking atten- dent, chauffeur)	99 - 359	
Protective service occupation (eg. police, fire, military, NOS)	99 - 379	
Building service occupations (eg. janitor)	99 - 389	
Packaging and materials handling occupations (eg. longshoremen)	99 - 929	
Utilities production and distribution occupations	99 - 959	
Unemployed	99 - 995	
Never worked - Housewives	99 - 996	
Retired, NOS	99 - 997	
Known, cannot classify	99 - 998	
Unknown	99 - 999	

APPENDIX G:

Distribution of Reproductive Outcome Categories
for Analysis of Maternal Occupation

Outcome Frequencies of the 14,944 Case and Control Pregnancies
Included and Excluded During Screening

Outcome Category	Included in Screening			Excluded from Screening			Total
	Number Exposed	Number Non-Exposed	Total Included	Period of Exposure	Unknown Occupation	Total Excluded	
Total	5,033	8,006	13,039	1,689	216	1,905	14,944
Referent (controls)	3,487	5,529	9,016	1,112	142	1,254	10,270
Stillbirth	250	417	666	80	16	97+	763
Neonatal death	249	404	653	111	8	119	772
Infant death	110	212	322	46	7	53	375
All Malf. (with live birth)	937	1,444	2,381	340	43	383	2,764
All Malformations	1,064	1,683	2,747	390	49	439	3,186

Malformation Number¹

100	300	447	747	114	10	124	871
101	124	186	310	52	6	58	368
102	11	17	28	1	1	2	30
103	14	26	40	6	2	8	48
104	46	57	103	13	3	16	119
105*	2	4	6	0	0	0	6
106*	4	7	11	1	0	1	12
108*	4	8	12	0	0	0	12
110	35	46	81	10	0	10	91
112*	1	5	6	0	1	1	7
113*	4	8	12	4	0	4	16
114*	2	6	8	2	0	2	10
115*	1	1	2	1	0	1	3
117	7	11	18	2	0	2	20

¹See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number (n≤5) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
125*	4	3	7	1	0	1	8
126	12	97	159	28	1	29	188
132*	5	6	11	3	0	3	14
134*	1	1	2	2	1	3	5
135*	5	6	11	1	0	1	12
136*	4	5	9	1	0	1	10
139*	3	5	8	1	0	1	9
149*	3	7	10	0	1	1	11
150*	1	1	2	1	0	1	3
200	30	71	101	16	2	18	119
201*	4	6	10	0	1	1	11
202*	3	8	11	2	0	2	13
203	11	27	38	5	1	6	44
204*	1	6	7	2	1	3	10
205*	1	6	7	1	0	1	8
210*	1	1	2	2	0	2	4
225*	3	5	8	1	0	1	9
226	9	21	30	5	1	6	36
300	126	216	342	63	4	67	409
301*	2	1	3	1	0	1	4
302*	4	4	8	3	1	4	12
303	6	10	16	2	0	2	18
304*	4	6	10	1	0	1	11
305*	0	10	10	2	0	2	12
306	56	94	150	36	2	38	188
307	11	15	26	3	0	3	29
308*	3	8	11	0	0	0	11
313*	1	2	3	0	0	0	3
315*	3	6	9	0	0	0	9
319*	3	4	7	1	0	1	8
322	7	14	21	4	0	4	25
323*	4	14	18	1	0	1	19

¹ See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number (n<5) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
324*	1	4	5	0	0	0	5
325	35	44	79	11	1	12	91
327	41	53	94	13	1	14	108
350	7	14	21	3	0	3	24
351*	5	15	20	4	0	4	24
352	12	29	41	7	0	7	48
353	11	11	22	8	0	8	30
354	33	54	87	21	2	23	110
355*	2	3	5	2	1	3	8
400	326	502	828	115	16	131	959
401	9	13	22	0	0	0	22
402	10	9	19	7	0	7	26
404*	4	6	10	1	0	1	11
405	7	16	23	2	0	2	25
407*	5	6	11	2	0	2	13
408*	2	4	6	1	0	1	7
409*	2	4	6	1	0	1	7
410	229	351	580	79	15	94	674
411*	1	3	4	1	0	1	5
412*	1	4	5	1	0	1	6
413*	2	1	3	0	0	0	3
414*	1	4	5	0	0	0	5
415	31	48	79	12	1	13	92
416*	3	15	18	2	0	2	20
417*	0	3	3	0	0	0	3
418*	1	6	7	0	0	0	7
419*	3	2	5	0	0	0	5
421*	3	3	6	2	0	2	8
422*	3	11	14	1	0	1	15
423	6	13	19	2	0	2	21
424	20	24	44	6	0	6	50
425	250	377	627	85	15	100	727

¹See Appendix E. list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

-Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
426*	1	2	3	0	0	0	3
427*	2	8	10	1	0	1	11
500	131	217	347	44	6	51+	398
501	18	26	44	8	0	8	52
502	60	88	148	19	1	20	168
503	6	12	18	0	0	0	18
504	11	10	20	6	0	7+	27
505	17	45	62	7	4	11	73
506	8	5	13	3	0	3	16
507*	4	3	7	2	0	2	9
508	9	17	26	3	0	3	29
508*	3	12	15	2	0	2	17
510*	4	2	6	1	0	1	7
511*	0	3	3	0	0	0	3
512	15	28	43	1	1	2	45
513	13	20	33	2	0	2	35
514*	3	3	6	0	0	0	6
515*	2	7	9	0	0	0	9
516	9	15	24	1	0	1	25
517*	4	5	9	1	0	1	10
518*	0	5	5	1	0	1	6
519*	3	7	10	2	0	2	12
520*	0	1	1	1	0	1	2
521*	1	1	2	1	0	1	3
522*	4	0	4	2	0	2	6
523*	5	8	13	2	0	2	15
524*	6	4	10	3	0	3	13
525*	2	6	8	1	1	2	10
526*	0	2	2	1	0	1	3
527*	1	1	2	0	0	0	2
528*	2	2	4	0	0	0	4
529*	0	0	0	1	0	1	1

¹ See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
530*	4	0	4	1	0	1	5
531	15	16	31	7	0	7	38
532	9	14	23	5	0	5	28
533	6	2	8	2	0	2	10
534*	4	10	14	1	0	1	15
535*	0	8	8	1	0	1	9
536*	4	2	6	0	0	0	6
537	9	22	31	6	0	6	37
538	9	4	13	2	0	2	15
539	43	68	111	15	0	15	126
540	26	37	63	11	0	11	74
541	18	37	55	4	1	5	60
542	16	14	30	4	0	4	34
543	42	51	93	44	0	14	107
546	18	37	55	5	1	6	61
547*	3	9	12	0	0	0	12
548*	3	3	6	0	0	0	6
549*	4	7	11	4	0	4	15
550*	2	7	9	2	0	2	11
551*	2	0	2	2	0	2	4
552*	1	2	3	0	0	0	3
553*	1	5	6	0	0	0	6
554*	4	6	10	1	0	1	11
555*	4	3	7	0	0	0	7
556*	0	2	2	1	0	1	3
557*	2	3	5	0	0	0	2
558*	2	5	7	2	0	2	9
559	7	10	17	2	0	2	19
560*	3	8	11	3	0	3	14
561*	2	0	2	0	0	0	2
562	14	26	40	4	0	4	44
563	10	22	32	2	0	2	34

¹See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
564*	4	7	11	2	0	2	13
565*	2	0	2	2	0	2	4
566	13	33	46	6	4	10	56
567	6	17	23	3	3	6	29
568	7	16	23	3	1	4	27
569*	2	5	7	1	0	1	8
570*	0	5	5	0	0	0	5
571*	2	0	2	1	0	1	3
572*	2	7	9	0	0	0	9
574*	2	7	9	0	0	0	9
575*	0	1	1	1	0	1	2
576	6	22	28	3	3	6	34
577	11	23	34	4	1	5	39
578*	2	0	2	0	0	0	2
579*	4	2	6	1	0	1	7
580*	2	4	6	0	0	0	6
581	10	11	21	3	0	3	24
584*	1	0	1	0	0	0	1
585*	2	12	14	2	0	2	16
586*	2	3	5	0	0	0	5
587*	1	1	2	0	0	0	2
588*	1	2	3	0	0	0	3
589*	2	0	2	0	0	0	2
590*	2	1	3	0	0	0	3
591	7	16	23	3	0	3	26
592	12	15	27	1	1	2	29
593*	3	13	16	0	0	0	16
594*	3	5	8	1	0	1	9
595	6	10	16	0	0	0	16
598	7	10	17	2	0	2	19
599	6	10	16	0	0	0	16
600	151	202	353	42	9	51	404

¹ See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
601	77	85	162	17	5	22	184
602	21	37	58	7	1	8	66
604	15	11	26	3	0	3	29
605*	3	7	10	0	0	0	10
606*	3	6	9	2	1	3	12
607*	2	4	6	1	1	2	8
608*	2	2	4	0	1	1	5
609*	2	6	8	1	0	1	9
610*	4	5	9	0	1	1	10
611	6	13	19	6	0	6	25
612*	2	1	3	0	1	1	4
613*	3	5	8	2	3	5	13
616*	5	5	10	0	0	0	10
617*	2	4	6	2	0	2	8
619	84	100	184	20	8	28	212
621*	3	2	5	2	0	2	7
622	15	15	30	5	0	5	35
623*	1	3	4	1	0	1	5
624*	4	6	10	1	0	1	11
625*	1	3	4	0	0	0	4
626*	3	7	10	1	0	1	11
627*	4	12	16	3	0	3	19
628	8	7	15	3	0	3	18
629	15	20	35	8	0	8	43
630*	2	3	5	0	0	0	5
631*	3	6	9	1	0	1	10
632*	1	4	5	1	1	2	7
633	7	5	12	2	0	2	14
634	8	11	19	3	0	3	22
635*	4	2	6	0	0	0	6
636*	2	0	2	0	0	0	2
700	53	90	143	12	3	15	158

¹See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
702*	53	90	143	12	3	15	158
703	8	13	21	2	0	2	23
706*	0	3	3	1	0	1	4
707*	4	4	8	0	0	0	8
708*	2	5	7	1	0	1	8
709*	2	1	3	0	0	0	3
710	43	77	120	10	3	13	133
711*	5	7	12	0	0	0	12
712*	2	8	10	1	0	1	11
713	11	25	36	2	1	3	39
714*	4	11	15	3	1	4	19
715	9	11	20	1	0	1	21
716	11	10	21	3	0	3	24
717*	1	5	6	0	1	1	7
800	78	145	222	32	7	40+	262
801	11	11	22	4	0	4	26
803*	1	1	2	2	1	3	5
804	13	16	29	5	2	7	36
805*	2	5	7	0	0	0	7
806*	2	5	7	2	0	2	9
807*	1	2	3	0	1	1	4
808	22	40	62	11	1	12	74
810	19	44	63	11	0	11	74
811*	5	4	9	0	1	1	10
812*	2	5	7	0	0	0	7
813*	0	2	2	1	0	1	3
814	9	14	23	1	2	3	26
815*	5	10	15	3	0	3	18
816*	2	4	6	0	0	0	6
818*	5	5	10	0	1	1	11
820*	2	1	3	1	0	1	4
821*	4	1	5	1	1	2	7

¹See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

<u>Outcome Category</u>	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Period of Exposure</u>	<u>Unknown Occupation</u>	<u>Total Excluded</u>	<u>Total</u>
822*	3	5	8	0	0	0	8
823*	3	5	8	0	1	1	9
824*	3	4	7	0	1	1	8
825*	3	3	6	1	0	1	7
826	19	24	43	7	3	10	50
827	22	41	63	11	2	13	76
828*	4	5	9	1	0	1	10
829	69	132	201	31	6	37	238
830	21	28	49	5	3	8	57
900	46	95	141	28	1	29	170
902	13	37	50	8	0	8	58
903*	3	5	8	3	1	4	12
909*	2	3	5	0	0	0	5
912	10	11	21	5	0	5	26
913*	1	5	6	0	0	0	6
914*	3	10	13	3	0	3	16
915*	0	3	3	1	0	1	4
918*	0	1	1	2	0	2	3
920*	1	2	3	1	0	1	4
935*	1	4	5	1	0	1	6
936*	1	3	4	1	0	1	5
937*	5	3	8	1	0	1	9
938*	3	10	13	1	0	1	14
939*	0	1	1	1	0	1	2
940*	3	2	5	0	0	0	5
941	16	41	57	9	0	9	66
942*	0	1	1	0	0	0	1

¹See Appendix E, list of malformations and codes.

*Excluded from analysis due to the small number ($n \leq 5$) of exposed mothers.

+Additional exclusion due to maternal occupation in an excluded industrial category.

APPENDIX H: Maternal Occupation and Industry Categories

Combined Occupational Categories Used in the Present Study and the
Occupations (Occupational Codes) Included in Each Category

<u>Industry</u> (Industry Code)	<u>Occupation</u> (Occupational Code)
Agriculture, Forestry, Fishing (01)	Office Work (209)
	Plant Farming (401-409)
	Animal Farming and Animal Care (411-419, 466, 15-356)
	Fishery and Related Occupations (439)
	Other Agricultural, Forestry, Fishing (429, 040, 469, 929, 461, 449)
Construction (03)	Office Work (209)
Paper and Wood (04)	Office Work (209, 265, 183)
	Processing and Production (530-539, 229)
	Paper Working (649, 17-649)
	Printing (659, 17-659)
	Woodworking and Product Fabrication (669, 17-669, 769)
	Material Handling (929)
Glass, Clay, Stone (05)	Office Work (209, 271)
	Processing and Other Production (570-579, 229)
	Glass, Clay, Stone, Machining and Products Fabrication (679, 779, 856)
	Material Handling (929)

Metal (06)	Office Work (209) Metal Working and Machining (609, 619, 819) Metal Products Fabrication and Production, NOS (709, 229, 509) Material Handling (929)
Machinery and Electrical (07)	Office Work (003, 209) Metal Working and Machining (609, 619) Metal Products Fabrication (709) Electrical Products Fabrication (729) Other Production, NOS (229, 749, 829) Material Handling (929)
Transportation (08)	Office Work (209, 180) Stewardess (359) Motor Vehicle and Ship Building (229, 999, 619, 609, 729) Garage Services, Drivers and Material Handling (849, 900, 915, 929)
Food and Tobacco (09)	Office Work (012, 187, 209) Clerks, Cashiers, Sales (grocery) (185, 262) Processing (520, 262) Other Production, NOS (229) Domestic Cooks (305) Waitress (310) Bartender (312)

Food and Tobacco (continued)
(09)

Cooks (Establishments)
(313)
Other Food Service Occupations
(316, 319)
Material Handling
(929)

Textiles
(10)

Office Work
(183, 209)
Sales
(263)
Processing
(500-589)
Textile Machining
(693)
Sewers
(789)
Fabrication of Textile and Related
Products, NOS
(780, 783, 784)
Other Production
(229)
Laundry
(363)
Other apparel service occupation
(302, 369)
Material Handling
(929)

Chemical, Drugs, Paints
(11)

Office Work
(183, 209)
Processing and Production
(022, 550-559, 229)
Material Handling
(929)

Rubber, Plastics
(12)

Office Work
(209, 268)
Processing and Production
(550-559, 022, 229)
Machine Trades (Metal, Rubber,
Plastic Machining)
(609, 690)
Rubber, Plastics Product Fabrication
(751-759)
Material Handling

Fuel
(13)

Office Work
(183, 209)

Leather
(14)

Office Work
(209)

Sales
(264)

Leather Products Fabrication
(365)

Processing and Production, NOS
(380-389, 229, 364)

Material Handling and Apparel
Services, NOS
(369, 929)

Medicine and Science
(15)

Pharmacists and Lab
Occupations
(015-041, 074)

Nurses
(075, 354)

Dental Assistants
(078)

X-ray Technicians
(199)

Nurses aids and attendants
(355, 307)

Other Medical and Health
(045, 338, 079)

Office Work
(282, 188, 209)

Housekeepers
(382, 321)

Hospital Laundry
(361)

Dietetics, hospital kitchen,
and other service
(077, 389)

Entertainment
(16)

Dance, Drama, Music and
other Entertainment
(150-159)

Office Work
(189, 209)

Hairdresser-Cosmetics
Demonstration and Sales
(339, 11-266)

Art; Products of Assorted Materials (17)	Office Work (199, 209) Art Occupations (099, 141, 142, 149, 970, 972, 979) Photography and Darkroom Occupations (143, 976) Engravers (619) Fabrication of Products of Assorted Materials (714-789) Book Binders (977) Material Handling (929)
Unknown Industry	Office Work (169, 189, 209, 219, 249) Switchboard Operator (235) Sales (269) Stitcher (699) Factory Work (799, 99-229) Laborer (899) Material Handling (929)
Low Exposure	Students (089) Teachers (099) Library Work (109) Managers and Professionals (00-051, 119-139, 189, 199) Office Work (209, 219, 249) Switchboard (235) Sales (259, 269) Domestic Work and Babysitting (309)

Low Exposure (Continued)

Lodging and other Personal
Services

(239, 329, 359)

Amusement Attendants

(349)

Protective Services

(379)

Building Services

(389)

Material Handling

(929)

Never Worked

(996)

Unknown

(998, 999)

APPENDIX I:

Distribution of Reproductive Outcome
Categories for Analysis of Paternal Occupations

Outcome Frequencies of the 14,944 Case and Control Pregnancies
Included and Excluded During Screening

Outcome Category	<u>Included in Screening</u>			<u>Excluded From Screening</u>				
	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Occupation Unknown</u>	<u>Age Over 55</u>	<u>Age Unknown</u>	<u>Total Excluded</u>	<u>Total</u>
Total	8674	1712	10,386	3371	1155	32	4558	14,944
Referent (controls)	6080	1233	7313	2174	756	27	2957	10,270
Stillbirth	427	67	494	199	70	0	269	763
Neonatal Death	418	66	484	225	63	0	288	772
Infant Death	188	23	211	124	39	1	164	375
All Malformations/ Live Birth	1561	323	1884	649	227	4	880	2764
All Malformations	1807	363	2170	751	261	4	1016	3186
Malformation ¹ <u>Number</u>								
100	483	96	578	220	71	1	293 ⁺	871
101	176	24	200	128	39	1	168	368
102	19	5	24	4	2	0	6	30
103	29	6	35	10	3	0	13	48
104	72	23	95	17	7	0	24	119
105*	3	0	3	3	0	0	3	6
106	7	2	9	2	1	0	3	12
108	10	1	11	1	0	0	1	12
110	54	19	73	16	2	0	18	91
112*	3	1	4	2	1	0	3	7
113	9	1	10	4	2	0	6	16

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

⁺Additional exclusion due to paternal occupation in an excluded industrial category

<u>Malformation¹ Number</u>	<u>Included in Screening</u>			<u>Excluded From Screening</u>				<u>Total</u>
	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Occupation Unknown</u>	<u>Age Over 55</u>	<u>Age Unknown</u>	<u>Total Excluded</u>	
114*	5	1	6	2	2	2	4	10
115*	3	0	3	0	0	0	0	3
117	12	2	13	5	1	0	7 ⁺	20
125*	5	0	5	1	2	0	3	8
126	112	24	136	37	15	0	52	188
132	7	3	10	4	0	0	4	14
134*	2	1	3	2	0	0	2	5
135	7	0	7	2	2	0	4	11
136	3	3	6	4	0	0	4	10
139	7	1	8	1	0	0	1	9
149*	3	1	4	3	3	0	6	10
150*	1	0	1	2	0	0	2	3
200	74	13	87	20	12	0	32	119
201	6	1	7	3	1	0	4	11
203	27	8	35	8	1	0	9	44
204	5	0	5	4	1	0	5	10
205*	4	1	5	2	1	0	3	8
210*	3	0	3	1	0	0	1	4
225*	5	0	5	3	1	0	4	9
226	25	3	28	3	5	0	8	36
300	247	43	288	87	31	1	121 ⁺	409
301*	0	0	0	3	1	0	4	4
302	7	0	7	4	1	0	5	12
303	10	2	12	3	3	0	6	18

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

⁺Additional exclusion due to paternal occupation in an excluded industrial category

<u>Malformation¹ Number</u>	<u>Included in Screening</u>			<u>Excluded From Screening</u>				<u>Total</u>
	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Occupation Unknown</u>	<u>Age Over 55</u>	<u>Age Unknown</u>	<u>Total Excluded</u>	
304	7	1	8	3	0	0	3	11
305	10	1	11	1	0	0	1	12
306	107	13	119	47	20	1	69 ⁺	188
307	20	2	22	7	0	0	7	29
308	9	0	9	1	1	0	2	11
313*	2	1	3	0	0	0	0	3
315	4	2	6	1	2	0	3	9
319	5	2	7	1	0	0	1	8
322	13	2	15	7	3	0	10	25
323	10	2	12	6	1	0	7	19
324*	1	1	2	3	0	0	3	5
325	63	17	80	9	2	0	11	91
327	72	19	90	12	5	0	18 ⁺	108
350	18	3	21	2	1	0	3	24
351	16	2	18	5	1	0	6	24
352	34	5	39	7	2	0	9	48
353	21	2	22	5	2	0	8 ⁺	30
354	52	6	58	35	16	1	52	110
355	7	0	7	1	0	0	1	8
400	537	112	647	227	83	0	312 ⁺	959
401	10	2	12	6	4	0	10	22
402	16	1	17	7	2	0	9	26
404	7	1	8	2	1	0	3	11
405	9	7	16	6	3	0	9	25

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

⁺Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	<u>Included in Screening</u>			<u>Excluded From Screening</u>				Total
	Number Exposed	Number Non-Exposed	Total Included	Occupation Unknown	Age Over 55	Age Unknown	Total Excluded	
407	7	2	9	0	4	0	4	13
408*	3	1	4	3	0	0	3	7
409*	4	72	5	1	1	0	2	7
410	375	0	446	168	59	0	228 ⁺	674
411*	2	0	2	2	1	0	3	5
412*	4	1	4	2	0	0	2	6
413*	1	0	2	1	0	0	1	3
414*	3	16	3	2	0	0	2	5
415	59	2	74	15	2	0	18 ⁺	92
416	12	1	14	4	2	0	6	20
417*	2	0	3	0	0	0	0	3
418	7	0	7	0	0	0	0	7
419*	3	2	3	1	1	0	2	5
421*	3	2	5	3	0	0	3	8
422	10	5	12	3	0	0	3	15
423	11	4	16	2	3	0	5	21
424	29	76	33	12	5	0	17	50
425	405	1	480	182	64	0	245 ⁺	727
426*	1	0	2	1	0	0	1	3
427	7	45	7	4	0	0	4	11
500	229	9	273	101	23	0	125 ⁺	398
501	29	21	38	12	2	0	14	52
502	106	4	127	34	7	0	41	168
503	8	6	12	5	1	0	6	18

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

⁺Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	<u>Included in Screening</u>			<u>Excluded From Screening</u>				Total
	Number Exposed	Number Non-Exposed	Total Included	Occupation Unknown	Age Over 55	Age Unknown	Total Excluded	
504	12	6	18	6	3	0	9	27
505	42	6	48	20	5	0	25	73
506	9	3	12	2	2	0	4	16
507	6	2	8	1	0	0	1	9
508	12	6	17	9	2	0	12+	29
509	9	4	13	4	0	0	4	17
510*	1	2	3	3	1	0	4	7
511*	2	0	2	1	0	0	1	3
512	23	5	28	16	1	0	17	45
513	23	2	25	9	1	0	10	35
514*	4	0	4	2	0	0	2	6
515*	4	0	4	5	0	0	5	9
516	16	2	18	6	1	0	7	25
517	7	0	7	3	0	0	3	10
518*	3	0	3	3	0	0	3	6
519	6	1	7	4	1	0	5	17
520*	2	0	2	0	0	0	0	2
521*	2	0	2	1	0	0	1	3
522*	3	1	4	1	1	0	2	6
523	12	2	14	1	0	0	1	15
524	7	2	9	2	2	0	4	13
525	6	1	7	2	1	0	3	10
526*	1	0	1	2	0	0	2	3
527*	2	0	2	0	0	0	0	2
528*	2	0	2	2	0	0	2	4
530*	3	1	4	0	1	0	1	5
531	20	7	27	10	1	0	11	38
532	15	3	18	9	1	0	10	28
533	5	4	9	1	0	0	1	10
534	10	2	12	2	1	0	3	15
535	6	1	7	1	1	0	2	9
536*	4	1	5	1	0	0	1	6

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

†Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	<u>Included in Screening</u>			<u>Excluded From Screening</u>				Total
	Number Exposed	Number Non-Exposed	Total Included	Occupation Unknown	Age Over 55	Age Unknown	Total Excluded	
537	21	4	25	10	2	0	12	3
538	8	5	13	2	0	0	2	1
539	80	17	97	24	5	0	29	12
540	45	10	55	14	5	0	19	7
541	39	8	47	12	1	0	13	6
542	22	3	25	8	1	0	9	3
543	66	13	79	22	6	0	28	10
546	40	8	48	12	1	0	13	6
547	6	3	9	2	1	0	3	1
548*	2	1	3	3	0	0	3	
549	6	4	10	4	1	0	5	1
550	3	3	6	4	1	0	5	1
551*	3	1	4	0	0	0	0	
552*	1	0	1	2	0	0	2	
553*	3	0	3	3	0	0	3	
554	7	1	8	2	1	0	3	1
555*	5	0	5	2	0	0	2	
556*	2	0	2	1	0	0	1	
557*	4	0	4	1	0	0	1	
558	6	1	7	2	0	0	2	
559	12	1	13	4	2	0	6	1
560	8	1	9	4	1	0	5	1
561*	2	0	2	0	0	0	0	
562	28	6	33	9	1	0	11+	4
563	19	6	25	7	2	0	9	3
564	5	3	8	4	1	0	5	1
565*	3	1	4	0	0	0	0	
566	34	5	39	15	2	0	17	5
567	15	1	16	12	1	0	13	2
568	19	4	23	3	1	0	4	2
569*	3	1	4	1	3	0	4	
570*	1	0	1	1	3	0	4	
571*	2	1	3	0	0	0	0	

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number ($n \leq 5$) of exposed fathers

+Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	Included in Screening			Excluded From Screening				Total
	Number Exposed	Number Non-Exposed	Total Included	Occupation Unknown	Age Over 55	Age Unknown	Total Excluded	
572*	5	0	5	4	0	0	4	9
574*	5	0	5	4	0	0	4	9
575*	1	1	2	0	0	0	0	2
576	16	1	17	13	4	0	17	34
577	25	5	31	7	1	0	8	39
578*	2	0	2	0	0	0	0	2
579	5	1	6	1	0	0	1	7
580*	2	1	3	2	1	0	3	6
581	14	3	17	4	3	0	7	24
584*	1	0	1	0	0	0	0	1
585	8	4	12	4	0	0	4	16
586*	2	0	2	2	1	0	3	5
587*	0	0	0	0	1	0	1	1
588*	2	0	2	1	0	0	1	3
589*	2	0	2	0	0	0	0	2
590*	1	0	1	1	1	0	2	3
591	11	6	17	8	1	0	9	26
592	14	4	18	10	1	0	11	29
593	9	1	10	6	0	0	6	16
594	6	0	6	2	1	0	3	9
595	10	2	12	4	0	0	4	16
598	13	0	13	5	1	0	6	19
599	10	2	12	4	0	0	4	16
600	234	42	276	92	35	1	128	404
601	105	19	124	45	14	1	60	184
602	34	8	42	15	9	0	24	66
604	19	2	21	5	3	0	8	29
605	7	0	7	2	1	0	3	10
606	7	1	8	2	2	0	4	12
607*	4	0	4	3	1	0	4	8
608*	2	0	2	3	0	0	3	5
609	5	1	6	3	0	0	3	9
610	6	0	6	3	1	0	4	10

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

~Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	<u>Included in Screening</u>			<u>Excluded From Screening</u>				<u>Total</u>
	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Occupation Unknown</u>	<u>Age Over 55</u>	<u>Age Unknown</u>	<u>Total Excluded</u>	
611	16	2	18	6	1	0	7	25
612*	1	1	2	2	0	0	2	4
613*	5	0	5	7	1	0	8	13
616	8	0	8	1	1	0	2	10
617	8	0	8	0	0	0	0	8
619	122	20	142	52	17	1	69	211
621	6	1	7	0	0	0	0	7
622	23	4	27	5	3	0	8	35
623*	3	0	3	1	1	0	2	5
624	5	2	7	4	0	0	4	11
625*	4	0	4	0	0	0	0	4
626	7	1	8	2	1	0	3	11
627	14	1	15	4	0	0	4	19
628	14	1	15	2	1	0	3	18
629	28	4	32	9	2	0	11	43
630*	4	0	4	1	0	0	1	5
631	7	0	7	2	1	0	3	10
632*	5	0	5	1	1	0	2	7
633	13	0	13	3	1	0	4	17
634	10	5	15	5	2	0	7	22
635*	4	0	4	1	1	0	2	6
636*	0	1	1	1	0	0	1	2
700	89	27	116	27	14	1	42	158
702*	1	1	2	0	0	0	0	2
703	16	3	19	4	0	0	4	23
706*	1	1	2	2	0	0	2	4
707	5	2	7	1	0	0	1	8
708	7	0	7	1	0	0	1	8
709*	3	0	3	0	0	0	0	3
710	73	23	95	23	14	1	38	133
711	5	1	6	3	3	0	6	12
712	9	1	10	0	1	0	1	11
713	18	6	24	8	6	1	15	39

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

+Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	Included in Screening			Excluded From Screening				Total
	Number Exposed	Number Non-Exposed	Total Included	Occupation Unknown	Age Over 55	Age Unknown	Total Excluded	
714	9	5	14	4	1	0	5	19
715	11	4	15	5	1	0	6	21
716	16	5	21	1	2	0	3	24
717*	4	1	5	2	0	0	2	7
800	158	26	184	58	20	0	78	262
801	20	2	22	3	1	0	4	26
803*	2	0	2	2	1	0	3	5
804	17	7	24	8	4	0	12	36
805	5	1	6	1	0	0	1	7
806	7	1	8	0	1	0	1	9
807*	2	0	2	1	1	0	2	4
808	45	3	48	18	8	0	26	74
810	44	9	53	18	5	0	23	76
811	5	1	6	3	1	0	4	10
812	6	0	6	1	0	0	1	7
813*	1	0	1	2	0	0	2	3
814	15	1	16	8	2	0	10	26
815	14	4	18	0	0	0	0	18
816	6	0	6	0	0	0	0	6
818	6	0	6	4	1	0	5	11
820*	2	0	2	1	1	0	2	4
821*	4	0	4	2	1	0	3	7
822	6	0	6	2	0	0	2	8
823*	3	1	4	5	0	0	5	9
824	6	0	6	1	1	0	2	8
825	7	0	7	0	0	0	0	7
826	29	8	37	11	5	0	16	53
827	46	3	49	19	8	0	27	76
828	10	0	10	0	0	0	0	10
829	149	20	169	50	19	0	69	238
830	30	9	39	14	4	0	18	53
900	108	17	125	35	10	0	45	170
902	32	8	40	13	5	0	18	58

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number (n≤5) of exposed fathers

+Additional exclusion due to paternal occupation in an excluded industrial category

Malformation ¹ Number	<u>Included in Screening</u>			<u>Excluded From Screening</u>				<u>Total</u>
	<u>Number Exposed</u>	<u>Number Non-Exposed</u>	<u>Total Included</u>	<u>Occupation Unknown</u>	<u>Age Over 55</u>	<u>Age Unknown</u>	<u>Total Excluded</u>	
903*	3	1	4	8	0	0	8	12
909*	5	0	5	0	0	0	0	5
912	21	1	22	3	1	0	4	26
913*	5	0	5	1	0	0	1	6
914	11	1	12	3	1	0	4	16
915*	3	0	3	1	0	0	1	4
918*	3	0	3	0	0	0	0	3
920*	3	0	3	1	0	0	1	4
935*	3	0	3	3	0	0	3	6
936*	4	0	4	0	1	0	1	5
937	7	2	9	0	0	0	0	9
938	8	3	11	1	2	0	3	14
939*	2	0	2	0	0	0	0	2
940*	3	1	4	1	0	0	1	5
941	38	9	47	14	5	0	19	66
942*	1	0	1	0	0	0	0	1

¹See Appendix E, list of malformations and codes

*Excluded from analysis due to small number ($n \leq 5$) of exposed fathers

+Regional exclusion due to paternal occupation in an excluded industrial category

APPENDIX J:

Paternal Occupation and Industry Categories

Industry and Occupational Categories
Included in the Analysis of Paternal Occupation with the
Codes of the Occupations Included in Each Category

<u>Industry</u> (Industry Code)	<u>Occupational Category</u> (Occupational Codes)
Agriculture, Forestry, Fishing (01)	Office Work* (013 to 072, 074 to 277) Plant Farming (401 to 409, 461) Animal Farming (411 to 419) Other Farming and Related Work (429, 465, 469) Veterinarians and Animal Care (073, 466, 15-073, 15-356) Logging and Forestry Occupations (449, 949, 04-949) Fishing and Fishery Related Work (435, 439) Material Handling (929)
Mining (02)	All Occupations
Construction (03)	Office Work* (005 to 209, 276) Painters, Plasterers (849) Glass, Clay, Stone Related Work (679, 779) Masons (861, 05-856, 05-861) Carpenters (860, 04-860) Roofers (866) Metal Structural Work (809, 819) Electricians (829)

*included in non-exposed category

Construction (continued)
(03)

Plumbers
(862)

Pavers
(859)

Construction, NOS
(229, 899, 863)

Paper and Wood
(04)

Office Work*
(183, 209, 265)

Paper and Wood Processing
(229, 530 to 569)

Paper Working
(649)

Printers
(659, 17-659, 17-972)

Wood Machining
(669, 03-669, 17-669)

Wood Product Fabrication
(769, 03-769, 17-769)

Material Handling
(929)

Glass, Clay, Stone
(03)

Office Work*
(006 to 209, 271)

Processing
(229, 570 to 579)

Machining and Fabrication
(679, 779, 17-779)

Material Handling
(929)

Metal
(06)

Office Work*
(011 to 209, 273)

Processing
(500 to 509, 17-509)

Ore Refining
(510 to 519)

Metal Machining
(609)

Metal Working
(619, 17-619)

Structural Work
(809, 819)

Metal Product Fabrication
(709, 17-709)

*included in non-exposed category

Metal (continued)
(06)

Other Production
(229)

Material Handling
(929)

Machinery and Electrical
(07)

Engineers
(003, 012)

Office Work*
(183, 209)

Sales*
(276 to 281)

Metal Working and Machining
(609, 617, 509)

Metal Mechanics
(639)

Electrical Products Fabrication
(729)

Other Production, NOS
(709, 229, 749)

Linemen and Service Men (elect., tele.)
(829)

Material Handling
(929)

Transportation
(08)

Office Work*
(002 to 184, 209)

Radio, Radar work
(193, 729)

Sales
(280)

Personal Services
(359)

Metal Working and Machining
(509, 609, 619)

Engine Mechanics
(625)

Service Station Work
(915)

Autobody Work
(849)

Drivers
(900)

*included in non-exposed category

Transportation (continued)
(08)

Railroad Personnel
(905)

Motor Vehicle Manufacturing
(229, 999)

Material Handling
(929)

Food and Tobacco
(09)

Managers and Clerks
(185)

Office Work*
(187, 209)

Sales
(260 to 275)

Cooks
(305, 313)

Waiters
(310)

Bartenders
(312)

Meat Cutters
(316)

Food Preparation and Service Work
(319)

Butcher
(525)

Bakers
(526)

Other Food Processing
(012, 229, 520 to 523, 529)

Material Handling
(929)

Textile
(10)

Office Work*
(012 to 209, 263)

Processing
(229, 580 to 589)

Textile Machining
(693, 628)

Product Fabrication
(780 to 789)

Laundering
(363, 364)

Material Handling
(369, 929)

*included in non-exposed category

Chemicals, Drugs, Paints
(11)

Chemistry Occupations
(008, 022)

Chemistry Educators
(090, 091)

Office Work*
(090, 091)

Chemical Processing
(550 to 559, 229)

Material Handling
(929, 849)

Rubber, Plastics, Synthetics
(12)

Processing
(008 to 022, 229, 550 to 559, 609)

Office Work*
(183 to 270)

Machining
(690)

Product Fabrication
(750 to 759, 17-759)

Material Handling
(929)

Fuel
(13)

Office Work*
(183, 209, 267)

Processing
(008 to 024, 229, 540 to 900, 939)

Material Handling
(929)

Utilities Production
(959)

Leather
(14)

Office Work*
(183, 209, 264)

Processing
(229, 580 to 589)

Product Fabrication
(364 to 366, 17-789)

Material Handling
(929)

*included in non-exposed category

Medicine and Science
(15)

Office Work*
(187, 188, 209, 266, 282)
Physicians
(070)
Dentists
(072, 078)
Pharmacists
(074)
Nurses, Attendants
(307, 354, 355)
Other Medical Work, NOS
(079, 199)
Laboratory Work
(041, 049)
Other Science Work, NOS
(015 to 029)
Psychology Occupations
(045)
Dietitian and Assistants
(077)
Morticians
(338)
Hospital Laundry, Cleaning
(361, 321, 382)
Other Hospital Service
(389)

Entertainment and Recreation
(16)

Drama, Dance, Music
(150 to 152)
Office Work*
(189, 209)
Bordering and Related Work
(334, 339)
Other Entertainment and Recreation
Related Work
(153, 159, 194)

Miscellaneous Occupations
(Art and Products of Assorted
Materials)
(17)

Artists
(099, 141, 142)
Photography
(143, 976, 714)

*included in non-exposed category

Miscellaneous (continued)
(17)

Other Art Related Work, NOS
(144, 148, 149, 749, 970 to 975, 977)
Office Work*
(199, 109, 209)
Fabrication of Products of
Assorted Materials
(739)
Material Handling
(929)

Unknown Industry
(98)

Engineers
(019)
Office Work*
(169 to 219, 235 to 269)
Labroer
(799, 899)
Factory Work
(99-229)
Material Handling
(929)

Few Chemical Exposures
(99)

Architects and Draftsmen*
(001, 17-979)
Science Occupations*
(020 to 059)
Students*
(098)
Educators*
(099)
Lawyers*
(119)
Clergy*
(129)
Accountants*
(169)
Other Professional and Technical
Work, NOS*
(109, 139, 189, 199)
Office Work*
(209, 219, 235, 249)
Mail Carriers
(239)

*included in non-exposed category

Few Chemical Exposures
(99)

Sales*

(259, 269)

Personal Services*

(309, 359)

Food & Lodging Services*

(319, 329)

Recreational Attendants*

(349)

Protective Services

(379)

Building Services

(389)

Material Handling*

(929)

Utilities Distribution

(959)

Never Worked*

(996)

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