THE PREVENTION AND REMEDIATION OF DOWN SYNDROME

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ABSTRACT

The effect of preventive and remediative procedures on the incidence and impact of Down syndrome in Montreal was examined. Two birth cohorts of Down syndrome infants for the years 1965-66 and 1975-76 were identified and compared for maternal age-specific incidence rates for five-year and single-year intervals. The age-specific rates for 1975-76 were generally higher than those for 1965-66 except for women aged 24 years and under. The effect of amniocentesis for the purpose of prenatal diagnosis on the prevention of Down syndrome in the later cohort was minimal. A clinical trial was conducted to assess the effect of early intervention on the development of a group of infants with Down syndrome. After insuring the comparability of the experimental and control groups and determining the extent to which the results of the trial could be generalized, no statistically significant differences in development between the experimental and control groups were demonstrated.

RESUME

Nous avons étudié l'effet des méthodes préventives et curatives sur l'incidence du syndrome de Down à Montréal. Deux groupes d'enfants nés en 1965-66 et en 1975-76 respectivement et présentant ce syndrome ont été identifiés et comparés quant aux taux d'incidence en rapport avec l'âge de la mère; aux fins de cette étude, les âges des mères ont été regroupés en tranches d'un an et de cinq ans. En général, le pourcentage de 1975-76 était plus élevé que celui de 1965-66, sauf en ce qui avait trait aux mères âgées de moins de 25 ans. L'amniocentèse à des fins de diagnostic prénatal n'a eu que très peu d'effet sur la prévention du syndrome de Down dans le deuxième groupe. Une étude clinique a été menée pour évaluer l'effet d'une intervention anticipée sur le développement d'un groupe d'enfants atteints du syndrome de Down. Une fois vérifiée la comparabilité entre le groupe témoin et le groupe d'enfants atteints et déterminé jusqu'à quel point les résultats de l'étude pouvaient être généralisés, aucune différence significative sur le plan statistique n'a été démontrée entre ces deux groupes quant au développement.

PREFACE

The birth of a child with Down syndrome is an unexpected event surrounded by grief and anguish. Yet it is not uncommon; approximately one-third of the severely mentally retarded in North America and Western Europe have Down syndrome (Drillien et al., 1966). Because the syndrome exhibits classic physical and genetic features, an affected child is easily identified and labeled as mentally retarded at birth. And, since no recognized cure exists, the diagnosis of Down syndrome implies a life-long handicap. While no specific cause of this chromosomal anomaly is known, its occurrence has long been associated with advanced maternal age. Recently, detection of the syndrome has become possible in utero through amniocentesis. Prenatal diagnosis coupled with subsequent selective pregnancy termination offers new hope in the area of primary prevention.

These factors, the relatively common occurrence, the early identification of the syndrome, the association with advanced maternal age, and the availability of prenatal diagnosis, offer the researcher in the field of mental retardation a unique opportunity to assess two forms of intervention. Prenatally, the prevention of this syndrome is theoretically possible by reduced conception in high risk women or selective abortion of prenatally diagnosed fetuses. Postnatally, the remediation of the retardation characteristic of this syndrome is also

presumably feasible by initiating stimulation and training procedures immediately following birth. Thus, the effect of both preventive and remediative procedures can be examined.

The primary objective of this study is to assess the effect of preventive and remediative procedures on the incidence and impact of Down syndrome in one Canadian city, Montreal. This study focused on (1) the effects of a decrease in overall maternal age and increased availability of amniocentesis for prenatal diagnosis on the incidence of Down syndrome, and (2) the effect of an early intervention program on the remediation of retarded development characteristic of Down syndrome during infancy. These issues of prevention and remediation are considered in this thesis.

The thesis has been organized in three parts. The first part contains a literature review of two content areas, prevention (Chapter 1) and remediation (Chapter 2). First, the effect of the two primary preventive factors, the change in the maternal age structure over time and the advent of amniocentesis for prenatal diagnosis is discussed. This chapter also includes, for background information, a description of the physical, mental and frequency characteristics of the syndrome. Chapter 2 considers the possibility of remediating the mental retardation associated with Down syndrome. The role of early intervention is examined by first discussing its contribution in deterring mental retardation in children defined as being "at risk" for retardation at some later date,

and more importantly, by studying the effect of early intervention in remediating delays in children with diagnosed forms of mental retardation. The distinction between these two populations of children, those "at risk" for mental retardation and those defined as mentally retarded, although essential when discussing the effect of early intervention, is often overlooked. By defining the intent of early intervention in this manner, the literature review is organized according to the objective of the intervention, deterring potential retardation or remediating retardation already known to be present.

Part II presents the specific objectives and hypotheses as well as the methods and results of the two aspects of the study. The methodology utilized for each section, prevention and remediation, is immediately followed by the appropriate results and a discussion of the findings; thus, Chapter 3 deals with the methods and results of the prevention segment; Chapter 4, the remediation. Finally, Part III summarizes the findings in light of their implications for public policy, clinical practices, and future research.

The benefits of prevention or remediation in the field of mental retardation are numerous. Economic factors warrant an investigation of possible preventive or remediative measures as does the desire to reduce the amount of individual distress associated with the birth of a retarded child. The impact of such an evaluation will, hopefully, provide direction

for future planning for all conditions associated with mental retardation, regardless of their nature or cause.

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PART I: REVIEW OF THE LITERATURE

CHAPTER 1

PREVENTION

Physical and Mental Characteristics

Down syndrome was first characterized and distinguished from other forms of mental retardation in 1866 by Langdon Down, a London physician (Bleyer, 1934). Although his description of the physical stigmata of the syndrome was correct, his racial explanation proved inaccurate, resulting in the terminology "mongolism".

As early as 1909, Shuttleworth, in a study of 350 cases, implicated advanced maternal age as an associated factor. Subsequent studies helped confirm this association (Jenkins, 1933; Penrose, 1933, 1934; Oster, 1953). A variety of additional hypotheses dealing with causative factors were suggested, but it was not until 1959 that Lejeune, Gautier and Turpin discovered the chromosome anomaly underlying Down syndrome, tissue cultures showing 47 chromosomes rather than the normal 46. Thereupon, it was demonstrated that in most cases the extra chromosome is found in what is classified as chromosome pair 21.

In 1960, Polani et al. established that not all cases of Down syndrome were characterized by trisomy. They observed a Down syndrome child with only 46 chromosomes and hypothesized that a reciprocal translocation had occurred between two

chromosomal groups. The extra chromosome was not independently present, but rather was attached to another chromosome and produced the same clinical picture as in trisomy 21. Translocations are considered important because the translocated chromosome may be carried by a normal person and passed through several generations, resulting in the familial occurrence of the disorder. It has been established that 2-3 percent of the Down syndrome population are translocations (Cowie, 1966; Penrose and Smith, 1966).

The third cytological type of Down syndrome is mosaicism. With this condition, certain clones of cells contain the extra chromosome, but the remaining cells have the normal number of chromosomes. Surveys indicate that about 2 percent of the Down syndrome populations are chromosomal mosaics (Cowie, 1966).

Prior to the onset of cytogenetic studies to confirm the diagnosis of Down syndrome, facial features and other physical signs characteristic of the syndrome were used to identify cases. These physical characteristics are well described by Penrose and Smith (1966) and more recently by Smith and Berg (1976). Although some of the signs are present in the normal population and few patients exhibit all of the features, most of those affected can be clinically identified at birth (Preus, 1977). The more common signs include: prominent forehead; flattened and broad nasal bridge; small, short nose; slanting, almond-shaped eyes with epicanthal folds and oblique palpebral fissures; bilateral palmar simian creases; speckling of the

iris or "Brushfield spots"; lens opacities; strabismus; ear deformities, i.e. angular overlapping helix, prominent antihelix, small or absent ear lobe; broad, short neck; cardiac anomalies; congential duodenal obstruction.

Physical growth patterns of these infants also differ significantly from those of normal children throughout the first three years of life (Cronk, 1978). Both length and weight measurements have been shown to be between one and two standard deviations below the norm. Similarly, prenatal growth patterns as well as subsequent birth weights tend to be below those of the unaffected infant (Smith and McKeown, 1956; Pueschel et al., 1976).

But by far, the most crucial characteristic of Down syndrome is the retardation in mental development. Although past studies concerning the level of intelligence in Down syndrome children demonstrated a wide range of IQ scores, they concurred that the level of subnormality is severe in the majority of children. Bleyer (1937) believed that the IQ of children with Down syndrome never exceeded 60; Penrose and Smith (1966) cited the range of intelligence to be from 15 to 29; Tennies (1943), 7 to 48. Dunsdon et al. (1960) estimated that of 390 children with Down syndrome only 6-7 percent had IQs over 45. Recently Horrobin and Rynders (1975) classified most Down syndrome children as moderately rather than severely retarded, with IQs ranging between 40 and 54. Dey (1971), too, classified 50% of the tested Down syndrome population as moderately

retarded (IQs 36-51) with 34% being severely retarded and the remaining 16% to be in the mildly retarded range.

A critical factor when reporting IQs is the age of the child at the time of testing. A variety of investigations (Centerwall and Centerwall, 1960; Dameron, 1963; Stedman and Eichorn, 1964; Koch et al., 1963; Shipe and Shotwell, 1965; Dicks-Mireaux, 1972; Melwyn and White, 1973; Cornwell and Birch, 1969) demonstrated an average IQ of about 70 at 6 months declining to 30 or 40 at 6 to 9 years. Several explanations for this decline over time have been advanced. The possibility of a true regression in development is raised by Dicks-Mireaux (1972), who described the rate of development of Down syndrome infants as progressively declining over time. Bilovsky and Share (1965) proposed that the apparent drop in IQ is a statistical artefact of the tests used during infancy. For example, many IQ tests do not require language skills until two years of age, thereby giving higher scores for the retarded child under age two and lower scores at later ages (Freeman, 1978).

In an attempt to see if in fact the IQ is affected by the Down syndrome child's slow language development, Carr (1975) analyzed her data by removing the verbal items from the intelligence testing of Down syndrome children. She reported a further decline in scores with the removal of these items, hence refuting this particular explanation. Koch et al. (1963) suggested that the gradual decrease in intelligence as expressed

by a developmental quotient (DQ) or an intelligence quotient (IQ) is simply a reflection of the formula DQ = Mental Age/ Chronological Age x 100, or in other terms, the chronological age increases at a faster rate than the mental age. They argued that an examination of DQs would thereby exhibit deterioration or arrested development over time, whereas investigation of the mental age (MA) scores over the same period would demonstrate steady developmental progress. They noted, however, that the rate of progress of mental age drops from an average increase of 6.26 months within the first year to 3.57 months during the third year.

Furthermore, there is controversy over the point in time when mental retardation becomes apparent. Fishler et al. (1964) followed 71 children with Down syndrome over a seven-year period with periodic developmental assessments and found that these children did not necessarily exhibit retarded development during the first six months of life. However, a similar study showed the measured intelligence of infants with Down syndrome to be below normal at 16 weeks (Dicks-Mireaux, 1972), and, more recently, both mental and motor developmental scores were found to be retarded as early as 6 weeks (Carr, 1975).

Different intelligence levels have been associated with various forms of residential care. Home-reared children exhibited higher IQ scores than institutionalized children (Centerwall and Centerwall, 1960; Stedman and Eichorn, 1964; Shipe

and Shotwell, 1965; Carr, 1970). While these studies theoretically supported the importance of the environment, caution is necessary when interpreting these results since the children compared were not randomly assigned to either institutions or homes. Selective factors may be at work resulting in biased samples with institutionalized children being more defective initially than those home-reared (Birch and Belmont, 1961). Because it is false to assume that the two groups are equal initially, it is similarly false to accept the theory that institutionalization results in more defective development.

Other factors have been cited as potential causes of variability within the measured levels of intelligence. Melwyn and White (1973) suggested that the degree of hypotonia combined with the genetic potential and environmental stimulation affect the eventual intelligence. Positive correlations between the intellectual status of the parent, measured either by IQ or education, and the measured developmental level of the Down syndrome child have been demonstrated (Fraser and Sadovnick, 1976; Golden and Pashayan, 1976). Clearly, the difficulties of separating the genetic component from the environmental factor are as great with the Down syndrome child as with the normal.

While it has been established that intellectual functioning is not related to the number of physical stigmata present (Baumeister and Williams, 1967; Shipe et al., 1968), the type

of Down syndrome, mosaic or trisomy 21, has been associated with the level of intelligence. Following reports of normal intelligence in mosaic Down syndrome individuals (Clarke et al., 1961; Hamerton et al., 1965), Fishler et al. (1976) compared the IQ levels of 25 trisomy 21 and 25 mosaic Down syndrome subjects matched for age and sex. They found the scores of the mosaics to be significantly higher than those of the trisomics.

As with the measured intelligence levels, there is considerable variability in the eventual functional capabilities of a person with Down syndrome. Motor skills are most consistent, with the majority able to walk, run and climb stairs (Share, 1975). Similarly, there is little controversy regarding their trainability in self-help activities, such as dressing, feeding, and toileting (Share, 1975; Pitt, 1977). Language development is the most delayed area, with the acquisition of functional speech occurring at a considerably slower rate than normal (Horrobin and Rynders, 1975; Share, 1975). At present most Down syndrome children receive special education throughout their school years with the emphasis being placed on functional rather than academic skills. Down syndrome adults often work in sheltered workshops or participate in daytime activity programs which emphasize self-help, social and leisure-time skills (Horrobin and Rynders, 1975).

In summary, it is obvious that a wide range of measured intelligence levels exist, as well as a number of potential

causative factors which may account for this variation. Any interpretation and application of intelligence quotients requires discretion, since factors such as age at the time of testing, residential status, and the cytological type of Down syndrome have been demonstrated to affect the measured developmental or intelligence quotient. The decline of the quotient over time is well documented, but the cause of the decline remains an enigma. However, average ages for attainment of developmental milestones are available (Fishler et al., 1964; Melwyn and White, 1973) and clearly indicate that children with Down syndrome exhibit a pattern of development which, while similar to the normal sequence, proceeds at a much slower rate.

Incidence and Prevalence

The incidence of Down syndrome among liveborns is thought to be approximately one in 700 (Penrose and Smith, 1966). During the past twenty years a great many incidence studies have been conducted throughout the world, several are summarized in Table 1. In Canada, recent figures are available for three provinces: Lowry et al. (1976) reported an overall rate of 1.27/1000 livebirths for the period 1952-1960 in British Columbia; Uchida (1970) cited a frequency of 1.35/1000 livebirths in Manitoba; and McDonald (1972), in Quebec, for the years 1958 through 1967 found a rate of 1.86/1000 livebirths. In both Manitoba and British Columbia, data from

TABLE 1

Summary of Selected Studies of Incidence of Down Syndrome (Per 1,000 Births)

Study	Geographical Area	Incidence Rate Per 1,000 Births
Carter and MacCarthy (1951)	London, England	1.5
Collmann and Stoller (1962)	Victoria, Australia	1.45
Baird and Miller (1968)	British Columbia, Canada	1.27
Lindsjo (1974)	Sweden	1.32
Mikkelsen et al. (1976)	Copenhagen, Denmark	1.15

registries for handicapped children were used, whereas in Quebec cases were obtained from a variety of sources. Although these rates differ slightly, incomplete ascertainment and under-reporting may explain some of the variation (Zappella and Cowie, 1962).

Given the proven association between maternal age and Down syndrome, the well-documented fall in the number of older women giving birth over the past twenty years (Statistics Canada, 1973) should theoretically have resulted in a decline in the incidence of Down syndrome during the same period. Stein et al. (1973) estimated a drop in incidence of Down syndrome in New York from 1.25/1000 livebirths in 1953 to 1.05/1000 livebirths in 1970. While they attributed this decline to factors such as a slight decline in the fertiility of older women, the major reason cited was a decrease in the proportion of older women among women of childbearing age. Reports from Dublin (O'Brien and Gill, 1972) likewise demonstrated a fall in the proportion of deliveries to women aged 35 years or more over a six-year period, and a subsequent decline in the incidence of Down syndrome. Similarly, the observed incidence of Down syndrome births in Victoria, Australia, for 1942 to 1957 was in agreement with the corresponding rates expected on the basis of decreased maternal age (Collman and Stoller, 1969).

In contrast, experience in both Sweden (Lindsjo, 1974) and Denmark (Mikkelsen et al., 1976) has been dissimilar, with

the two countries reporting unchanged incidence rates over time. Two Canadian provinces, Manitoba and British Columbia, also failed to demonstrate a decrease in the incidence of Down syndrome, although both provinces reported a drop in the proportion of mothers aged 35 and over (Uchida, 1970; Jones and Lowry, 1975). One possible explanation advanced by both Lindsjo (1974) and Jones and Lowry (1975) for the increase in incidence rather than the hypothesized decline is better ascertainment in the more recent studies. However, the possibility of a true biological change resulting in a real increase in the incidence of Down syndrome has also been proposed (Uchida, 1970; Lindsjo, 1974; Lowry et al., 1976; Stein and Susser, 1977).

Incidence figures for Down syndrome are considerably higher than the prevalence figures, since there is significant mortality, particularly within the first year of life. The gap between the two figures is narrowing as a result of advances in cardiac and general pediatric surgery (Stein, 1975). Increased protection from antibiotics and immunization is also now preventing many deaths from the characteristic congenital anomalies. Table 2 demonstrates the steady decrease in mortality over the first year of life during the past 30 years. Although the representativeness of the samples used in several of these studies might be criticized, the decreasing trend in case-fatality rates is impressive.

Since prevalence measures the amount of a disorder existing

TABLE 2

Summary of Selected Infant Mortality Studies of Down Syndrome

Study	Geographical Area	Infant Mortality Rate (deaths under 1 year of age per 1,000 livebirths)
Carter (1958)	London, England 1944-1955	530
Collmann and Stoller (1963)	Victoria, Australia 1948-1957	290
Fabia and Drolette (1970)	Massachusetts 1950-1966	236
Carr (1975)	Surrey, England 1963-1968	160
Gallagher and Lowry (1975)	British Columbia 1952-1971	106

in a population at a specific point in time, it may also be considered to be an indicator of the size of the burden placed on a community by that disorder. In regard to Down syndrome, prevalence figures help determine the care required, in terms of health, education and residential needs. The above evidence suggests that independent of a possible decrease in incidence, the need to provide care or services for this population may be increasing in spite of any decline in incidence.

In summary, although it is not clear if the incidence of Down syndrome at birth is decreasing, there is substantial evidence that due to medical advances, the prevalence of Down syndrome is rising. Because the prevalence of a disorder is a function of the incidence and the average duration of the disorder from onset to termination (MacMahon and Pugh, 1970), and because there most likely will not be a reduction in the duration of Down syndrome, reducing the incidence must be considered the first step in alleviating this disorder (Stein, 1975). Primary preventive procedures offer the best means to do so.

Maternal Age

Maternal age is the one demographic variable known to be associated with the rate of occurrence of Down syndrome at birth. A disproportionate number of all Down syndrome infants are born to older mothers. The risk of having a Down syndrome

child increases from one in every 1600 births for a twenty-year-old woman to approximately one in every 40 births for a woman 45 years or older (Collmann and Stoller, 1969). Figure 1 illustrates the increased risk associated with advanced maternal age. Thus, the number of older women in a population giving birth should directly affect the incidence of Down syndrome.

Support of this association is also found by comparing the proportion of all livebirths in a specific maternal age group with the proportion of livebirths with Down syndrome contributed by the same group of women. For example, Stein (1975) estimated that in New York City approximately 35% of all Down syndrome babies are born to women 35 years and over who account for only 7% of the total births. While the comparative proportions differ according to time and place (see Table 3), the unbalanced distribution is apparent.

While the overall birth rate has been falling during the past twenty years in Quebec as in Canada generally, the number of older women giving birth has diminished more rapidly than the number of younger women (Statistics Canada, 1973). Theoretically, this decline in the fertility of older women should result in (1) a decrease in the proportion of all livebirths to women 35 years and over, (2) a decrease in the proportion of affected babies delivered by women 35 years and over, and most importantly, (3) a corresponding decrease in the total incidence of Down syndrome.

FIGURE 1. Variation of Incidence of Down syndrome with Maternal Age, Collmann and Stoller (1962).

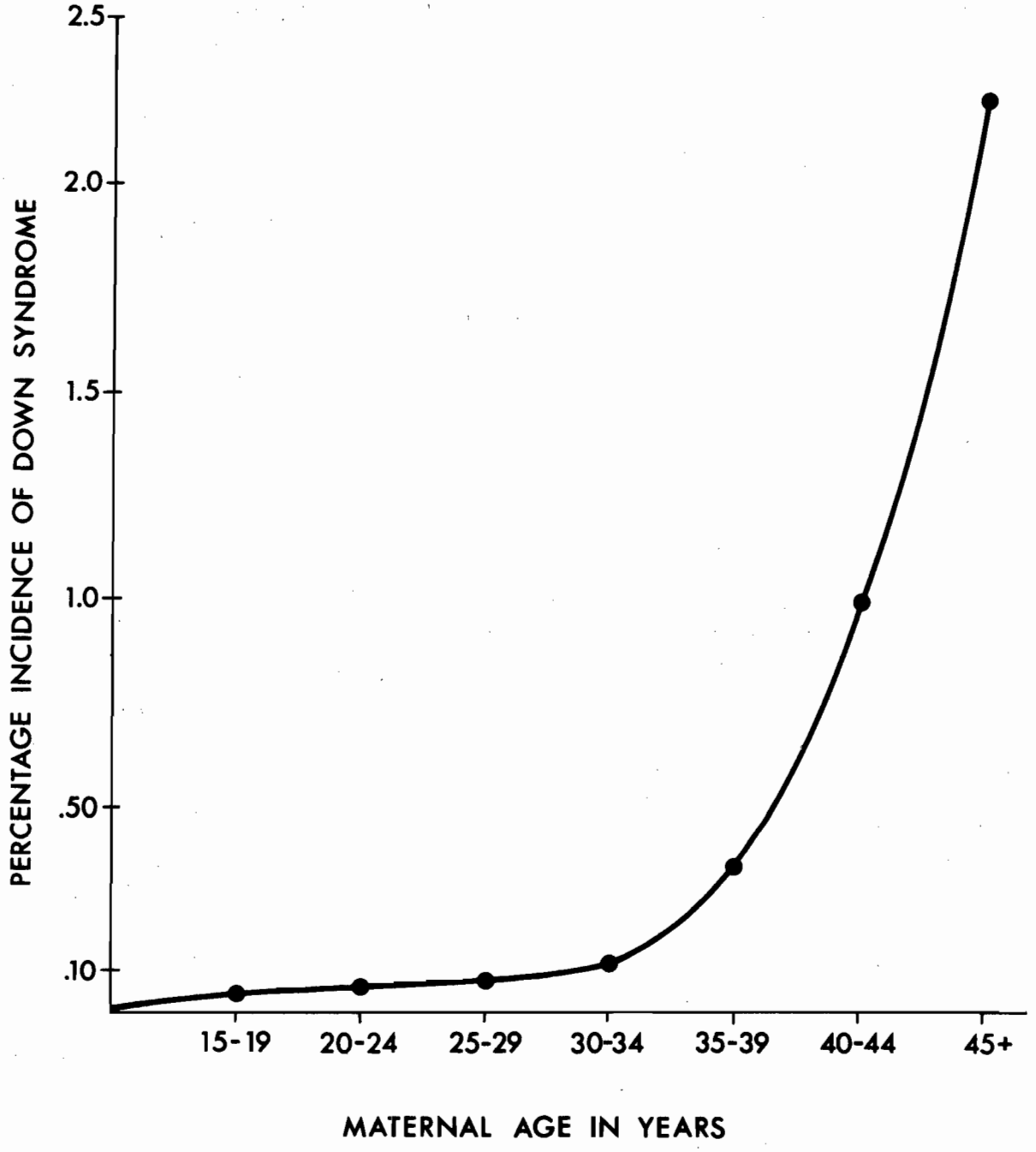

2.5
2.0
1.5
1.0
.50
.10
PERCENTAGE INCIDENCE OF DOWN SYNDROME
15-19
20-24
25-29
30-34
35-39
40-44
45+
MATERNAL AGE IN YEARS

TABLE 3

Percent Maternal Age Distribution of All Livebirths and of Down Syndrome Births

	Collmann & Stoller (1962) Victoria, 1942-57		Kuroki et al. (1977) Japan, 1950-54		Mikkelsen et al. (1976) Copenhagen, 1966-68		Lowry et al. (1976) B.C., 1972-73	
Age Group	% Livebirths	% D.S. Births	% Livebirths	% D.S. Births	% Livebirths	% D.S. Births	% Livebirths	% D.S. Births
15-19	4.54	1.34	2.0	0.0	12.5	12.7	13.5	10.1
20-24	26.66	11.44	26.4	14.7	43.1	27.0	35.7	20.2
25-29	32.00	18.59	36.3	26.5	29.3	20.6	33.3	30.4
30-34	21.98	17.34	21.7	26.5	10.2	17.5	12.7	19.0
35-39	11.08	26.54	10.5	23.5	3.8	11.1	3.8	12.7
40-44	3.14	21.45	2.9	8.8	1.0	11.1	0.9	7.6
45+	.22	3.31	0.1	0.0	0.1	-	0.1	-

This predicted decline is the rationale for any preventive program which advocates family planning based on maternal age as a means of diminishing the number of affected children born in the future. The deterrence of conception in older women as a method of decreasing the total incidence of Down syndrome has been proposed (Stein, 1975). Whether the reduction of fertility in older women occurs because of educational programs which stress family planning or because of a natural drop in the age-specific fertility of older women, the results should be the same: fewer infants with Down syndrome should be born, thereby lowering the total incidence. In actuality, however, reports regarding the expected change in incidence over time are conflicting. Several studies (Penrose, 1967; Collmann and Stoller, 1969; O'Brien, 1972; Kuroki et al., 1977) confirmed the fall in incidence associated with diminished maternal age. Dissimilarly, Uchida (1970) in Manitoba, Jones and Lowry (1975) and Lowry et al. (1976) in British Columbia and Mikkelsen (1977) in Copenhagen observed an unchanged or increased incidence of Down syndrome over varied time periods with concurrent reductions in maternal age.

Obviously, the extent of the impact of deterring conception in older women on the incidence of Down syndrome is determined by the proportions of affected babies delivered by women 35 years and over. Women over 35 years now deliver only 20-30% of the Down syndrome children whereas previously they contributed 50% or more of the cases (Lowry et al., 1976;

Holmes, 1978). Consequently, primary prevention of Down syndrome through family planning appears to be more limited now than in the past.

There are two possible explanations for the increase or unchanged incidence patterns versus the expected decline. Better ascertainment of cases in recent years would result in the calculation of higher rates for later cohorts. A change in the age-specific rates might also cause an increase in the overall incidence. Lindsjo (1974) investigated the age-specific rates in Sweden and found them to be higher than those most commonly employed when calculating expected births (Penrose, 1967; Collmann and Stoller, 1962). Lowery et al. (1976) likewise found the age-specific rates in British Columbia to be higher than those in Australia. Furthermore, they noted no appreciable change in age-specific rates over the 20-year period, but did note a rise from .726 to .961/1000 livebirths in women under 35 (Jones and Lowry, 1975). Similarly, in Denmark (Mikkelsen, 1976), an increase in the age-specific rates in the age groups 20-24, 30-34 and 35-39 between 1960 and 1971 was reported. Evans et al. (1978) recently reported an increase in the age-specific rates for women aged 35 to 39 years in Manitoba between 1965 and 1974. Scotland's experience has been similar (Holloway and Emery, 1977), with published data indicating a rise in the incidence in women 35 years and older. Such a change in these rates in a population over time, regardless of the cause, i.e. environmental or social factors,

would interact with the maternal age distribution and influence the total incidence figures.

The expected decline in incidence is dependent, therefore, not only on the drop in the number of older women giving birth but also on the age-specific rates remaining stable over the examined time period. Table 4 displays a hypothetical situation where the total number of livebirths and the proportion of women 35 years and over drops from Time A to Time B. If the age-specific rates remain constant over this period, as expected, the crude incidence rate declines. If, however, the age-specific rates were to change over time, the expected number of Down syndrome births could not be accurately predicted by applying previous age-specific rates. Table 5 demonstrates a second hypothetical situation where the age-specific rates have increased for the women from Time A to Time B. This particular situation would not result in the predicted drop in the crude incidence rate despite the decline in the fertility of older women.

The argument for the computation of individualized maternal age-specific rates for specific geographic locales is a compelling one. The frequent practice of using Australian rates (Collmann and Stoller, 1962) for genetic counseling in North America must be questioned on several counts. First, the Australian rates were compiled 20 years ago. Second, the premise that Australian rates are applicable to North Americans is debatable, particularly in light of epidemiological

TABLE 4

Hypothetical Situation Depicting Interaction of Decline in Livebirths with Constant Age-Specific Rates Over Time

	TIME A			TIME B		
	Number of Livebirths	Age-Specific Rate/1,000 Livebirths	Expected Number of D.S. Births	Number of Livebirths	Age-Specific Rates	Expected Number of D.S. Births
15-19	5,000	0.75	3.75	4,000	0.75	3.00
20-24	10,000	0.50	5.00	9,000	0.50	4.50
25-29	20,000	0.75	15.00	18,000	0.75	13.50
30-34	10,000	1.50	15.00	9,000	1.50	13.50
35-39	2,000	3.00	6.00	1,000	3.00	3.00
40-44	500	10.00	5.00	200	10.00	2.00
45+	100	25.00	2.50	25	25.00	0.625
Total	47,600		52.25	41,225		40.125
All ages (crude) =	1.1			= .97		

TABLE 5

Hypothetical Situation Depicting Interaction of Decline in Livebirths with Changing Age-Specific Rates Over Time

	TIME A			TIME B		
	Number of Livebirths	Age-Specific Rate/1,000 Livebirths	Expected No. of Down Syndrome Births	Number of Livebirths	Age-Specific Rates	Expected No. of Down Syndrome Births
15-19	5,000	0.75	3.75	4,000	1.00	4.00
20-24	10,000	0.50	5.00	9,000	0.75	6.75
25-29	20,000	0.75	15.00	18,000	1.00	18.00
30-34	10,000	1.50	15.00	9,000	2.50	22.50
35-39	2,000	3.00	6.00	1,000	5.00	5.00
40-44	500	10.00	5.00	200	15.00	3.00
45+	100	25.00	2.50	25	30.00	0.75
Total	47,600		52.50	41,225		60.00
		All Ages (Crude) = 1.1			All Ages (Crude) = 1.4	

evidence that incidence may vary in different ethnic groups (Stevenson et al., 1966; Harlap, 1974; Lillienfeld, 1969). Even within Australia, Collmann and Stoller (1962) reported a higher incidence in urban than in rural areas.

The necessity to limit the delivery of prenatal diagnostic services to those women "at risk" for giving birth to an affected baby, dictates the importance of defining those women who are currently "at risk" in the specific area being served by the screening program. An arbitrary age qualification, 35 years or 40 years and older, may not always be the most efficient criterion for determining who will receive services. If specific locales generated their own maternal age-specific rates, it is feasible that differing communities might screen different sets of women. Similarly, it has recently been suggested (Hook, 1976) that maternal age-specific rates for single years are needed to better define women at risk, rather than basing prenatal diagnosis programs on the usual five-year interval rates. The availability of one-year maternal age-specific rates would assist genetic counseling programs whose objective is the primary prevention of Down syndrome.

In summary, in the past, childbearing women over 35 years of age have contributed a disproportionate number of Down syndrome births. The recent decline in the proportion of older women giving birth should in itself be a major form of prevention of Down syndrome. However, the effect of this

reduction in the fertility of older women on the incidence of Down syndrome is still uncertain. Although the mean maternal age of Down syndrome births may be falling, the observed incidence may be rising or remaining constant as a result of a change in the age-specific rates over time. Prevention of Down syndrome by deterring conception is contingent upon the accurate definition of "at risk" women, i.e. the determination of the appropriate age-specific rates for the population in question.

Prenatal Diagnosis

Recent advances in prenatal diagnosis have resulted in another approach to the prevention of Down syndrome. Midtrimester amniocentesis to enable fetal cells to be cultured and karyotyped permits the identification of a Down syndrome fetus in utero. Contrary to a preconception prevention program based on maternal age, prenatal diagnosis coupled with selective abortion offers a postconception preventive procedure which, theoretically, can be utilized by all pregnant women regardless of age or past genetic history.

Amniocentesis involves the withdrawal of a small sample of amniotic fluid by introducing a needle through the abdominal skin and uterine wall and into the cavity of the uterus between the 14th and 16th weeks of gestation (Miller and Erbe, 1978). Ultrasonic scanning aids the obstetrician in avoiding the placenta and the fetus (Gerbie and Shkolnik, 1975). The

fetal cells are then removed from the amniotic fluid and are carefully cultured and karyotyped in the laboratory.

Presumably, universal prenatal diagnosis through amniocentesis with subsequent abortion could prevent the birth of any child with Down syndrome. Stein et al. (1973) present the rationale for a universal screening program for the prevention of Down syndrome. Although the elimination of Down syndrome, with its ever-increasing prevalence, is a desirable goal, such a comprehensive program is unlikely to be implemented in the near future. In reality, the impact of this technology on the eradication of Down syndrome is still negligible (Lowry et al., 1976). For several reasons the actual delivery of this form of prenatal diagnosis has been limited. Aside from the controversy surrounding selective abortion, there has been continued uncertainty associated with the risk of the surgical procedure to the fetus, mother, and subsequent child (Goldstein and Dumars, 1977).

In order to determine the actual risks involved with the procedure, two independent collaborative studies each collected data prospectively on approximately 1000 subjects who underwent midtrimester amniocentesis (NICHD, 1976; Simpson et al., 1976). Both concluded that "midtrimester amniocentesis is a safe, accurate and reliable procedure that does not significantly increase the risk of fetal loss or injury when it is monitored by ultrasound, performed by a trained obstetrician, and carried out in a major health science center". The short-

term effects on the children born after prenatal diagnosis have also been reported (NICHD, 1976 ; Robinson et al., 1975). The results of these two studies indicated no deviations from the norm in mental, physical or neurological functioning at one year of age. Although the long-term effects have not as yet been evaluated fully, these preliminary findings are promising. Studies such as these should assist physicians and parents alike in the decision-making process concerning the relative risks of a preventive procedure versus that of giving birth to a child with Down syndrome.

The practical argument, aside from the risk factors, against a mass screening program is the lack of manpower and expertise needed to carry out the amniocentesis, tissue culture and karyotyping (Holmes, 1978). In a cost-benefit analysis of providing universal prenatal diagnosis in Scotland, Hagard and Carter (1976) found that the potential economic benefits would be greater than the costs for women aged 40 and over, equal to costs for those aged 35 and over, and less than costs if the service were offered to women under 35 years. Yet as Hagard and Carter succinctly state: "the problem of Down syndrome cannot rest solely on the consideration of economic costs and benefits." In an attempt to put the debate on universal screening in perspective, they continue, "If Down syndrome is socially unacceptable, provision of a programme to reduce its birth prevalence by scarcely a third would be an inadequate response. Conversely, failure to

implement a programme for all maternal age groups would imply that there were other, perhaps more appropriate, responses to the problem of Down syndrome."

Except for Stein et al. (1973), few authorities openly advocate amniocentesis for all pregnant women. Rather, it is suggested (Laurence and Gregory, 1976; Gerbie and Simpson, 1976) that amniocentesis should be offered to those women who are defined to be at risk, that is pregnant women who have had a previous infant with Down syndrome or other chromosomal abnormality, women who themselves or whose husbands are known to be translocation carriers, and women who are 35 years and older.

Even with these restrictions regarding who is eligible for this diagnostic service, present evidence suggests that this particular preventive procedure is underutilized within this subset of high risk women. Milunsky (1975) found that in Massachussetts, where 3,979 women 35 years of age and older had babies in 1974, only 4.1% availed themselves of the opportunities afforded by prenatal diagnosis. In the Canadian collaborative study (Simpson et al., 1976), similar underutilization by older mothers was noted (see Table 6). One should recognize, however, the general trend towards increasing utilization from 1973 to 1974. For Canada as a whole, excluding Newfoundland, the rate of utilization doubled for women over 40 from 1973 to 1974. The experience in Great Britain resembles that of North America (Forster and Davison, 1977;

TABLE 6

Number of Canadian Women Per 1,000 Giving Birth Who Underwent Amniocentesis in 1973 and 1974

Region	1973 Mother's Age (Yr) 35-39	1973 Mother's Age (Yr) ⩾ 40	1974 Mother's Age (Yr) 35-39	1974 Mother's Age (Yr) ⩾ 40
Maritimes	6.0	2.6	8.6	18.9
Quebec	1.5	8.3	5.6	17.2
Ontario	6.1	12.7	9.5	38.1
Manitoba	9.0	28.6	1.4	24.9
Saskatchewan	0.0	10.9	1.5	8.4
Alberta	13.0	26.6	20.6	59.9
British Columbia	17.7	56.7	10.6	106.2
All provinces (excluding Newfoundland)	5.9	15.2	8.4	34.1

Source: Reprinted from: Simpson, N.E. et al. Prenatal diagnosis of genetic disease in Canada: report of a collaborative study. Canadian Med. Ass. J., 115: 739-746, 1976.

Polani, 1977). Furthermore, these figures, in both the United States and Canada, represented utilization prior to the publication of the collaborative studies. It is reasonable to assume that the conclusions presented in these studies regarding the risks involved in the procedure might alleviate some concerns and result in increased utilization in the future.

It is apparent that until mass screening of all pregnant women is initiated, the effectiveness of prenatal diagnosis in decreasing the incidence of Down syndrome will depend on the accurate identification and provision of services to those women who are at an increased risk. In terms of the maternal age factor, the need for precise age-specific incidence rates cannot be over-emphasized. If the age-specific rates are truly undergoing changes with the passage of time, the definition of the high risk mother is also changing. Estimates of the proportion of affected children who would be detected prenatally if all pregnant women 35 years and older were screened vary from as little as 20% (Lowry et al., 1976; Holmes, 1978) to as high as 45% (Evans et al., 1978). These estimates are based on the age-specific rates and their interaction with the maternal age distribution of the populations in the specific geographic locations being reported. In this time of limited resources, the uncertainty surrounding the age-specific rates has obvious ramifications for any prenatal diagnostic program in terms of determining which women are in most need of the service.

In summary, prenatal diagnosis for women "at risk" provides an opportunity for the primary prevention of Down syndrome. The ability to influence the incidence of Down syndrome through midtrimester amniocentesis is presently limited by both the decline in mean maternal age and the underutilization of this service by eligible women. Actual documentation of the effect of amniocentesis on the incidence of Down syndrome has yet to be reported, undoubtedly because so few women have availed themselves of the service. Although this situation is somewhat discouraging for those advocating primary prevention through prenatal diagnosis, the means for eliminating Down syndrome as a form of mental retardation exist. Accordingly, there is a pressing need to monitor the effectiveness of this preventive procedure in terms of future incidence rates.

CHAPTER 2

REMEDIATION

Early Intervention: Description

Given the fact that a considerable gap still exists between the primary preventive services that are available and those that are utilized, the challenge remains to find a means to ameliorate the severity of the mental handicap associated with Down syndrome. Until genetic counseling and prenatal diagnosis are more widely and efficaciously practiced, attempts must be made to remediate the retardation of children born with Down syndrome (Meir, 1975).

The search for methods of remediation is not new. A variety of drug treatment programs have been tried over the years in an attempt to alter the mental functioning of Down syndrome including dessicated thyroid gland, pituitary extract, thymus extract, glutamic acid and dehydroepiandrosterone (Smith, 1975; de la Cruz, 1977). However, none of these have proven efficacious (Coleman, 1975; Weise et al., 1975).

Another major approach to remediation that is being developed involves early intervention strategies for modifying the learning environments of Down syndrome children. These procedures are based on past experience suggesting first, that the early years of life provide the foundation for later development, and second, that increased stimulation within this

early growth period may alter the development of a young child (Caldwell, 1967; Tjossem, 1976). The theoretical value of intervention assumes greater importance with developmentally disabled or environmentally deprived infants whose early experiences are so often less than adequate. Recognition of the importance of the early years for a child's development has accordingly resulted in an increased application of intervention programs for high risk infants, including those with Down syndrome.

Early intervention is the formal attempt to facilitate an infant's growth and development by manipulating his social and physical environments. Tjossem (1976) defines early intervention as "A stimulus environment adapted to the infant's immediate capacities for response, which consistently and systematically creates learning environments responsive to his gradually expanding response capabilities."

There are three basic categories of infants who, because of their definition of being "at risk" could be considered potential candidates for an early intervention program (Tjossem, 1976): (1) those manifesting delayed development related to a medical disorder, such as Down syndrome; (2) those at "environmental risk" as a result of depriving life experiences, such as familial cultural deprivation; and (3) those at "biological risk" as determined by an increased probability for delayed or aberrant development subsequent to biological insult(s), such as prematurity. These risk categories are not

mutually exclusive. It is not uncommon to find an infant who is at risk for more than one reason, as in the case of a premature Down syndrome infant with congenital heart disease or a low birth weight infant born to an adolescent mother who herself is a victim of poverty.

Currently, a variety of activities and programs are labeled as forms of early intervention. Simple handling and rocking of premature infants, verbal stimulation for an infant from a socially deprived environment, or a complex individualized program stressing motor, verbal, social and cognitive development for a brain injured child are all examples of intervention procedures. Intervention approaches vary according to where, how often, and by whom they are offered. Mothers may be trained by nurses, or physical and occupational therapists to provide the stimulation activities in the home. Infants may be seen at a child development centre by a medical or educational specialist; child care workers may treat the infant in a residential care facility. The focus of a specific program dictates the approach used, as well as factors such as age and type of population being served, funding, personnel, and community resources.

Early intervention programs are being provided for infants with Down syndrome by a variety of agencies in both the United States and Canada (Zausmer et al., 1972; Wolpert et al., 1978; Podilchak and Gouse-Sheese, 1978), all of which involve activities designed to help develop those skills in

which the Down syndrome infant is behind his normal peer (Zausmer et al., 1972). In substance the infant curricula include:

Visual Stimulation:

Provision of interesting and developmentally appropriate objects--differing in colour, shape, and distance.

Optimal positioning to enable the child to make the best use of the eyes--particularly in the upright position.

Provision of experience in visual tracking as well as visual permanency.

Combining visual with other sensory-motor experiences.

Auditory Stimulation:

Introduction of sounds of variable quality, frequency and intensity--derived from different directions and distances.

Sounds reinforced with visual and tactile stimuli--particularly with facial expressions and gestures.

Repetition of sounds which the infant produces.

Additional Sensory Stimulation Relating to Sound Production and Speech:

Oral stimulation to encourage sucking, licking, closure of the mouth, tongue movements, and chewing.

Motor Stimulation:

Activities which encourage symmetrical and alternate or reciprocal movement patterns appropriate to specific developmental stages.

A model of an early intervention program specifically designed for Down syndrome infants is provided by the University of Washington. Their program involves an interdisciplinary team, including a nurse, nutritionist, physical therapist and

pediatrician and is described by the Center as follows (Hayden and Dmitriev, 1977):

> The Down Syndrome Programs are designed to accelerate and maintain the development of children with Down syndrome 0-6 years old and to give help and training to their parents. There are five programs in which children and parents participate; Infant Learning, Early, Intermediate and Advanced Pre-schools and Kindergarten. The Infant Learning class provides individualized instruction in early motor and cognitive development in children from birth to 18 months of age. Parent and child come to the center for weekly 30-minute sessions. Training is also continued and maintained by parents in the home. Pre-school and Kindergarten classes meet for two hours four days a week. In addition to a variety of classroom activities which foster physical, personal-social, communication, and cognitive development each child receives 10-20 minutes of daily individualized instruction in pre-academic and academic skills. Parents participate weekly as teacher aides and data-takers to learn techniques for maintaining the child's progress at home.

In summary, early intervention strategies have a wide focus and include many types of developmental activities. Opportunities for early intervention span the entire pre-school period, from birth to school entry. Programs are located in the high risk newborn nursery, the infant's home, the well baby clinic, the community child development centre, the mental retardation facility, and the nursery school. Prevention or remediation of a developmental delay, or both, regardless of cause, is the objective of early intervention. The medical, educational and social aspects of early intervention programs employed with the Down syndrome infant offer guidance and techniques for children and parents to maintain the child's

developmental progress as close as possible to that of established child development norms.

Early Intervention: Rationale

Throughout the past decade there has been an increased emphasis on the importance of early childhood education and intervention programs (Bronfenbrenner, 1975). Motivation and support for this upsurge came from research on both animal and human populations. Well-designed studies demonstrated that experiences in an animal's early life have a significant effect on later development. Levine (1956) found that stimulation of infant rats accelerated the maturation of their central nervous system. Stimulated rats exhibited a more rapid rate of development and achieved motor co-ordination at an earlier age when compared with non-stimulated ones. Rosenweig et al. (1972) also showed that rats raised in an enriched environment for 30 days had heavier and thicker cortical tissue than comparison animals from an impoverished setting. Likewise, Shapiro and Vukovich (1970) reported an increase in the number of dendritic spines in rats given a wide range of sensory stimulation.

Inevitably, the generalizability of animal findings to humans must be questioned. There is little evidence in the literature to support the premise that external stimulation of an infant's environment results in morpho-physiological changes in the brain. One case study (Purpura, 1976) compared

the cortical dendritic development of two premature infants. Both were the same gestational age at death, 33 weeks, but one infant had lived for 4 weeks following birth at 29 weeks, the other had died immediately after birth at 33 weeks. Comparisons of their brains revealed that the former child had more highly differentiated neurons as assessed by dendritic branch thickness and dendritic spine characteristics than the latter. Three explanations are possible: (1) the differences represent gross errors in calculating gestational ages, (2) prematurity may result in "acceleration" of cortical neuronal development, (3) accelerated development of the dendrites in the infant born at 29 weeks may be attributed to the 4 weeks of extra-uterine existence (Purpura, 1976).

The third explanation is doubtful, to say the least. Nonetheless, the lack of data from studies on humans documenting the physiological effects of stimulation need not necessarily be interpreted as evidence that environmental enrichment does not result in physiological brain changes. Since the problems involved in human brain research are many, the dearth of such investigations is understandable.

Somewhat more information is available on the capacity of the brain to recover from damage. Hebb (1942) made an important contribution to the study of the effects of brain damage early in life. He suggested that an intact and functional cerebrum is a prerequisite for the development of language and other mental abilities, but that once these skills have been

mastered their retention is not dependent on an intact brain. Due to the importance of the integrity of the brain for "early learning", Hebb (1947) argued that early brain damage has more severe consequences than that experienced later in life.

The belief that early brain damage is more amenable to change as a result of the greater plasticity of the young brain has also been disputed. Following extensive study of brain damaged infants, Isaacson and Nonneman (1972) concluded that early brain damage has more severe effects on cortical function than originally believed. Similarly, Purpura (1975) has proposed that the human brain at birth is a great deal more "mature" than was previously thought, rendering it less receptive to change through intervention.

Because the neurophysiological effects of stimulation are unclear and the capacity of the infant human brain to recover from injury is debatable, major support for early intervention, aside from the animal studies, is derived chiefly from human "deprivation" studies. This series of studies examined the repercussions of institutionalization and impoverishment on growth and development in infancy. In institutionalized infants, absence of consistent contact with a stimulating adult was associated with severe developmental delays resulting in intellectual, motor and emotional impairment (Spitz, 1945; Goldfarb, 1945; Dennis, 1960; Provence and Lipton, 1962).

Following these early studies, more attention was focused on the relative importance of the mother figure versus the

necessity of a stimulating environment. Evidence now suggests that both human and inanimate stimulation are important to infant development (Yarrow et al., 1972). The variety and type of objects available to the infant have been correlated with exploratory behaviour (Rubenstein, 1967) and sensorimotor development (Wachs et al., 1971).

Recently, studies dealing with premature infants have been added to the deprivation literature. The early environment of an isolette, with its carefully controlled temperature, humidity and oxygen levels, may result in prolonged social isolation and stimulus deprivation. Solokoff et al. (1969) implemented a clinical trial where handling of premature infants produced increased weight gain and better motor development. Further support of the positive effects of increased handling comes from Siqueland (1973) who, in a study with ten sets of premature twins, found significant differences in visual exploratory behaviours, at four months of age.

In summary, the results of these studies have provided support for the concept that the early years of a child's life comprise the most important period for priming physical, cognitive, social and emotional development. And, because a deprived environment has been shown to interfere with a child's development, it has been hypothesized that an enriched setting will be beneficial. Acceptance of these principles has resulted in an outpouring of early education programs for educationally "at risk" children, those who are economically and culturally disadvantaged (Bronfenbrenner, 1975).

Early Intervention: Prevention of Mental Retardation in "at risk" Children

Intervention advocates, encouraged by the findings of the animal and human deprivation studies, began to apply stimulation techniques to children labeled "disadvantaged", "culturally deprived" or "economically impoverished". Hence, programs to prevent a mild form of mental retardation in a culturally deprived but organically normal population were developed. These initial efforts followed traditional patterns of education and removed the child from the home, using the preschool as the site of intervention. This strategy was considered more efficient than attempts to influence an adult caretaker or change a family's lifestyle. Initial results from these pre-school enrichment programs were encouraging (Palmer, 1972; Caldwell and Richmond, 1968; Specter and Cowen, 1971; Lally and Honig, 1975). However, later research indicated that positive findings were short-lived with most IQ gains disappearing with the termination of the program (Ryan, 1975; Bronfenbrenner, 1975).

In an effort to alleviate this problem, Heber and Garber (1975), in a classic study in Milwaukee, initiated a long-term intervention program with low socioeconomic status infants. Their objective was to prevent "cultural-familial mental retardation". This population exhibited no identifiable gross pathology of the central nervous system but was considered at risk for mental retardation because of low socioeconomic status and a maternal IQ less than 80. Infants were

selected for the study and assigned on a monthly basis to either an experimental or a control group. Their intervention strategy included two major components: maternal intervention, consisting of career training and instruction in child care; and infant intervention commencing between 3-6 months of age and continuing to age 6. Beginning with two mornings a week at 3-6 months, the intervention was increased to an all-day program, five days per week, twelve months per year by 1-2 years of age. The hypothesis that cultural-familial mental retardation can be prevented by appropriate intervention was supported by the final results: at 66 months of age there was a 30 point difference in IQ between the experimental and control groups.

Recent endeavours have emphasized the mother's role in the intervention process. Programs involving maternal instruction in child-rearing techniques and appropriate play activities were initiated (Schaefer, 1972; Levenstein, 1970; Karnes et al., 1970; Morris et al., 1976). The experimental groups in the majority of these projects not only made substantial gains initially, but also retained them for at least several years after termination of the intervention. Bronfenbrenner (1975), in a critical review of early intervention, concluded that parental involvement and active participation of the child's family are essential in fostering and sustaining developmental gains.

In summary, there is convincing evidence regarding the

efficacy of early intervention as a preventive procedure for children who do not exhibit central nervous system deficits but who are considered at risk for retardation at some later point in time. The joint involvement of both the nursery school setting and the home, the teacher and the parent, has proven most efficacious in terms of sustaining initial cognitive gains. The purported success of these programs in preventing retardation has contributed to the development of similar services for mentally handicapped children in hopes of ameliorating their retardation. However, the relevance of these findings to remediating retardation stemming from organic deficits or specific brain damage must be considered separately.

Early Intervention: Remediation of Mental Retardation

While the reported success of intervention programs in preventing future retardation is compelling, much less is known about the efficacy of early intervention for children with mental handicaps. Nonetheless, the available evidence from animal research, studies of early intervention with disadvantaged children, and subjective clinical reports have prompted the development of early intervention programs for mentally retarded and brain damaged infants throughout the United States, Canada and Western Europe.

As with the disadvantaged child, early intervention for the retarded has taken many forms. Stimulation programs are

conducted in institutions, pre-schools, community retardation centers, and within the home. Some provide services for all mentally retarded children; others offer programs only to those with specific diagnoses. Regardless of the location of the intervention or the population receiving services, the basic principle that enrichment of the environment will remediate or alter the pattern of retardation is questionable. Unfortunately, research documenting the efficacy of such programs is lacking. Furthermore, the few evaluative studies which have been completed are difficult to interpret. Methodological problems plague these efforts and often overshadow the reported results. Lack of adequate control or comparison groups, the absence of "blind" evaluators, and the failure to assess the contribution of possible confounding variables, are examples of the problems encountered.

The Skeels and Dye (1938) classic study on the effects of differential stimulation on institutionalized retarded children, is repeatedly cited as evidence that early intervention does in fact remediate retardation. While the study subjects "appeared" mentally retarded, they had no signs of physiologic deficiences or organic diseases and therefore may, in reality, have only been "culturally deprived". This being the case, the positive results merely concur with those previously cited for disadvantaged children.

The effect of pre-school training on the mentally handicapped child has also been considered (Kirk, 1958). By

evaluating nursery programs operating within the community, Kirk assessed the development of four groups of mentally retarded children who were already either receiving or not receiving programming. Although he demonstrated higher IQs after intervention in the experimental groups, Kirk found it more difficult to affect the rate of growth of children with biological defects than children not so affected.

Likewise, home intervention programs have been reviewed (Santostefano and Stayton, 1967; Sandow and Clarke, 1978). In the earlier study, mothers were trained in a procedure emphasizing focal attention; in the latter, children received stimulation programs provided by home visitors. Santostefano and Stayton reported significant differences on several sensory and perceptual measures favouring the experimental children, but failed to document the training the "controls" were receiving at the time of the study from the various nursery programs they were attending. Consequently, it is difficult to interpret the reported findings as a product of intervention; they may only be due to differences at the time of the study in the routine nursery programs.

Sandow and Clarke published contradictory results. Children frequently visited in the home, following an initial increase in measured intelligence, demonstrated a decrease in intellectual growth. Conversely, less frequently visited children displayed an increase in performance after an initial drop.

In summary, early intervention programs for the mentally retarded child have been administered in institutions, preschool settings and the home itself. Evaluative studies of these programs have failed to unequivocally establish the efficacy of early intervention techniques for this population of special children. Moreover, these investigations have considered many forms of mental retardation and not Down syndrome exclusively. Because it is conceivable that Down syndrome represents a unique organic deficit, and that these children may respond differently than those with other forms of retardation, the efficacy of early intervention for this specific population will be considered in detail.

Early Intervention: Remediation of Down Syndrome

Because Down syndrome is easily identified at birth, stimulation procedures may be initiated immediately, permitting the earliest postnatal intervention available. This diagnosis alleviates the necessity for screening for developmental delays or retardation prior to recommending treatment. As a result of this almost certain diagnosis of mental retardation, infants with Down syndrome are prime candidates for early intervention.

Many early intervention programs were, hence, developed to provide services to these children and their families from birth forward. Unfortunately, it appears that the rapid establishment of such services has precluded appropriate evaluation (Tjossem,

1976). This entrenchment of programs has interfered with past research in terms of the provision of adequate comparison or control groups, the use of "blind" evaluators, the consideration of potential confounding variables, and the determination of the representativeness of the study population. In effect, the evaluative research of early intervention for Down syndrome children that has been conducted contains similar problems as those identified with mental retardation in general.

Historically, the results of early intervention on development were studied by comparing institutionalized Down syndrome children with those children reared in the home (Centerwall and Centerwall, 1960; Kugel and Reque, 1961; Stedman and Eichorn, 1964; Shotwell and Shipe, 1964; Shipe and Shotwell, 1965; Stimson et al., 1968; Carr, 1970). In general, these studies claimed adverse effects associated with residential care, by reporting differences in favour of the home-reared children in physical size, age of walking, and in both mental and social development. Interpreting these findings is extremely difficult since the children compared were not randomly assigned to either institutions or homes. Rather, a selective factor may be at work resulting in biased samples, such as the institutionalized child might have been more defective initially than the home-reared (Birch and Belmont, 1961).

Since Down syndrome infants were often institutionalized at birth, many intervention programs were implemented in residences for the mentally retarded. Evaluations of these

programs have consisted of one descriptive report (Kugel, (1970), a comparison study (Bayley et al., 1971) and more recently a controlled trial (Aronson and Fallstrom, 1977).

In a longitudinal study comparing the development of institutionalized and home-reared Down syndrome children, Bayley et al. (1971) initiated a program of language stimulation for the hospital children after the fifth year of life. Follow-up evaluations at 6 and 8 years of age of both populations demonstrated a reduction in the marked initial differences that had favoured the home-reared children. Although these findings are suggestive of the positive value of specific interventive techniques, the advanced ages of the children detracts from the applicability to younger populations. Moreover, in spite of the authors' attempts to prove the comparability of the two groups, the fact remains that the subjects represented two distinct populations.

The objective of the Aronson trial was to assess the immediate and long-term effects of early, systematic mental training with institutionalized Down syndrome children. Although significant increases in mental age were reported initially, a follow-up study one year after termination of the training revealed that the effects were no longer apparent.

In view of the fact that many more Down syndrome children are now being reared in natural or foster homes (Pueschel and Murphy, 1976), many early intervention programs are conducted in the pre-school setting or the home itself. One of the most

widely acclaimed is the Model Pre-school Center for Handicapped Children at the University of Washington. Since 1971 the Model Pre-school has provided four separate yet complementary programs: the Infant Learning Program (0-18 months), Early Pre-school (18 months-3 years), Advanced Pre-school (3-5 years) and Kindergarten (4½-6 years), with the objective of all four being "to bring these Down syndrome children's developmental patterns as close as possible to sequential developmental norms based on normal children's performance" (Hayden and Haring, 1976). Published accounts (Mills, 1974) of impressive accomplishments of pre-schoolers (successful performance of independence skills such as toilet training, dressing, feeding; academic skills; and near normal IQs) have drawn attention to the potential ramifications of early intervention for the Down syndrome infant.

Upon close examination, however, many questions remain. Hayden and Dmitriev (1975) claimed this particular approach was "remediating severe developmental lags usually exhibited by children in this population". They compared the IQ scores of two groups of Down syndrome pre-school children: Group I was composed of 14 children who had previously received the pre-school program; Group II contained children who were enrolling for the first time. Early intervention was credited for the discrepancy of 25 IQ points between the mean IQs for the two groups. After one year of additional intervention for both groups the difference in IQ between groups had

decreased approximately 13 points.

Basic problems with the design of this investigation may have biased the findings. Firstly, the major difficulty concerns the comparability of the two groups. Initially the mean age of Group I was 3.2 years, with Group II being 4.0 years. Such a difference in age may itself have accounted for or contributed to the difference in development due to the widely documented decrease in IQ with increasing age. Standard deviations are not reported, thereby making it difficult to assess the variance of ages within the groups. Secondly, no information was provided regarding the reasons why those in Group II did not avail themselves of the program at a younger age. Possibly, the child with medical problems was unable to attend at a young age because of repeated hospitalizations, and only after major surgery, etc. was physically well enough to participate in the Model Pre-school Program. Other factors, such as early institutionalization, foster home placement, increased family size and advanced maternal age might in effect have been the factors that determined which Group a child entered, and consequently, these factors in themselves, might be the reason for the observed difference in IQ. When an experimental design fails to provide for random allocation of subjects into groups, it is essential to demonstrate that the groups do not differ on potential confounding variables (Weiss, 1972). This study lacks such a demonstration.

In a more recent report, Hayden and Haring (1977) suggested that children entering the public school system functioned at a higher level after attending the Model Pre-school Center when compared with peers who lacked this experience. As before, the potential reasons why some children received services and others did not were not considered. Furthermore, the analyses used were described as being "cross-sectional"; they used only one score from each child and examined the relationship between age and developmental level. A cross-sectional analysis, when presented on a longitudinal basis, gives the impression of defining the average growth curve of a child enrolled in the program over time. In reality, however, the relationships presented here are not the means calculated from the same n children at specific ages. Rather the relationship depicted represents individual scores at varied times for different children. Such an analysis is difficult to interpret unless one is able to assume that the individual children contributing to the graph are homogeneous in terms of severity of retardation, home environment, heart conditions, etc. Obviously, this assumption cannot be made, thereby requiring extreme care when analyzing this data.

The more relevant studies to this thesis are those focusing on the effect of early intervention conducted in the home with an emphasis on maternal training. The lack of adequate comparison populations plague this area, as it has with the institutional and pre-school research. Brinkworth (1972)

attempted to demonstrate the importance of an enriched home environment by initiating a home training program in England for five newborns. Comparisons were made with 12 "control" Down syndrome infants who were born as much as six months prior to the initiation of the program; significant differences favouring the experimental group were reported. While Brinkworth attempted to compensate for the recognized drop in measured IQ over the first year of life, the age difference between the two groups may remain a crucial confounding variable. Moreover, because the pre-test, post-test design was not employed, the results may only reflect initial differences in the two groups.

Data collected by Fishler et al. (1964) on the development of children with Down syndrome were compared with the results of a home-based early intervention program for infants (Connolly and Russell, 1976). Historical controls are at best questionable; however, in this situation the choice of data is unacceptable because Fishler failed to mention whether his population was derived from homes or institutions. Furthermore, a simple comparison of mean values was employed with no mention of standard deviations or variances. This is most likely due to the lack of information regarding the Fishler data, such as individual scores or standard deviations. Because this comparison may be deceiving for several reasons, Connolly's claims of positive results are in question.

An adequate control group was used by Bidder (1975) in a

comparison study of maternal training in behaviour modification techniques. Significant differences were noted between the two groups of children in verbal and performance skills. Unfortunately, the outcome measures of this otherwise well designed study were changes in mental ages rather than changes in developmental quotients. Because mental age scores do not account for the chronological age of the child, the comparison of mental age scores is inappropriate unless all the children are the same age at the time of testing. That is to say, one mental age unit at chronological age A is not equivalent to another mental age unit at chronological age B (Anastasi, 1966). The use of developmental quotients is a more acceptable procedure since the quotient is derived by dividing the mental age by the chronological age and then multiplying by 100, thereby adjusting, theoretically, for the chronological age.

Bidder's decision to report changes in mental ages rather than developmental quotients might be a product of the observation by Koch et al. (1963) that while developmental quotients decline over time, mental ages slowly increase with age in the child with Down syndrome, thus rendering change scores positive rather than negative. Regardless, the selection of this outcome measure may have distorted the findings of this study.

Table 7 summarizes the studies cited above with regard to the type of program offered, the population served, and the methodology used. The most consistent and important

TABLE 7

Summary of Early Intervention Studies for Down Syndrome Children

Study	Method	Limitations
Brinkworth (1972)	Home training program for 5 infants; compared with 12 children not receiving program.	Uncertain comparability of 2 groups. No blind evaluator.
Kugel (1970)	Stimulation program for 7 institutionalized infants.	Descriptive report; no comparison group. No blind evaluator.
Hayden and Dmitriev (1975)	Pre-school training program for 14 children; compared with children enrolling for the first time in pre-school program.	Uncertain comparability of 2 groups. Pre-schoolers rather than infants. No blind evaluator.
Bayley, Rhodes, Gooch, and Marcus (1971)	Language stimulation program for 10 six-year-old institutionalized subjects matched for age with home-reared children.	Uncertain comparability of 2 groups. Approach not considered early intervention.
Connolly and Russell (1976)	Early intervention for 35 children; compared with historical data.	Uncertain comparability of 2 groups. No blind evaluators.
Bidder (1975)	Behaviour modification program for 8 children; compared with 8 matched controls.	Mean age at entry = 24 months. Mental age scores.
Aronson and Fallstrom (1977)	Systematic mental training program for 8 institutionalized children; compared with matched controls.	Mean age at entry = 51 months. Institutionalized children instead of home-reared. Mental age scores.

methodological deficiency is the absence of satisfactory control or comparison groups (Kugel, 1970; Brinkworth, 1970; Hayden and Dmitriev, 1975; Connolly and Russell, 1976). As the majority of the findings involved children aged two or more (Hayden and Dmitriev, 1975; Bidder, 1975; Aronson and Fallstrom, 1977), the effect of early intervention, immediately or shortly following birth, has also not been adequately explored. Finally, potential confounding variables are rarely considered in the designs. Except for age and sex there is no regard for other factors which may influence the results.

Thus, many questions remain about the efficacy of early intervention for remediating the mental retardation associated with Down syndrome. The effect of the age of the child at the time of initiating intervention on outcome is still unclear. However, since a definitive diagnosis at birth is usually possible, intervention during infancy is feasible. With the evidence that measured intelligence declines as the child with Down syndrome grows older, it is easily argued that intervention must be begun early in the infant's life. Unfortunately, the only two studies that included this time period (Brinkworth, 1972; Connolly and Russell, 1976) contained major methodological flaws.

The provision of an adequate comparison group is essential to an evaluative study. Often random allocation or the selection of an appropriate group is difficult, and, therefore, any potential factors which may bias the results should

be defined and evaluated in terms of their distribution between or among the groups being compared. With regard to Down syndrome, in addition to a variety of demographic variables, the quality of the home environment has been recognized as a potential factor that might influence development (Melwyn and White, 1973).

If early intervention is truly efficacious and environmental manipulation does change the rate of development, it is reasonable to propose that the quality of the home environment may also be a crucial factor influencing eventual outcome. Bradley and Caldwell (1976; 1977) have shown normal infants' home environments as measured by the Home Observation for Measurement of the Environment (HOME), an index of the quality of the stimulation found in the early environment, to be a relatively good predictor of intelligence as measured at 3 years of age. Oddly enough, no investigator has yet considered the contribution the home environment might make to the outcome of an early intervention program for mentally retarded children who are being reared in the home.

Finally, there has been no effort in previous reports to describe the representativeness of the particular group being studied. The absence of probability sampling to derive the study population necessitates comparison of the characteristics of the individuals included in and omitted from the investigation. Moreover, if differences are discovered, the possible bias contributed by such differences should be

explored (Abramson, 1974).

It may be that the infant who participates in early intervention services is not truly representative of all the Down syndrome children being born, thereby resulting in an evaluation of a service for a biased sample. For example, this population may be healthier and less seriously involved or have younger mothers and fewer siblings than the population that is not receiving intervention. This, certainly, would influence the generalizability of the results.

In summary, previous investigations of the efficacy of early intervention as it applied to Down syndrome have either failed to provide adequate comparison groups or "blind" evaluators. The few studies that employed both comparison groups and independent evaluators chose to evaluate outcome in older children rather than infants. Concern for the representativeness and the potential biases of the study population has not yet been displayed. Thus, at present, the need for a well designed investigation in this area is obvious and until such a study is conducted, the efficacy of early intervention as applied to Down syndrome infants will continue to be uncertain.

PART II: THE PRESENT STUDY

CHAPTER 3

ASSESSMENT OF PRIMARY PREVENTIVE MEASURES

Objectives

This study examined the effect of two primary preventive measures, decrease in maternal age and amniocentesis for prenatal diagnosis, on the incidence of Down syndrome in Montreal. Specifically, the incidence rates of Down syndrome in Montreal were determined and compared for two time periods, ten years apart, 1965-66 and 1975-76. The expected decline in maternal age over this time span contributed to the selection of this particular comparison. Furthermore, because amniocentesis was not available for prenatal diagnosis in 1965-66, the choice of these specific years permitted the evaluation of the impact of a newly acquired technology.

The number of Down syndrome infants born alive in Montreal between January 1, 1975 and December 31, 1976, was ascertained, and the incidence rate of Down syndrome was calculated. This rate was compared with the previous rate established by McDonald (1972) for Montreal in 1965 and 1966 in order to determine: (1) whether the incidence differed, and (2) if so, whether the difference could be attributed to the decrease in mean maternal age, change in age-specific rates or prenatal diagnosis and selective termination.

Methods and Materials

Ascertainment of Cases. All infants diagnosed as having Down syndrome, either clinically or cytogenetically, who were born alive in Montreal between January 1, 1975 and December 31, 1976, were ascertained. Montreal was defined as the geographic Island of Montreal including the Lakeshore and excluding the South Shore area. To be eligible for the study the infant was required to have been born in a hospital or home located in this area, but did not necessarily have to reside in the defined locale after birth. For example, a child of a mother who lived on the South Shore and gave birth at a hospital on the island, was included in the study.

Cases were ascertained from several sources, including the four Montreal social service agencies responsible for the placement of handicapped children in foster homes or institutions and the two early intervention programs currently providing services for Down syndrome infants. However, ascertainment of the cohort was done primarily through a request to all hospital cytogenetic laboratories on the Island of Montreal for information regarding all children born alive during the specified time period who were diagnosed as having Down syndrome with positive karyotypes. This particular method of ascertaining cases was selected for several reasons. Although birth certificates or birth records are often used as sources of information on congenital defects, the effectiveness of this method is questionable when applied to Down

syndrome. Zappella and Cowie (1962) reported 26% of cases in one series not to have been diagnosed as Down syndrome until 6 months of age or later. Similarly, Venters et al. (1976) found 52% of cytogenetically confirmed cases not to have been reported on matched birth certificates. Quebec's experience can be estimated by the reported incidence of 0.7 per 1000 livebirths in 1973 as recorded on a mandatory birth record, Attestation Medicale d'un Accouchement (Anonymous, 1973). This incidence is only 40% of that expected from studies elsewhere. Analysis on a regional basis revealed only one area (Cantons de l'Est) where the rate of reported diagnosis (1.4/1000) approached the expected frequency, with Montreal reporting a rate of 0.6/1000. Despite the fact that diagnosis in the neonatal period by physical examination alone is possible, confirmation through chromosomal studies requires an additional 1 to 2 weeks, thereby prohibiting the inclusion of this form of reporting on birth records which often must be completed within a specified period after birth. This reason in itself may explain some of the under-reporting in the above studies.

Therefore, the possibility of ascertaining cases from the cytogenetic laboratories where the chromosomal studies were performed was considered. Experience in Sweden (Lindsjo, 1974) has shown that this technique of ascertainment contributed 25% more cases than had been reported through pediatric or obstetric departments. In British Columbia only 40% of

the Down syndrome children born between 1952-73 had their chromosomes analyzed (Lowry et al., 1976). However, it was estimated (Lowry, 1977) that chromosomal studies were done in 95% or more of those infants born in 1970 or later, with 98%-99% of the cases being karyotyped in 1975 and 1976. This increased utilization was attributed to a "greatly increased knowledge of chromosome resources and the importance of excluding a translocation" (Lowry, 1977). Thus, requesting cases from cytogenetic laboratories was selected as a method of ascertainment instead of relying solely on reviewing birth certificates or hospital records.

Because no complete list of hospitals with cytogenetic laboratories in Montreal was available, letters were sent to 22 hospitals on the island which provided maternity or pediatric services. Twelve of the twenty-two had a cytogenetic laboratory. The information requested from these laboratories was:

(1) initials of the child's given and surnames, or the child's family name, if possible.
(2) birth date of the child.
(3) sex of the child.

It was felt that the above data would provide sufficient identifying information to prevent including the same child more than once in the cohort, while at the same time, retaining the confidentiality of medical information by preventing specific

identification of any child or family.

The procedure for requesting information was as follows:

(1) An initial letter explaining the study and requesting information was sent to all 22 hospitals. (See Appendix A.) Included with this letter was a form to be completed and a stamped envelope for its return. (See Appendix B.)

(2) A follow-up letter was sent to all non-responders (n = 7) in one month's time.

(3) A follow-up telephone call was made to all subsequent non-responders (n = 5) three weeks after the second letter was sent.

(4) Only one hospital required further personal contact in order to elicit the requested information.

100% compliance was obtained. (See Figure 2.)

The amount of identifying information obtained varied for each child according to the particular hospital's or agency's policies regarding disclosure of confidential patient information. Family names, birth dates, sex, and hospital of birth were obtained on 94% of the cohort. For the remaining 6%, the procured data consisted of the initial of the family name, the sex and date of birth of the child.

At the same time, in order to compare crude and age-specific incidence rates between 1965-66 and 1975-76, data collected by Dr. Alison McDonald (1972) on the Down syndrome

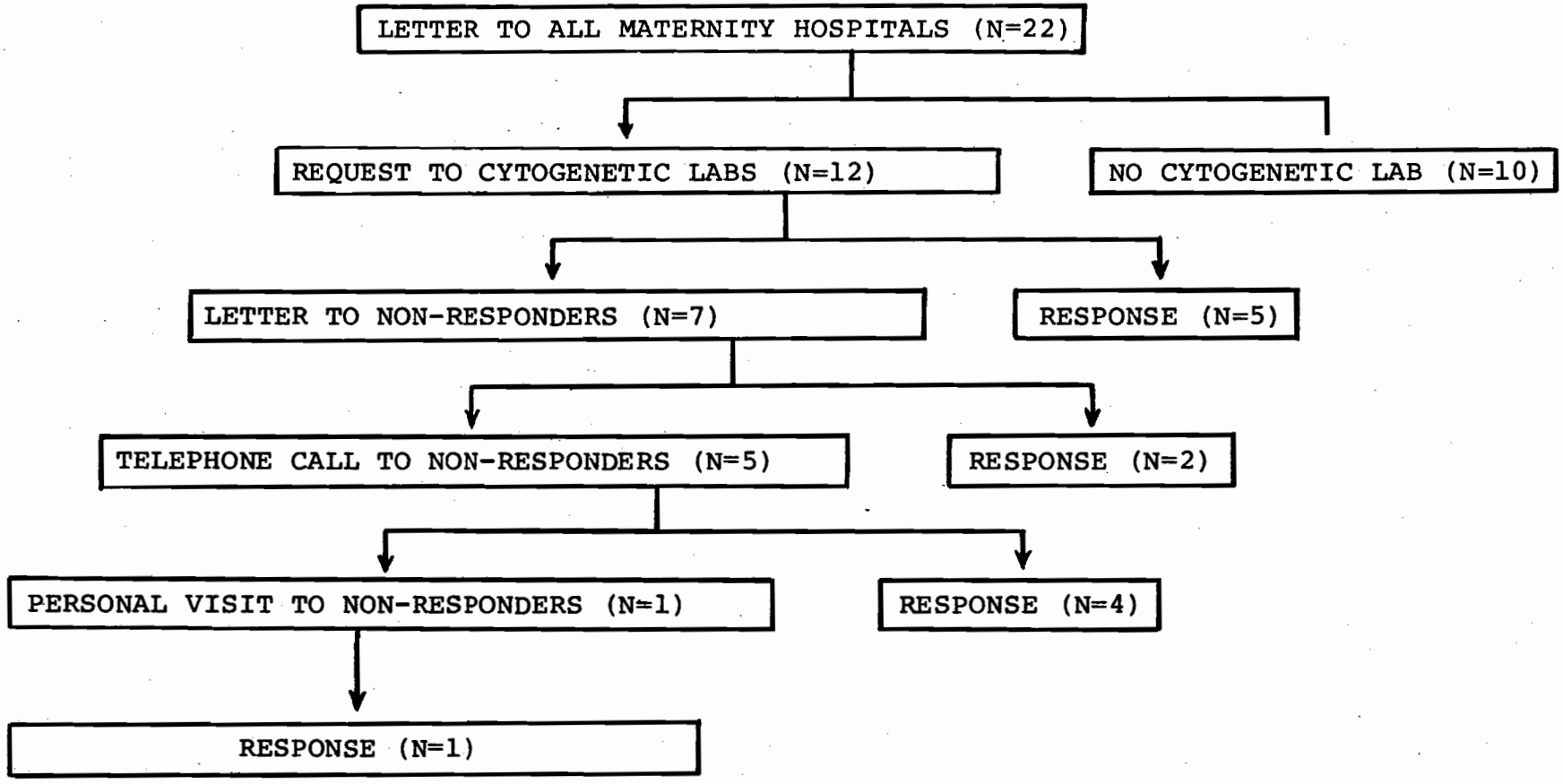


FIGURE 2. Flow Chart - Ascertainment of Down syndrome cases in cohort.

children born in 1965-66 in Quebec were re-analyzed. The 1965-66 birth cohort was composed of those children from the Quebec population who were identified as having been born in Montreal either by the hospital of birth or the parents' address at the time of birth.

The number of Down syndrome fetuses aborted following prenatal diagnosis who would have been born in 1975-76 were obtained from the two centres performing prenatal diagnoses on the Island of Montreal.

Determination of Maternal Age Structure. The maternal age structure for all livebirths on the Island of Montreal for the years 1965-66 and 1975-76 was obtained from Statistics Canada, Vital Statistics and Disease Registries Section. The maternal age groupings requested were those most often used in the literature to calculate age-specific rates: 15-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40-44 years, and 45 years and over (see Table 8).

Since the commonly employed five year age-specific rates are averages for those periods and do not necessarily reflect the variation within the groups, extreme differences may exist at the borders of the intervals. For example, the age-specific rate for age 35 may be very dissimilar to that for age 39. As Hook (1976) suggested, the limited resources available for prenatal diagnosis demand careful evaluation of arbitrary age cut-offs as determinants for amniocentesis. It could be argued on a cost-benefit basis that the difference between

TABLE 8

Maternal Age Structure by Five-Year Intervals for all Livebirths and of Those Ascertained with Down Syndrome in Montreal in 1965-66 and 1975-76. Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

	All Livebirths		Livebirths With Down Syndrome	
Maternal Age	1965-66	1975-76	1965-66	1975-76
15-19 years	4,754	3,351	6	4
20-24 years	24,422	14,381	26	11
25-29 years	21,349	17,966	23	31
30-34 years	13,271	7,829	24	16
35-39 years	7,077	2,324	29	9 (11)
40-44 years	1,980	448	29	11 (12)
45+ years	137	52	2	1 (2)
Unknown	189	1,295	9	5
TOTAL	73,179	47,646	148	88 (92)

screening all women older than 35 years versus women 37 years and over is significant.

Because the comparison of the five-year rates does not permit a precise evaluation of the age-specific rate, the maternal age structure by single years for all livebirths was requested from Statistics Canada in order to calculate the age-specific rates for single year intervals. While this agency was unable to provide single year statistics for the Island of Montreal, the requested figures for the metropolitain Montreal area for 1965-66 and 1975-76 were available. Using these vital statistics as a basis, the percentage of the total livebirths in metropolitain Montreal for each maternal age was calculated for both birth cohorts. Following this calculation, an estimate of the number of livebirths for each single year for the Island of Montreal was derived by applying the appropriate percents to the total number of births on the island. (See Table 9.)

Within the two birth cohorts the maternal age structure, by single years and five-year groupings, of the livebirths with Down syndrome was determined. Maternal age was defined as the age of the mother in years on the birth date of the index child. Maternal ages were acquired from the following sources: hospital and birth records, social service agencies, and hospital genetic counseling services. Similarly the maternal ages were ascertained for the fetuses aborted in 1975-76 following prenatal diagnosis. Maternal ages were

TABLE 9

Maternal Age Structure by Single Years for All Livebirths and of Those Ascertained with Down Syndrome in Montreal in 1965-66 and 1975-76. Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

	All Livebirths		Livebirths With Down Syndrome	
Maternal Age	1965-66	1975-76	1965-66	1975-76
<15	14	23	0	0
15	60	73	0	0
16	213	272	0	0
17	620	569	0	2
18	1,408	945	2	1
19	2,439	1,470	4	1
20	3,417	1,756	2	0
21	4,672	2,358	8	2
22	5,305	2,908	6	0
23	5,576	3,409	6	4
24	5,452	3,950	4	5
25	5,167	3,700	1	3
26	4,574	3,946	6	1
27	4,268	3,858	4	7
28	3,962	3,504	6	10
29	3,378	2,958	6	10
30	3,221	2,343	4	7
31	2,733	1,897	3	1
32	2,651	1,512	5	4
33	2,464	1,183	7	0
34	2,202	895	5	4
35	1,920	770	5	4
36	1,681	556	6	1
37	1,350	423	6	0 (2)
38	1,209	319	6	4
39	917	255	6	0
40	692	154	4	2
41	526	130	11	2
42	398	80	6	2 (3)
43	228	50	5	4
44	136	32	3	1
45+	137	52	2	1 (2)
Unknown	189	1,295	9	5

not available for nine children (6%) in the 1965-66 cohort and for 5 children (5.7%) in 1975-76. (See Tables 8 and 9.) The reason(s) for missing data for the 1965-66 cohort is unknown, however, the five children in the later cohort were identified by one cytogenetic laboratory that refused to disclose family names, thereby making the acquisition of the maternal ages from birth records impossible.

A crude assessment of the completeness of the ascertainment of cases for all four cohorts was done by calculating the expected number of cases and comparing this with the observed number of cases. Three age-specific rates were used (Collmann and Stoller of Australia, 1962; Lindsjo of Sweden, 1974; and McDonald of Quebec, 1972) to determine the expected number of affected births. (See Table 10.) The age-specific rates reported for Quebec were calculated by using all cases of Down syndrome ascertained in 1966 in Quebec. (See Table 11.) The observed numbers of cases in the 15-19, 35-39, and 45 plus age groups in both cohorts and the 20-24 age group in 1975-76 and the 40-44 age group in 1965-66 are similar to those expected. For the remaining groups the observed numbers are substantially higher than the expected. Because the discrepancies between the expected and observed cases are not uniform across all groups, the possibility of different age-specific rates (than those commonly cited in the literature) for certain Montreal women must be considered.

TABLE 10

Expected and Observed Cases of Liveborn Infants With Down Syndrome in Montreal According to Three Maternal Age-Specific Rates

Maternal Age		1965-66	1975-76
15-19 Years			
Total no. of births		4,754	3,351
Expect. Australia	(.42)	2.00	1.41
Expect. Sweden	(.59)	2.80	1.98
Expect. Quebec	(.99)	4.71	3.32
Observed		6	4
20-24 Years			
Total no. of births		24,422	14,381
Expect. Australia	(.61)	14.90	8.77
Expect. Sweden	(.74)	18.07	10.64
Expect. Quebec	(.70)	17.10	10.07
Observed		26	11
25-29 Years			
Total no. of births		21,349	17,966
Expect. Australia	(.82)	17.51	14.73
Expect. Sweden	(.88)	18.79	15.81
Expect. Quebec	(.78)	16.65	14.01
Observed		23	31
30-34 Years			
Total no. of births		13,271	7,829
Expect. Australia	(1.13)	15.00	8.85
Expect. Sweden	(1.46)	19.38	11.43
Expect. Quebec	(1.33)	17.65	10.41
Observed		24	16

TABLE 10
(continued)

Maternal Age	1965-66	1975-76
35-39 Years		
Total no. of births	7,077	2,324
Expect. Australia (3.45)	24,42	8.02
Expect. Sweden (3.75)	26.54	8.72
Expect. Quebec (4.42)	31.28	10.27
Observed	29	9
40-44 Years		
Total no. of births	1,980	448
Expect. Australia (9.80)	19.40	4.39
Expect. Sweden (14.96)	29.62	6.70
Expect. Quebec (13.13)	26.00	5.88
Observed	29	11
45+ Years		
Total no. of births	137	52
Expect. Australia (21.56)	2.95	1.12
Expect. Sweden (12.10)	1.66	0.63
Expect. Quebec (34.58)	4.74	1.80
Observed	2	1
Unknown Observed Livebirths	9	5
Total		
Total no. of livebirths	73,179	47,646
Expected Australia	96.18	47.29
Expected Sweden	116.86	55.91
Expected Quebec	118.11	55.76
Observed	148	88

TABLE 11

Determination of Quebec Age-Specific Rates for Those Cases Ascertained in Quebec in 1966

Maternal Age	Total No. of Quebec Livebirths (Statistics Canada)	Observed no. of Cases	Age-Specific Rates for Quebec (per 1000 livebirths)
15-19 years	7,101	7	.99
20-24 years	35,860	25	.70
25-29 years	30,775	24	.78
30-34 years	19,533	26	1.33
35-39 years	11,757	52	4.42
40-44 years	3,959	52	13.13
45+ years	347	12	34.58
Unknown		11	
TOTAL	109,332	209	

Results

The percentages of all livebirths and Down syndrome births within the five-year maternal age intervals were calculated for the two birth cohorts. Similarly the mean maternal age and proportion of births to mothers 35 years and over for each cohort were determined. (See Table 12.) In the earlier cohort, 12.6% of all livebirths were born to women 35 years and over; whereas 5.9% were born to this age group in the 1975-76 cohort. The mean maternal age dropped from 27.0 years for the 1965-66 cohort to 26.3 years for all women delivering in 1975-76. The mean maternal age of women giving birth to affected children declined from 32.6 years in 1965-66 to 30.4 years in 1975-76, as did the proportion of Down syndrome births to mothers 35 years and over, from 40.5% to 23.9%. Upon inclusion of the aborted fetuses the percentage of affected "births" in the 1975-76 cohort to women 35 years and over changed to 27.2%, the mean maternal age became 30.9 years.

Maternal age-specific rates for the five-year periods for both cohorts were calculated. Two rates for the 1975-76 cohort were reported: (1) those including abortions following amniocentesis, and (2) those excluding abortions following amniocentesis. (See Table 13.) A comparison of these age-specific rates reveals lower rates for the later cohort in the two youngest age groups, 15-19 and 20-24. The remaining rates, with the exception of the 35-39 age group, are higher in 1975-76 than in the 1965-66; upon inclusion of the aborted fetuses,

TABLE 12

Percent Maternal Age Distribution and Mean Maternal Age of All Livebirths and of Those Ascertained with Down Syndrome in Montreal in 1965-66 and 1975-76. Figures in ( ) include Aborted Fetuses Following Prenatal Diagnosis

	All Livebirths (%)		Livebirths with Down Syndrome (%)	
Age Group	1965-66	1975-76	1965-66	1975-76
Under 20	6.50	7.03	4.05	4.54 (4.35)[1]
20-24	33.37	30.18	17.57	12.50 (11.96)[1]
25-29	29.17	37.71	15.54	35.23 (33.70)[1]
30-34	18.13	16.43	16.22	18.18 (17.39)[1]
35-39	9.67	4.88	19.59	10.23 (11.96)[2]
40-44	2.70	.94	19.59	12.50 (13.04)[2]
45 and over	.19	.11	1.35	1.14 (2.17)[2]
Unknown	.26	2.72	6.08	5.68 (5.43)[1]
Total number of livebirths	73,179	47,647	148	88 (92)
% 35 years and over	12.56	5.93	40.54	23.86 (27.17)
Mean maternal age	27.00	26.27	32.60	30.42 (30.90)

[1]Aborted fetuses are included in the denominator only.

[2]Aborted fetuses are included in both the numerator and denominator.

TABLE 13

Maternal Age-Specific Rates for Five-Year Intervals of Ascertained Liveborn Infants with Down Syndrome per 1,000 Livebirths in Montreal for 1965-66 and 1975-76. Rates in ( ) Include Aborted Fetuses Following Amniocentesis

	1965-66	1975-76
Under 20	1.26	1.19
20-24	1.06	0.76
25-29	1.08	1.72
30-34	1.81	2.04
35-39	4.10	3.87 (4.73)
40-44	14.65	24.55 (26.73)
45 and over	14.60	19.23 (37.74)
All ages (crude)	2.02	1.85 (1.93)
Under 35 (crude)	1.24	1.42
35 years and over (crude)	6.53	7.44 (8.84)

the 1975-76 cohort exhibits higher rates in all five older age intervals. A plot of the rates is found in Figure 3.

Single year age-specific rates were also calculated and support the trend noted above; with the exception of women 22 years and younger, the age-specific rates are generally higher in 1975-76 than in 1965-66 with increased rates becoming most apparent from age 27 upward. (See Table 14 and Figure 4.) It is of special interest to note the major rise in the 1975-76 figures from 2.64 at age 32 to 4.47 at age 34. The rates for both ages, 34 and 35, are higher in the later cohort, increasing from 2.27 to 4.47 and 2.60 to 5.19 respectively. The increased rate in women aged 34 years is noteworthy due to the present policy to exclude these women from prenatal diagnosis. Indeed, the age 34 rate in 1975-76 is higher than the 35 year rate in 1965-66.

As rates have been based on data for the entire population of the Island of Montreal, the issue of sampling variation is not germane to the comparison of the two cohorts; the age-specific rates completely describe the underlying population experience. However, the data may be viewed as a sample from a larger population. A distribution-free method, the Wilcoxon signed rank test, was used to examine the statistical significance exhibited by the differences in the two cohorts experience. The difference scores and the ranks for the data which excludes the aborted fetuses following amniocentesis are presented in Table 15. Table 16 displays the

FIGURE 3. Plot of Maternal Age-Specific Rates for Five-Year Intervals of Liveborn Infants with Down syndrome for 1965-66 and 1975-76 in Montreal.

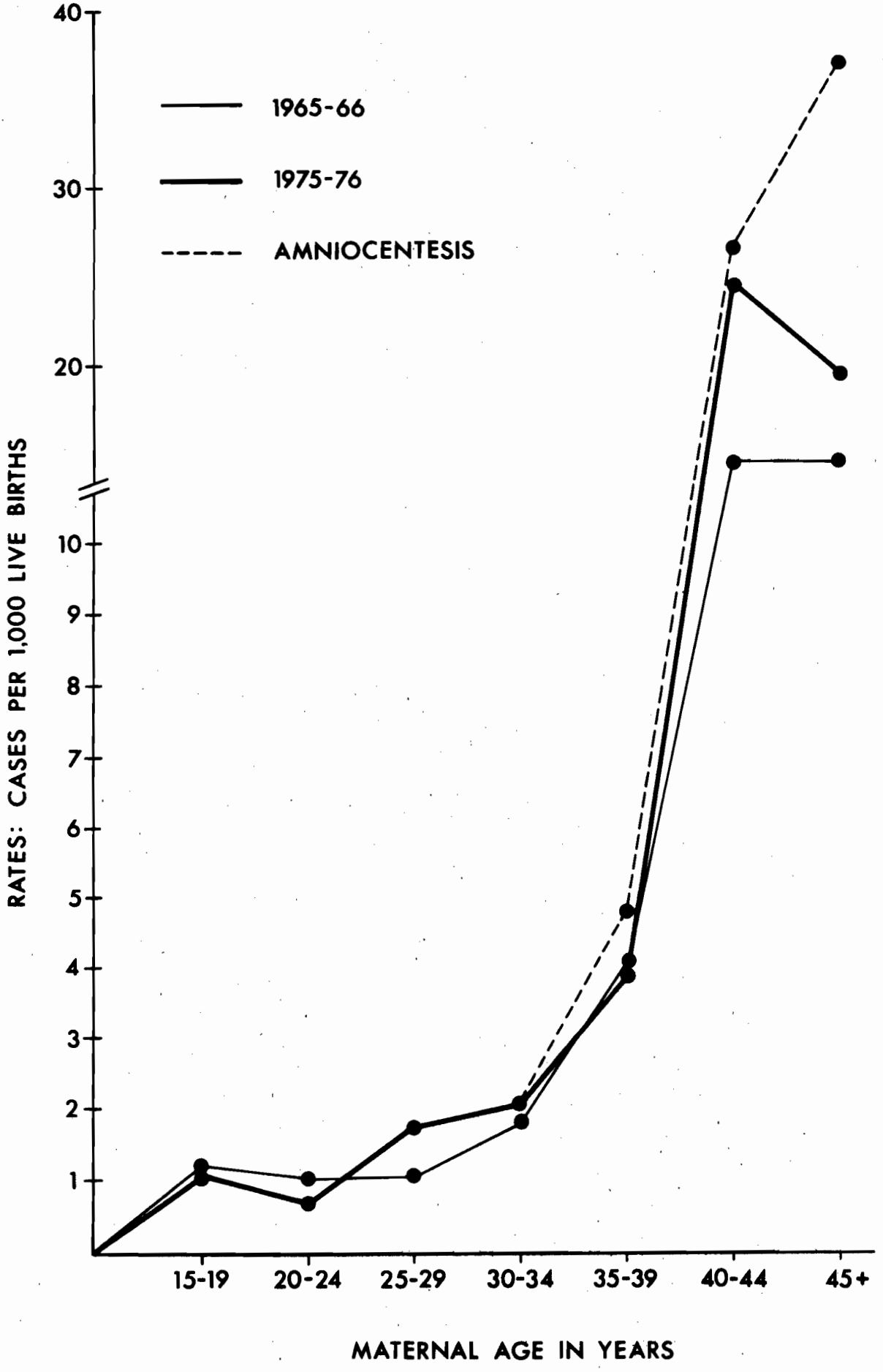
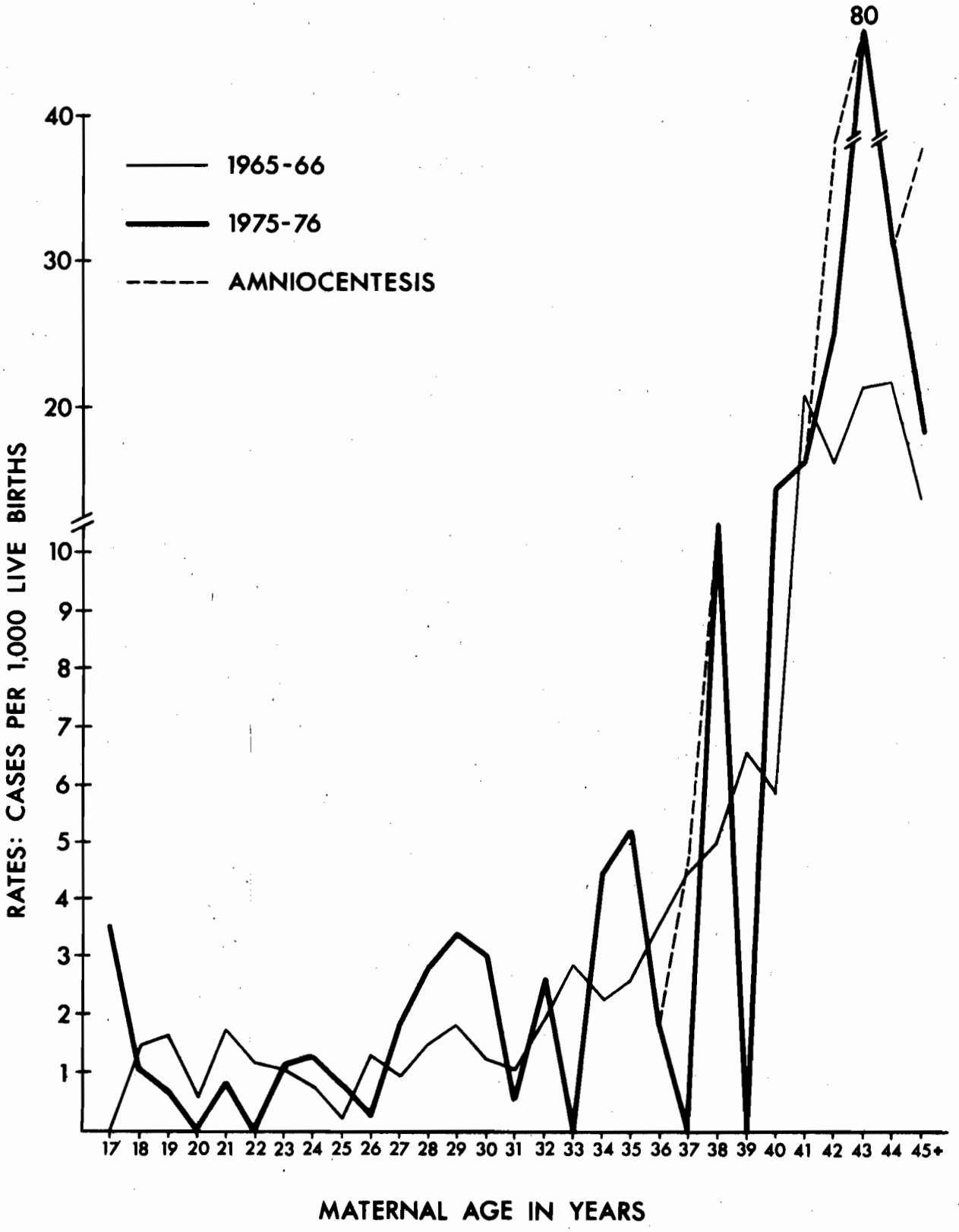

40
30
20
10
9
8
7
6
5
4
3
2
1
1965-66
1975-76
AMNIOCENTESIS
RATES: CASES PER 1,000 LIVE BIRTHS
15-19
20-24
25-29
30-34
35-39
40-44
45+
MATERNAL AGE IN YEARS

TABLE 14

Maternal Age-Specific Rates for Single Years of Ascertained Liveborn Infants with Down Syndrome per 1,000 Livebirths in Montreal for 1965-66 and 1975-76. Rates in ( ) Include Aborted Fetuses Following Amniocentesis

Maternal Age	1965-66	1975-76
17	0.00	3.51
18	1.42	1.06
19	1.64	0.68
20	0.58	0.00
21	1.71	0.85
22	1.13	0.00
23	1.08	1.17
24	0.73	1.27
25	0.19	0.81
26	1.31	0.25
27	0.94	1.81
28	1.51	2.85
29	1.78	3.38
30	1.24	2.99
31	1.10	0.53
32	1.89	2.64
33	2.84	0.00
34	2.27	4.47
35	2.60	5.19
36	3.57	1.80
37	4.44	0.00 (4.71)
38	4.96	12.54
39	6.54	0.00
40	5.78	12.99
41	20.91	15.38
42	15.08	25.00 (37.04)
43	21.93	80.00
44	22.06	31.25
45+	14.60	19.23 (37.44)

FIGURE 4. Plot of Maternal Age-Specific Rates for Single-Year Intervals of Liveborn Infants with Down Syndrome for 1965-66 and 1975-76 in Montreal.


80
40
30
20
10
9
8
7
6
5
4
3
2
1
1965-66
1975-76
AMNIOCENTESIS
RATES: CASES PER 1,000 LIVE BIRTHS
17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45+
MATERNAL AGE IN YEARS

data for the rates which include the aborted fetuses. Although neither test rejected the null hypothesis of equality of rates at the 0.05 level, the test including the aborted fetuses approached significance ($p = .08$).

While the most appropriate comparisons of incidence figures are made by comparing age-specific rates, it is often useful to have one single summary statistic. Therefore, the crude incidence rates for all women were calculated and are found in Table 13. These rates may be misleading since they are sensitive to the age distribution of the population and hence, may only reflect the age differential in the two cohorts. However, in this particular circumstance, the effect of the change in the maternal age structure is in itself a legitimate question; that is, has the crude incidence rate in 1975-76 decreased from that which was found ten years earlier as a result of a change in the maternal age distribution in the two cohorts? Upon examination, the crude overall incidence rate has declined from 2.02/1,000 livebirths in Montreal in 1965-66 to 1.85/1,000 livebirths in 1975-76, or when including the aborted fetuses, to 1.93/1,000 "births".*

If, however, one wished to examine whether the crude incidence rate has changed as a result of a change in the age-specific rates, prenatal diagnosis, or any other factors in addition to the change in the maternal age structure, one must

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*The aborted fetuses are considered to be livebirths for this calculation in both the numerator and denominator.

TABLE 15

Calculations for the Wilcoxon's Signed Rank Test for Single Maternal Age-Specific Rates for Down Syndrome (Excluding Amniocentesis) for the 1965-66 and 1975-76 Cohorts

Maternal Age	Rate 1965-66	Rate 1975-76	Difference (1975-76-1965-66)	Rank
17	0.00	3.51	+ 3.51	20
18	1.42	1.06	- 0.36	2
19	1.64	0.68	- 0.96	10
20	0.58	0.00	- 0.58	5
21	1.71	0.85	- 0.86	8
22	1.13	0.00	- 1.13	12
23	1.08	1.17	+ 0.09	1
24	0.73	1.27	+ 0.54	3
25	0.19	0.81	+ 0.62	6
26	1.31	0.25	- 1.06	11
27	0.94	1.81	+ 0.87	9
28	1.51	2.85	+ 1.34	13
29	1.78	3.38	+ 1.60	14
30	1.24	2.99	+ 1.75	15
31	1.10	0.53	- 0.57	4
32	1.89	2.64	+ 0.75	7
33	2.84	0.00	- 2.84	19
34	2.27	4.47	+ 2.20	17
35	2.60	5.19	+ 2.59	18
36	3.57	1.80	- 1.77	16
37	4.44	0.00	- 4.44	21
38	4.96	12.54	+ 7.58	26
39	6.54	0.00	- 6.54	24
40	5.78	12.99	+ 7.21	25
41	20.91	15.38	- 5.53	23
42	15.08	25.00	+ 9.92	28
43	21.93	80.00	+58.07	29
44	22.06	31.25	+ 9.19	27
45	14.60	19.23	+ 4.63	22

Sum of negative ranks = 155
Sum of positive ranks = 280
Number of pairs = 29
p = .14

TABLE 16

Calculations for the Wilcoxon's Signed Rank Test For Single Maternal Age-Specific Rates for Down Syndrome, Including Fetuses Aborted Following Amniocentesis, For the 1965-66 and 1975-76 Cohorts

Maternal Age	Rate 1965-66	Rate 1975-76	Difference (1975-76-1965-66)	Rank
17	0.00	3.51	+ 3.51	21
18	1.42	1.06	- 0.36	3
19	1.64	0.68	- 0.96	11
20	0.58	0.00	- 0.58	6
21	1.71	0.85	- 0.86	9
22	1.13	0.00	- 1.13	13
23	1.08	1.17	+ 0.09	1
24	0.73	1.27	+ 0.54	4
25	0.19	0.81	+ 0.62	7
26	1.31	0.25	- 1.06	12
27	0.94	1.81	+ 0.87	10
28	1.51	2.85	+ 1.34	14
29	1.78	3.38	+ 1.60	15
30	1.24	2.99	+ 1.75	16
31	1.10	0.53	- 0.57	5
32	1.89	2.64	+ 0.75	8
33	2.84	0.00	- 2.84	20
34	2.27	4.47	+ 2.20	18
35	2.60	5.19	+ 2.59	19
36	3.57	1.80	- 1.77	17
37	4.44	4.71	+ 0.27	2
38	4.96	12.54	+ 7.58	25
39	6.54	0.00	- 6.54	23
40	5.78	12.99	+ 7.21	24
41	20.91	15.38	- 5.53	22
42	15.08	37.04	+21.96	27
43	21.93	80.00	+58.07	29
44	22.06	31.25	+ 9.19	26
45	14.60	37.74	+23.14	28

Sum of the negative ranks = 141
Sum of the positive ranks = 294
p = 0.08

standardize the rates in order to remove the effect of the age differential in the two cohorts. The two most commonly employed methods were used, direct and indirect, and the results of both methods are reported for all women, women under 35 years, and women 35 years and over in Tables 17-22. Table 23 presents a summary of all the age-adjusted rates.

With the direct method the calculated age-specific rates for the two time periods are applied to a standard population. With the indirect method a set of standard rates are chosen and applied to the population in question. For the direct method the total number of livebirths in Quebec for 1966 was used as the standardizing population. The age-specific rates for Quebec in 1966 (see Table 11) were used with the indirect method.

By standardizing and thereby removing the age differential in the two populations, the adjusted rates support the trend noted earlier when comparing the age-specific rates. In the younger age group, women under 35 years, the adjusted rates for 1975-76 are slightly higher than those calculated for 1965-66. This reflects the decrease in age-specific rates from 1965-66 to 1975-76 for the younger members (19-24) and the increase for the older women (25-34). The age-adjusted rates for women, excluding abortions, 35 years and over, are substantially higher in the more recent cohort. With the inclusion of the aborted fetuses, the rates in 1975-76 are nearly twice as high as those compared for 1965-66. When

combined, the total age-adjusted rates for 1975-76 are greater than those calculated for 1965-66.

It should be remembered that these standardized rates are only weighted averages computed for the purpose of comparison. Yet, the best comparisons are those made between the age-specific rates, and no single figure can adequately replace those contrasts (Hill, 1971).

In summary, although fewer livebirths were born to Montreal women 35 years and over in 1975-76, and a decreased proportion of Down syndrome births were born to these same women, there is strong evidence suggesting that the age-specific rates for women 35 and over were greater in 1975-76 than in 1965-66. Moreover, women aged 25-34 years contributed a greater proportion of the affected births in 1975-76 and exhibited higher age-specific rates than ten years earlier. Only the young child-bearing woman was found to be unaffected, with both the proportion of births and the age-specific rates remaining relatively unchanged.

TABLE 17

Calculation of Age-Adjusted Rates by the Direct Method: Number of Down Syndrome Births Per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Adjusted to Total Number of Livebirths in Quebec, 1966. Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

Maternal Age	Number of Livebirths Quebec, 1966	Age-Specific Rates 1965-66	Age-Specific Rates 1975-76	Expected Births 1965-66	Expected Births 1975-76
15-19	7,101	1.26	1.19	8.95	8.45
20-24	35,860	1.06	0.76	38.01	27.25
25-29	30,775	1.08	1.72	33.24	52.93
30-34	19,533	1.81	2.04	35.35	39.85
35-39	11,757	4.10	3.87 (4.73)	48.20	45.50 (55.62)
40-44	3,959	14.65	24.55 (26.73)	58.00	97.19 (105.82)
45+	347	14.60	19.23 (37.74)	5.07	6.67 (13.13)
Total	109,332			226.82	277.84 (303.05)

Age adjusted rates: 1965-66 226.82/109,332 = 2.07
1975-76 277.84/109,332 = 2.54
1975-76 303.05/109,336 =(2.77)

(including abortions)

TABLE 18

Calculation of Age-Adjusted Rated by the Indirect Method: Number of Down Syndrome Births Per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Age-Specific Rates for Quebec, 1966, Chosen as Standard. Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

Maternal Age	Quebec Rates 1966	Number of Livebirths, Montreal 1965-66	1975-76	Expected Births 1965-66	1975-76
15-19	0.99	4,754	3,351	4.71	3.32
20-24	0.70	24,422	14,381	17.10	10.07
25-29	0.78	21,349	17,966	16.65	14.01
30-34	1.33	13,271	7,829	17.65	10.41
35-39	4.42	7,077	2,324 (2,326)	31.28	10.27 (10.28)
40-44	13.13	1,980	448 (449)	26.00	5.88 (5.89)
45	34.58	137	52 (53)	4.74	1.80 (1.83)
Total		72,990	46,351	117.86	55.76 (55.81)

Age-adjusted rates:

$$1965\text{-}66 = \frac{\text{observed}}{\text{expected}} = \frac{148}{117.86} = 1.26 \times 2.02 = 2.54$$

$$1975\text{-}76 = \frac{\text{observed}}{\text{expected}} = \frac{88}{55.76} = 1.58 \times 1.85 = 2.92$$

$$1975\text{-}76 = \frac{\text{observed}}{\text{expected}} = \frac{(92)}{(55.81)} = (1.65) \times (1.93) = (3.18)$$

(including abortions)

TABLE 19

Calculations of Age-Adjusted Rates for Women 35 Years and Over by the Direct Method: Number of Down Syndrome Births Per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Adjusted to Livebirths in Quebec, 1966. Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

Maternal Age	Number of Livebirths, Quebec, 1966	Age-Specific Rates 1965-66	Age-Specific Rates 1975-76	Expected Births 1965-66	Expected Births 1975-76
35-39	11,757	4.10	3.87 (4.73)	48.20	45.50 (55.62)
40-44	3,959	14.65	24.55 (26.73)	58.00	97.19 (105.82)
45+	347	14.60	19.23 (37.74)	5.07	6.67 (13.13)
Total	16,063			111.27	149.36 (174.57)

Age-adjusted rates: 1965-66 111.27/16,063 = 6.93

1975-76 149.36/16,063 = 9.30

1975-76 (174.57)/16,063 = (10.87)

(Including Abortions)

TABLE 20

Calculation of Age-Adjusted Rates for Women 35 Years and Over by the Indirect Method: Number of Down Syndrome Births per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Age-Specific Rates for Quebec, 1966, Chosen as Standard. The Figures in ( ) Include Aborted Fetuses Following Prenatal Diagnosis

Maternal Age	Quebec Rates, 1966	Number of Livebirths, Montreal 1965-66	1975-76	Expected Births 1965-66	1975-76
35-39	4.42	7,077	2,324 (2,326)	31.28	10.27 (10.28)
40-44	13.13	1,980	448 (449)	26.00	5.88 (5.89)
45+	34.58	137	52 (53)	4.74	1.80 (1.83)
Total		9,194	2,824 (2,828)	62.02	17.95 (18.00)

Age-adjusted rates:

1965-66 $\frac{\text{Observed}}{\text{Expected}} = \frac{60}{62.02} = 0.97 \times 6.53 = 6.33$

1975-76 $\frac{\text{Observed}}{\text{Expected}} = \frac{21}{17.95} = 1.17 \times 7.44 = 8.70$

1975-76 $\frac{\text{Observed}}{\text{Expected}} = \frac{(25)}{(18.00)} = (1.39) \times (8.84) = (12.29)$

(Including abortions)

TABLE 21

Calculations of Age-Adjusted Rates for Women Under 35 Years by the Direct Method: Number of Down Syndrome Births Per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Adjusted to Livebirths in Quebec, 1966

Maternal Age	Number of Livebirths Quebec, 1966	Age-Specific Rates 1965-66	Age-Specific Rates 1975-76	Expected Births 1965-66	Expected Births 1975-76
15-19	7,101	1.26	1.19	8.95	8.45
20-24	35,860	1.06	0.76	38.01	27.25
25-29	30,775	1.08	1.72	33.24	52.93
30-34	19,533	1.81	2.04	35.35	39.85
Total	93,269			115.55	128.48

Age-adjusted rates: 1965-66 115.55/93,269 = 1.24

1975-76 128.48/93,269 = 1.38

TABLE 22

Calculation of Age-Adjusted Rates for Women Under 35 Years by the Indirect Method: Number of Down Syndrome Births Per 1,000 Livebirths, Montreal, 1965-66 and 1975-76. Age-Specific Rates for Quebec, 1966, Chosen as Standard

Maternal Age	Quebec Rates 1966	Number of Livebirths, Montreal 1965-66	Number of Livebirths, Montreal 1975-76	Expected Births 1965-66	Expected Births 1975-76
15-19	0.99	4,754	3,351	4.71	3.32
20-24	0.70	24,422	14,381	17.10	10.07
25-29	0.78	21,349	17,966	16.65	14.01
30-34	1.33	13,271	7,829	17.65	10.41
Total		63,796	43,527	56.11	37.81

Age-adjusted rates: 1965-66 $\frac{\text{Observed}}{\text{Expected}} = \frac{79}{56.11} = 1.41 \times 1.24 = 1.75$

1975-76 $\frac{\text{Observed}}{\text{Expected}} = \frac{62}{37.81} = 1.64 \times 1.42 = 2.33$

TABLE 23

Age-Adjusted Incidence Rates of Down Syndrome Per 1,000 Livebirths Derived From the Direct and Indirect Standardization Methods. Rates in Parentheses Include Aborted Fetuses Following Prenatal Diagnosis

		Direct Method	Indirect Method
Total	1965-66	2.07	2.54
	1975-76	2.54 (2.77)	2.92 (3.18)
Under 35 Years	1965-66	1.24	1.75
	1975-76	1.38	2.33
35 Years and Over	1965-66	6.93	6.33
	1975-76	9.30 (10.87)	8.70 (12.29)

Discussion

The results of this section of the study will be discussed according to the contribution of three factors, maternal age, age-specific rates, and amniocentesis for prenatal diagnosis, to the primary prevention of Down syndrome in Montreal.

Effect of Maternal Age Distribution. A decline in both the total number of livebirths and mean maternal age was observed in this study between the two birth cohorts. There were approximately 25,000 fewer births in Montreal in 1975-76 than in 1965-66, and the proportion of births to women aged 35 years and over was halved. Similarly, a total of 88 infants with Down syndrome were born alive in Montreal in 1975-76 compared with 148 in 1965-66. The mean maternal age of the women giving birth to affected children also declined as did the proportion of the Down syndrome births to women aged 35 years and over.

Similar reductions have been noted by others, with equivalent Canadian findings reported in British Columbia (Lowry et al., 1976) and Manitoba (Evans et al., 1978). Experience in Japan (Shiono et al., 1975) and Sweden (Lindsjo, 1974) has resembled that in Canada. As in British Columbia, this study demonstrated a drop in the proportion of affected births to women aged 35-39 years as well as those 40 years and older, whereas Manitoba and Japan observed a decrease only in women 40 years and over.

Pertinent to these findings is the observed increase in the proportions of both livebirths and affected births to women under 35 years with these women contributing more than 75% of the Down syndrome births in 1975-76. Yet, unlike the British Columbia experience (Lowry et al., 1976), this increase in affected births was not uniform across the younger age groups. Instead the percentage of Montreal women under 24 years delivering babies with Down syndrome actually declined. Women aged 25-34 years solely accounted for the increase in the proportion of affected births to women under 35 years.

These data suggest that a Down syndrome infant is now most likely to be born to women aged 35 years and under. This results in part from the fact that fewer women are bearing children after the age of 35 due to reduced family sizes, reliable contraceptive measures, and the recent legalization of abortion (Stein and Susser, 1977). These demographic trends have ramifications for a primary prevention program based on advanced maternal age. A smaller proportion of the cases will be detected through prenatal diagnosis than 10 years earlier by screening only women aged 35 years and over. And, if this shift to the younger childbearing woman continues, the goal of primary prevention of Down syndrome through prenatal diagnosis will be threatened.

At present approximately one-quarter of the Down syndrome births in Montreal would be detected if prenatal diagnosis

were offered to and accepted by all women 35 years and over. This is a substantial decrease from the 40% which would have been identified under the same circumstances in 1965-66. This reduction in the potential effectiveness of this preventive procedure evokes concern for whether the criteria for prenatal diagnosis should be changed and, if so whether the procedure should be offered to women younger than 35 years who do not fulfill other screening specifications. The justification of limiting screening to a selected group of women considering that the procedure has been deemed safe and reliable has been questioned (Philip et al., 1977).

Using the 1965-66 and 1975-76 data for Montreal women and assuming 100% acceptance rates of amniocentesis and abortion, the number of screenings as well as the number and percentage of cases prevented for each maternal group were calculated and are presented in Table 24. There is no doubt that the most efficient results are obtained by screening older women only. On the other hand, in order to prevent the same proportion of affected births in 1975-76 that was preventable in 1965-66 by screening women aged 35 years and over, prenatal diagnosis would now have to be made available to all women 30 years and over. As interesting, however, is the fact that if all women aged 30 years and over had been screened in 1975-76 the actual number of screenings would not have differed substantially from the number which would have been completed in 1965-66 by screening only women aged 35 years and over.

TABLE 24

Effectiveness of Prenatal Diagnosis Screening Program According to Maternal Age for the Years 1965-66 and 1975-76 in Montreal (Adapted from Stein et al., 1976)

Maternal Age (years)	Total Number Screened**		Number of Cases Aborted**		% Down Syndrome Births Prevented	
	1965-66	1975-76	1965-66	1975-76	1965-66	1975-76
40+	2,117	500	31	14	21.0	15.2
35-39	7,077 (9,194)	2,324 (2,824)	29 (60)	11 (25)	19.6 (40.6)	12.0 (27.2)
30-34	13,271 (22,465)	7,829 (10,653)	24 (84)	16 (41)	16.2 (56.8)	17.4 (44.6)
25-29	21,349 (43,814)	17,966 (28,619)	23 (107)	31 (72)	15.5 (72.3)	33.7 (78.3)
24 and under	29,176 (72,990)	17,732 (46,351)	32 (139)	15 (87)	21.6 (93.9)	16.3 (94.6)
Unknown	189	1,295	9 (148)	5 (92)	6.1 (100)	5.4 (100)
Total	73,189	47,646	148	92		

** Assuming 100% acceptance rates for amniocentesis and abortion.

Figures in ( ) are cumulative of all prior age groups.

These observations lend support to the suggestion that amniocentesis for prenatal diagnosis be made available, in phases, to younger groups of women (Stein et al., 1973). In reality, however, the two prenatal diagnostic units in Montreal would at present be unable to perform screenings if requested on all pregnant women aged 35 years and over due to limited personnel and laboratory resources (Mackenzie, 1978). Hence, the feasibility of extending prenatal diagnosis to additional women without supplementing the present facilities is doubtful. Invariably the justification for any screening program is presented in economic terms. Prenatal diagnosis has been estimated to be cost-beneficial in Scotland if all pregnant women 35 years and over are screened (Hagard and Carter, 1976) and in New York City if mothers over 30 years of age are monitored (Stein et al., 1973). To date, no cost-benefit analyses have been reported for Canada.

Yet, ideally the criteria determining eligibility for screening should not be based on numbers and resources, but rather on risk and a community's commitment to prevention. For example, if a woman aged 34 has as high or higher risk of having an affected Down syndrome child than a woman aged 35, the extension of services to include these women seems reasonable. Or, similarly, if a community desires to prevent a larger proportion of affected births than possible by only screening women 35 years and over, the accommodation of additional women is justified. Either of these two situations,

a documented increased risk to a specific group of women or a commitment to prevent more affected births, is reason to alter age specifications for prenatal diagnosis.

Effect of Age-Specific Rates. It has been convenient to categorize women into three age groups for the interpretation of the age-specific rates: young women, less than 24 years; middle aged women, 25-34 years; and older women, 35 years and over. The comparison of the maternal age-specific rates between the two cohorts for these three age groups reveals a striking trend.

For women aged 24 years or less the age-specific rates tend to be lower in 1975-76 than 1965-66. Indeed, it is only at the older boundary of this group that the 1975-76 rates overtake those of 1965-66 and continue to be generally higher for women aged 25 years and over.

The high risk women, 35 years and over, on the other hand, exhibit higher age-specific rates in 1975-76 than previously. Specifically, the rate for women aged 40-44 years is substantially higher with the rate for women aged 45 years and over being moderately higher. Unlike Evans et al. (1978) who observed the largest increase in Manitoba within the 35-39 age group, this study found the rate for these women to be higher in 1975-76 only when the aborted fetuses were included. This finding, however, may be partially explained by examining the single year rates for these ages (Table 16). The fact that no cases are reported for age 39 and that the two cases for

age 37 were diagnosed and aborted prenatally influence the overall rate for this particular group.

More disconcerting are the rates recorded for the middle aged women. For both age groups, 25-29 years and 30-34 years, the 1975-76 rates are higher than those for 1965-66. A similar rise over the past 20 years has also been found in British Columbia (Lowry et al., 1976). These findings are particularly relevant to the determination of future age boundaries for prenatal diagnosis. Particularly, the possible increase in risk to the 34 year-old woman must be carefully evaluated. In the past, this particular age-specific rate has been camouflaged in the five-year age group to which it contributes. Because at present these women are excluded from screening, and because the 1975-76 rates for 34 and 35 year-old woman are very similar, the arbitrary cut-off of 35 years for prenatal diagnosis in Montreal must be questioned.

An evaluation of the crude incidence rates for the two periods provides additional evidence of a change in the age-specific rates. It has been postulated that a decline in mean maternal age will result in a corresponding decrease in the total incidence of Down syndrome (Penrose, 1967; Collmann and Stoller, 1969). The crude incidence rate for all Montreal women did, in fact, drop from 2.02 to 1.85/1,000 livebirths. However, if the age-specific rates for the five-year intervals for 1965-66 had been constant and had been applied to the maternal age structure of the 1975-76 population, the crude

incidence rate would have declined even further to 1.51/1,000 livebirths.

Moreover, the crude rates for both women under 35 years and women 35 years and over were slightly higher in 1975-76 than in 1965-66. The increase in the age-adjusted rates in the more recent years is further reason that the expected decline based on the drop in mean maternal age has not transpired. Thus, the crude rate of 1.85/1,000 livebirths in 1975-76 is higher than expected and signals the necessity to consider the possibility of a real change in age-specific rates.

Several possible biases that may have influenced these results must be considered. Better ascertainment of cases in 1975-76 could inflate the differences in the rates between the two cohorts. The likelihood of this is difficult to assess accurately since the ascertainments of cases were done ten years apart and by two separate investigators. Although such a possibility exists, it fails to explain the increase in rates for older women occurring simultaneously with a decrease in rates for younger women.

In addition, the determination of the denominators utilized for calculating age-specific rates may have been biased in some fashion resulting in higher rates for 1975-76 than 1965-66. This possibility, it seems, is less likely to be a cause for concern than the first. For both cohorts the figures were obtained from the identical source at the same point in time, and although the figures may be incorrect, it is

improbable that the 1975-76 numbers were biased in any one direction more than those for 1965-66.

However, the larger proportion of livebirths with the maternal age unknown in the 1975-76 cohort is disturbing. If for some reason the majority of these births were to older women, this would have affected the calculation of the denominators and subsequent rates for these women, yielding higher rates for the older women in 1975-76 than actually existed. The possibility of the "unknown" women being disporportionately distributed according to maternal age was explored with Statistics Canada. It was their impression that, if anything, this unknown category would be weighted in the direction of the younger woman. That is, the very young woman or adolescent mother with an illegitimate birth is more likely to fail to report her age than the older woman (Nagnur, 1978). Nevertheless, due to the relatively large number of "unknowns" reported in 1975-76, the chance of inflated rates for this period must be acknowledged.

The cause of these increases is not known, but the possibility of either better ascertainment or biased denominators for the 1975-76 cohort must be entertained. Two additional explanations for the possible rise in recently reported rates have been advanced (Stein and Susser, 1977). Firstly, with the advent of neonatalogy as a medical subspecialty and its associated specialized care for the "high risk" newborn, the chance for survival of a Down syndrome infant in the neonatal

period may be greater now than in the past. Diagnosis of infants dying in the perinatal period may not be carefully recorded, thereby affecting the enumeration of cases. If, in fact, more unidentified Down syndrome infants died shortly after birth in 1965-66 than in 1975-76 the calculated incidence rates for the later period would be higher. However, this interpretation fails to explain the observed rate increases in older women versus the decrease for younger women between the two time periods.

Secondly, the possibility of a real rise in the age-specific rates for older women as a result of some prolonged environmental exposure must be explored. Several studies (Uchida et al., 1968, Sigler et al., 1965; Alberman et al., 1972) have demonstrated an increased risk of Down syndrome birth to be associated with increased irradiation exposure of the mother. Presumably, due to their advanced age older women have had more opportunity for such exposure by increased utilization of either therapeutic or diagnostic irradiation.

An additional explanation may be appropriate for this particular Quebec population. Medicare as a form of provincial health insurance was not operating in Quebec in 1965-66. Consequently, it might be argued that more pregnant women were receiving prenatal care in 1975-76 than ten years earlier, resulting in fewer miscarriages of Down syndrome fetuses. This change in health care patterns could preferentially affect older women, more at risk for spontaneous abortions than

younger women, thus explaining the recent increase in the older age groups.

The results of this study indicate that the age-specific rates were different in 1975-76 than in 1965-66, with women under 25 years having lower rates and those aged 25 years and over exhibiting higher rates. These differences are apparent by comparing either rates for the five-year intervals or the single year rates. The increase in rates is not limited to women 35 years and over but is also evident in the middle-aged women, aged 25-34 years; hence, the importance of evaluating the age criterion for prenatal diagnosis was discussed. Although it is not within the scope of this thesis to explain the cause of the noted changes, several possible explanations were presented.

Effect of Prenatal Diagnosis. A total of four pregnancies with expected birth dates in 1975-76 were prenatally diagnosed and terminated in Montreal. By assuming that these four pregnancies would have resulted in Down syndrome livebirths, less than 5% of the potential affected deliveries were prevented as a result of prenatal diagnosis.

This assumption, however, is questionable since it has recently been shown that the rates of Down syndrome in prenatally diagnosed pregnancies are on the average 33% above those calculated from livebirths (Hook and Chambers, 1977; Ferguson-Smith, 1976). This phenomenon is seen at all ages over 35 years and is not unique to any subset of older women (Fergu-

son-Smith, 1978). Explanations for this discrepancy between prenatal and postnatal rates include the occurrence of fetal loss after 16 weeks gestation, possible selective factors other than maternal age which make those receiving prenatal diagnosis different from those not receiving it (Polani et al., 1976), and selective reporting by the prenatal diagnostic centres observing increased rates (Hook, 1978). The most recently advanced interpretation deals with the real possibility of an increase in age-specific rates for older women (Ferguson-Smith, 1978). And, since most livebirth data has been collected for births prior to that obtained for prenatal diagnosis rates, the two rates are not easily compared or combined. As Ferguson-Smith (1978) suggests, the prenatal rates for Down syndrome may actually reflect accurately the present postnatal rates. Nevertheless, the assumption that a fetus diagnosed and aborted prenatally would have been carried to term is debatable.

If, however, we suppose that approximately three of the four aborted fetuses in this study had been born alive, the total number of Down syndrome births for 1975-76 would have been 91 instead of 88, thereby preventing approximately 3.3% of the potential cases. Likewise, the crude incidence rate in 1975-76 would have been 1.91/1,000 livebirths instead of 1.85/1,000 livebirths, or for women over 35, 8.50/1,000 livebirths rather than 7.44/1,000 livebirths.

A comparison of the age-specific rates is more definitive.

Because evidence suggesting the risk of prenatal wastage after 16 weeks gestation is slightly higher in the 35-39 year age group (Ferguson-Smith, 1978), it will be assumed that the one fetus in this study that would have been spontaneously aborted during the course of the pregnancy was from this age group. The age-specific rates per 1,000 livebirths including and excluding fetuses aborted prenatally, based on this assumption, for 1965-66 and 1975-76 are as follows:

	1965-66	1975-76 (Excluding Fetuses)	1975-76 (Including 3 Fetuses)
35-39 years	4.10	3.87	4.30
40-44 years	14.64	24.55	26.73
45+ years	14.60	19.23	39.22

Except for the 35-39 year age group the age-specific rates excluding aborted fetuses are still higher in 1975-76 than in 1965-66. That is to say, given amniocentesis for prenatal diagnosis, other than in the 35-39 year age group, the age-specific rates for the later cohort have not been diminished. The effect, of prenatal screening has been confined to the 35-39 age group and has not as yet been reflected in lower age-specific rates for women 40 years and older.

There are several possible explanations for this situation. As previously suggested a real increase in age-specific

rates in women 35 years and over would camouflage any effect. The potential biases discussed in the earlier section could inflate the 1975-76 rates or deflate the 1965-66 rates, and in turn disguise any decrease in rates as a result of preventive measures. Finally, the possibility of artificially inflated rates as a product of the small numbers in both the numerators and the denominators in the 1975-76 cohort must be considered. Any one or combination of these explanations may have masked an effect, however slight, of prenatal diagnosis and selective pregnancy termination.

Relevant to this discussion are the 21 women in the 1975-76 cohort who were 35 years or over at the time of the birth of their Down syndrome child and were eligible for prenatal diagnosis because of their advanced age. It is impossible to say, due to the limited scope of this present study, if: (1) these women were offered prenatal diagnosis but refused it for personal or other reasons, (2) these women had prenatal diagnosis but refused to terminate the pregnancy or (3) these women were not offered prenatal diagnosis early enough within their pregnancies. Whatever the reason, these 21 births must be considered "potentially preventable." Had these pregnancies been diagnosed and terminated prenatally the incidence of Down syndrome for 1975-76 in Montreal would have been reduced to 1.28/1,000 livebirths. Although to date no eligible woman has been refused screening because of limited resources, the prenatal detection of these 21 cases would have required

2,824 screenings, exceeding the present capacity of the laboratory facilities available in Montreal (Mackenzie, 1978).

More feasible, in terms of laboratory space, is the situation presented by the screening of all pregnant women 40 years and over. This limited amount of primary prevention would have prevented 14 of the 21 cases or 15% of all Down syndrome births in 1975-76. The impact of these 500 screenings is augmented by the sizeable increase in age-specific rates to these women. The importance of offering screening to this subset of women can not be overemphasized.

The fact that prenatal diagnosis has had no measurable effect in reducing the incidence of Down syndrome in women aged 40 years and over is disturbing and demands additional attention. Although these women are the most likely candidates, in terms of maternal age, for prenatal diagnosis, they may find selective termination an unacceptable form of prevention. Unlike their earlier peers, these contemporary women may be attempting to have their first or second child after many previous unsuccessful pregnancies. Or, perhaps because the typical Down syndrome birth is no longer seen predominantly in older women, physicians are less aware of the increased risks for these women. In effect, they may consider the birth of a Down syndrome child to be a chance happening, with no group of women more likely to experience it than another. On the contrary, because these women have the highest risk of giving birth to an affected child and because the

goal of screening this group is technically feasible, an additional effort should be made, in Montreal, to inform, counsel, and offer prenatal diagnosis to these women.

There is little evidence to support the notion that amniocentesis for prenatal diagnosis was an effective measure in preventing Down syndrome in Montreal in 1975-76. Whereas 27.2% of the affected births could have been prevented by screening all pregnant women 35 years and over, only 3.3% of the potential cases were in fact prenatally detected and selectively terminated. Explanations for this finding include a possible increase in age-specific rates, potential methodological biases, and lack of utilization of prenatal diagnosis by women considered at risk.

In summary, the effects of maternal age distribution, the change in age-specific rates, and amniocentesis for prenatal diagnosis have been examined in terms of their contribution to the primary prevention of Down syndrome in Montreal. Although there has been a shift in childbearing to younger women and the mean maternal age has declined, there is evidence that due to increases in age-specific rates for women aged 25 years and over, the predicted fall in incidence has not occurred. The impact of amniocentesis for prenatal diagnosis on the problem of Down syndrome has also been minimal. It would appear, therefore, that the goal of primary prevention of Down syndrome was not attained in Montreal in 1975-76.

CHAPTER 4

ASSESSMENT OF REMEDIATIVE PROCEDURES

Objectives and Hypotheses

In addition to assessing the primary preventive measures, this study examined the effect of an early intervention program in Montreal on the development of Down syndrome infants. The objective of the examination was to determine if early intervention was efficacious in remediating the mental retardation in the infancy period of Down syndrome.

A trial was conducted to compare the development of an experimental group of infants receiving early intervention with the development of a control group not receiving treatment. The distribution of a variety of potential confounding variables within the two trial groups was examined to assess the initial comparability of the groups. The representativeness of the sample of Down syndrome children participating in the Early Intervention Program was also addressed. Two groups of children, those participating and not participating in the program, were compared on several variables; maternal age, birth weight, number of siblings, presence or absence of congenital heart disease, hospital of birth and type of residential care, to determine whether children involved in the Early Intervention Program differed from those not so involved.

The main null hypothesis tested was: There will be no

significant differences between the experimental group receiving early intervention and a control group receiving no treatment in the amount of change in development over a six-month period as assessed by a developmental measure.

In order to rigorously examine this question various subsidiary issues were raised. The comparability of the experimental and control groups was assessed by determining if they differed on a variety of confounding variables: quality of the home environment as measured by the home environment measure; initial prescores on the developmental measure; and several demographic variables, sex, chronological age at the time of entry into the trial, birth weight, maternal age, number of siblings, presence or absence of congenital heart disease and type of residential care. The extent to which the results of the trial may be generalized was also examined by comparing the group of Down syndrome infants participating in the Early Intervention Program and the group of Down syndrome infants in Montreal who did not so participate on several factors: birth weight, maternal age, number of siblings, presence or absence of congenital heart disease, hospital of birth, type of residential care.

Methods and Materials: Trial

A trial was conducted with the co-operation of the Early Intervention Program (EIP)* operating in Montreal since 1973

*Future reference to the Early Intervention Program will be made by using the initials EIP.

designed for developmentally delayed infants and pre-schoolers. Children with mental and physical delays are referred to this intervention program from a variety of sources: hospitals, social service agencies, pediatricians, parents. This particular program provides services for infants from birth to two years of age and a pre-school nursery curriculum for children aged two to five years. It operates on an academic calendar (September-June) and recommends home programs for the summer months. A physical examination, a requisition for physical and occupational therapy, and permission to collect pertinent medical information are required prior to enrollment of the child.

Inclusion Criteria. In order to be included in the present study, the Down syndrome infant had to have been accepted into the above early intervention program, be less than two years of age and living in a natural or foster home.** The diagnosis of Down syndrome was based on either a clinical or cytogenetic examination. Written parental permission was obtained for all subjects to participate in evaluative research and video-taping.

Program and Staff. The treatment program involved bi-weekly therapy sessions of one hour with the parent and infant at the centre. The program demonstrated and taught the parent specific activities to facilitate the sequence of development

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** Children over two years of age were referred to the pre-school program and not included in the trial.

seen in unaffected children. Activities to stimulate rolling, sitting, reaching and/or speaking were emphasized rather than specific exercises or manipulations. The normal pattern of child development was pursued by recommending to the parent techniques to encourage the child's acquisition of successive developmental levels. In addition to individual sessions at the centre, a set of written instructions was given to the mother to follow at home between sessions. These included activities that had been demonstrated during the therapy session. For examples of the activities prescribed see Appendix C.

The staff consisted of two special educators, one child care worker, one social worker, one occupational therapist and one physical therapist. Upon acceptance, a child was assigned to one staff member who then became the primary care giver, following the child over time.

The comparability of the EIP with other intervention programs with similar objectives was assessed. Descriptions of several early intervention programs for mentally retarded infants were reviewed (Moersch and Wilson, 1976; Hayden and Haring, 1976; Wolpert et al., 1978; Podilchak and Gouse-Sheese, 1978). (See Table 25.) The objectives, frequency of treatments, as well as the curriculum and staffing patterns of all those reviewed appeared similar to those of the program being studied. Except for the Seattle project (Hayden and Haring, 1976) all others were home-based. Consequently, the place of

TABLE 25

Description of Early Intervention Programs

Program	Objectives	Frequency and Site of Treatment	Staff
Moersh and Wilson 1976	To facilitate developmental milestones in the areas of language, self-care, perceptual fine motor, gross motor, cognitive and social emotional development.	(Hour session, weekly or bi-weekly). Centre and home sessions.	Occupational and physical therapists, speech pathologist, psychologist and special educator.
Hayden and Haring 1976	To bring Down syndrome children's developmental patterns as close as possible to sequential developmental norms based on normal children's performances.	Weekly 30-minute session at centre.	Special educators, speech and hearing specialist, psychologist.
Wolpert et al. 1978	To accelerate development in gross motor, five motor, social-cognitive, self-care, communication and co-operation areas.	Intensive 6 week program with intervention in the home.	Physiotherapist, psychologist, occupational therapist, speech pathologist.
Podilchak and Gouse-Sheese 1978	To stimulate the rate of development of Down syndrome infants as assessed by the Bayley Scales of Infant Development.	Bi-weekly parent training sessions in the home.	Psychologist, occupational therapist, physiotherapist, early childhood educator, speech pathologist, nurse.

treatment, rather than the method, appears to be the only important difference among the comparison of programs, and it is assumed that with some obvious limitations the findings could apply equally to all such forms of early intervention.

Design. A pre-test, post-test design utilizing an experimental group which received treatment for a six-month period and a control group which received no treatment for a six-month period was followed. Treatment was initiated immediately following the post-test for all control subjects. Allocation to the two groups was not random, but rather was determined by the date of referral to the centre. Infants referred to the program between July and December were placed in the experimental treatment group. Children referred between March and June were placed in the control group and received no treatment throughout the summer months until the following fall. Those referred to the centre in either January or February were not included in the trial because the summer holiday period prevented them from having a full six-month period of treatment. Therefore, these children received treatment but were not included in the study group. This procedure was repeated over a two-year period, in order to obtain an adequate number of subjects.

This method of allocation, based on the date of referral, was necessitated by the ethical issues raised from denying treatment for families requesting service. Although the EIP was unwilling to withhold treatment throughout the major portion of their academic year, the method of not providing

treatment during a time that the centre is normally closed, the summer months, was acceptable.

Measures of the independent and dependent variables were collected at the time of admission into the study (pre-test). Post measures on the same dependent variables were gathered six months later. (See Figure 5.) Outcome data were tabulated according to the change scores on the assessment measures. All evaluators were never informed of the child's group assignment or to the objectives of the study, thus, in effect "blinding" them to both the hypotheses and group status.

Data collection began in the fall of 1976 and continued through the fall of 1978. Pre-test measures were collected on a total of 41 children, 23 experimentals and 18 controls. Post-test measures were collected on 37 children, 21 experimentals and 16 controls. One experimental child was institutionalized and another died prior to the final assessment. Two control children moved out of the city and were lost to follow-up. See Table 26 for a time table of the trial.

Several potential confounding biases were assessed. Firstly, the two groups (experimental and control) were compared for the following groups of factors: (1) demographic variables, chronological age, sex, maternal age, birth weight, number of siblings, presence or absence of congenital heart disease, type of residential care; (2) developmental quotients

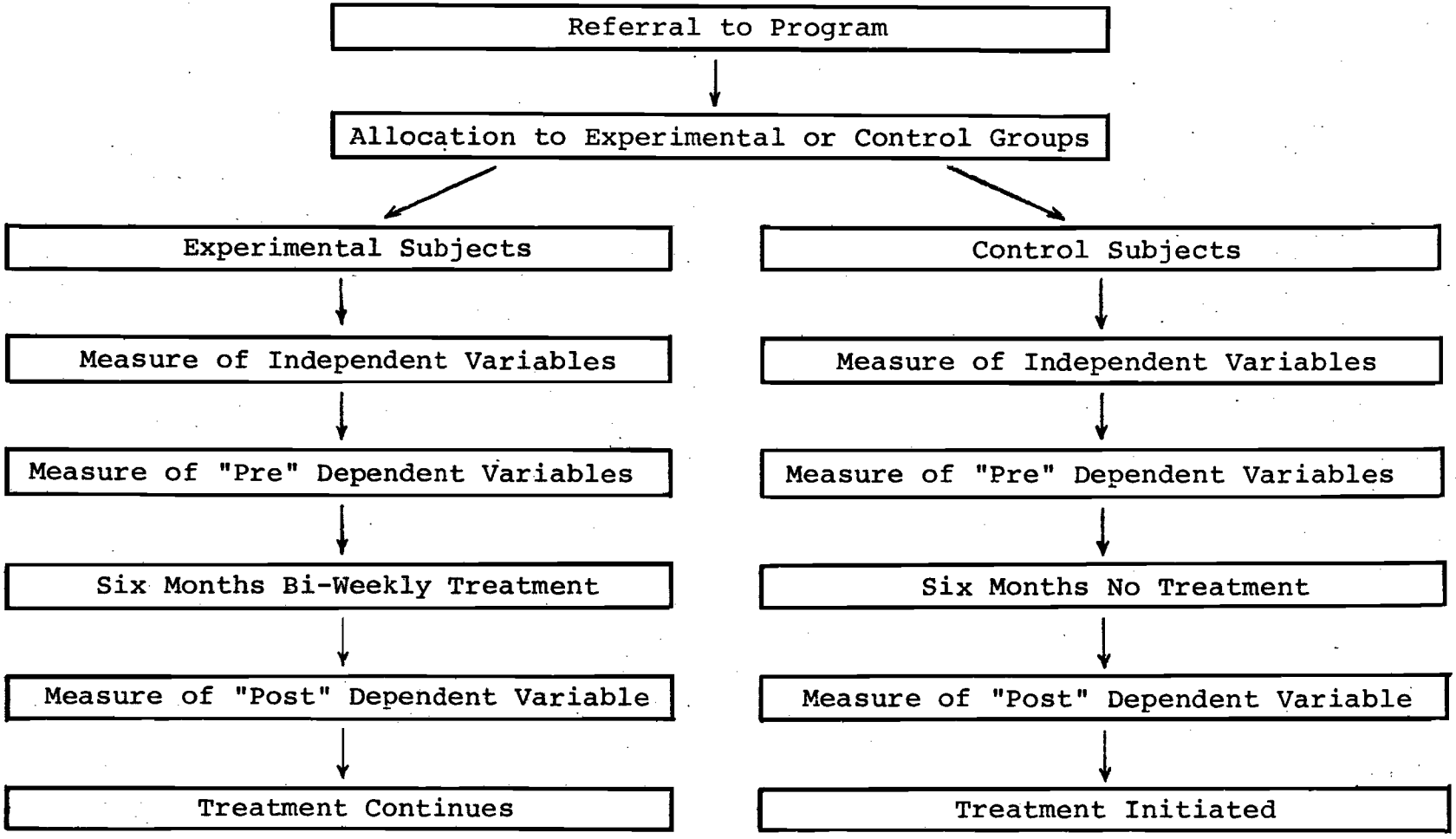

FIGURE 5. Flow Chart of Study Design

TABLE 26

Time Table for Trial

Fall, 1976	- Collection of Independent Variables and "Pre" Dependent Variables on 13 Experimental Subjects.
Spring, 1977	- Collection of "Post" Dependent Variables on 13 Experimental Subjects. - Collection of Independent Variables and "Pre" Dependent Variables on 10 Control Subjects.
Fall, 1977	- Collection of "Post" Dependent Variables on 10 Control Subjects. - Collection of Independent Variables and "Pre" Dependent Variables on 10 Experimental Subjects.
Spring, 1978	- Collection of "Post" Dependent Variables on 8 Experimental Subjects. - Collection of Independent Variables and "Pre" Dependent Variables on 8 Control Subjects.
Fall, 1978	- Collection of "Post" Dependent Variables on 6 Control Subjects.

at the time of entry into the study; and (3) home environment scores obtained upon admission into the trial.

Secondly, the cytological type of Down syndrome was ascertained for each subject. Three of the 37 study children were mosaics; the remaining 34 being trisomy 21. Because all three mosaics happened to be allocated to the control group, the developmental quotients upon entry into the trial of the mosaic infants were examined to check for discrepancies. All three scores were within the expected ranges for their chronological ages: 102 at 1.5 months, 78 at 3.2 months, and 69 at 15 months. Due to the previously cited association of higher IQs with mosaics (Fishler et al., 1976), it was decided that in the analyses special attention would be given to these three subjects to see if their performance was substantially different from others. Nevertheless, if present, this bias would, if anything, affect the control group's results, and therefore could not be considered the cause of any significant findings favouring the experimental group.

Measures

Dependent variables. The Griffiths Mental Development Scales (Griffiths, 1954, 1970) were used to measure the change in developmental status of both groups of children. This particular instrument was selected because it provides developmental quotients and mental age scores for five sub-scales as well as a general developmental quotient. The five scales

are: (See Appendices D-H)

(1) Locomotor Scale - measures gross motor skills.

(2) Personal-Social Scale - measures social adaptation.

(3) Hearing and Speech - measures active listening, progress in acquisition of first vocabulary sounds, vocalization or pre-speech as well as final language acquisition.

(4) Hand and Eye Development - graded measure for assessing the child's level of manipulation.

(5) Performance - a scale of graded performance tests, drawing on the developing ability to reason in practical situations or to manipulate materials intelligently.

Each scale contains fifty-two graded items; total of 260 items for the first two years based on 3 items for each week of life in the first year and 2 items for each week in the second year. Additionally, unlike the Bayley Scales of Infant Development (Bayley, 1969), all five skills are equally represented at all ages allowing a detailed analysis of any child at any age (Ramsay and Fitzhardinge, 1977).

Testing was performed by a psychologist who is both certified to assess infants using this particular scale and who has had a great deal of experience with infant testing. The psychologist was hired exclusively for this investigation and was kept unaware of the group status of the children and the basic design of the study. The same psychologist administered both pre- and post-measures to all children. All children were tested with their mothers present at the centre, with the exception of one control child who was tested in the home.

Independent Variables. Independent variables were grouped into three categories: demographic, home environment and "pre" developmental quotients. The demographic category included: chronological age at the time of entry into the trial, birth weight, presence or absence of congenital heart disease, sex, number of siblings, maternal age, and type of residential care. It was judged that any one or more of these might affect the development of the infants. For example, chronological age had been demonstrated previously to be strongly associated with measured intelligence or developmental quotients in the Down syndrome child, that is the younger the child the higher the quotient (Melwyn and White, 1973; Carr, 1970).

Likewise the severity of the condition was assessed by birth weight and presence or absence of congenital heart disease. Low birth weight has long been associated with deficiencies such as intellectual impairment (Harper et al., 1959; Weiner et al., 1966), slow learning (Harmeling and Jones, 1968; Drillien, 1961) and other handicapping conditions (Lubcheno et al., 1963; McDonald, 1967; Drillien, 1969). Down syndrome children are known to be at risk of growth retardation in utero (Smith and McKeown, 1956; Kucera and Dolezalova, 1973) and subsequent low birth weight (Pueschl et al., 1976). Because of these possible associations, the birth weights (in grams) of all infants enrolled in the program were acquired by maternal interview or review of medical records.

Similarly the presence or absence of congenital heart

disease was documented for each subject. This factor was considered important due to its potential impact on the health of the infant and subsequent performance of the infant on the dependent measures. Congenital heart disease was defined as any heart condition noted on the medical record compiled by the EIP by obtaining information from the hospital of birth or pediatrician.

Furthermore, information was collected on sex, number of siblings, maternal age and type of residential care. There is some support for a sex difference in the rate of development of Down syndrome infants (Clements et al., 1976; LaVeck and LaVeck, 1977). In addition, it was hypothesized that family structure, in terms of number of other siblings present, maternal age and type of residential care (natural or foster home) might enhance or deter the development of a mentally retarded child.

The Home Observation for Measurement of the Environment (HOME) Inventory (Caldwell et al., 1966) was used to evaluate the home environment at the time of referral to the program. This inventory was developed in an effort to determine features within an infant's environment most likely to influence development. The nature of the home as measured by this Inventory, has been shown to be a good predictor of a normal infant's intelligence (Bradley and Caldwell, 1976; 1977). While no studies have been conducted with retarded children using this measure, it is reasonable to postulate that the quality

of a retarded infant's home environment could influence the results of an intervention program.

The HOME Inventory uses 45 items to assess six categories of stimulation available to the infant in the home: emotional and verbal responsivity of the mother; avoidance of restriction and punishment; organization of the physical and temporal environment; provision of appropriate play materials; maternal involvement with the child; and opportunities for variety in daily activities. (See Appendix I.) Scoring of the Inventory is based partly on observation and partly on answers to a semi-structured interview. It is administered in the home when the child is awake and requires approximately 60 minutes to complete. A composite score, as well as scores for each of the six categories, are obtained.

At present, extensive standardization data do not exist for the Inventory. Data gathered from 176 families in central Arkansas indicate that the instrument is sensitive enough to register a wide range of scores for families with identical social status designations (Elardo et al., 1975). According to its authors, raters can be quickly trained with the use of their manual to achieve a 90% level of agreement. A Kuder-Richardson 20 reliability coefficient for the Inventory was computed at r = .89 (Bradley and Caldwell, 1977).

Throughout the course of the study the HOME Inventory was administered by the same social worker at the time of admission into the trial. The social worker was trained to score

this Inventory by following the Instruction Manual. As in the case of the psychologist, the social worker did not know either the design of the study or each infant's group assignment. For those children residing in foster homes, the HOME Inventory scores applied to that environment.

Finally, the amount of retardation present at the time of referral was assessed using the "pre" developmental quotient scores obtained on the Griffiths Mental Development Scales at the time of entry into the trial.

Representativeness of Sample. The sample of children participating in the EIP was assessed to determine to what extent it was representative of the entire population of Down syndrome children eligible for services. All infants diagnosed as having Down syndrome either clinically or cytogenetically, born alive on the Island of Montreal between January 1, 1975 and December 31, 1976 and who survived the first year of life were identified. These infants were then placed in either the EIP or Non-EIP groups according to the following allocation criteria:

EIP Group	Non-EIP Group
1. Born either in 1975-76. Survived first year of life.	1. Born either in 1975-76. Survived first year of life.
2. Receiving care from EIP, but not necessarily subject in trial.	2. Not receiving care from EIP.

After identification of the entire 1975-76 birth cohort, demographic information was collected on 94% of all the survivors within the population; data were not available for 6% of cases due to the absence of family names for these infants. These particular cases had been ascertained through a hospital cytogenetic laboratory, which due to its perception of ethical considerations, provided only initials, sex and date of birth as identifying information. No other source of further information on these cases was available.

Survivors were defined as all children within the cohort who remained alive throughout the first year of life. Identification of the survivors within the cohort was done by a search of death certificates conducted by the Service des Affaires Sociales, Montreal. A list of all known family names of the identified cases, as well as their sex and date of birth were submitted to the Service. After searching death certificates, the list was returned to the investigator with the date of death noted on the appropriate cases. As stated above, the search was incomplete in 6% of the cohort due to the lack of sufficient identifying information for those cases. The results of this search are printed in Figure 6.

The demographic information collected is as follows:

(1) Age of mother at the birth of the child.

(2) Number of siblings prior to the birth of the child.

(3) Birth weight in grams.

(4) Presence or absence of congenital heart disease,

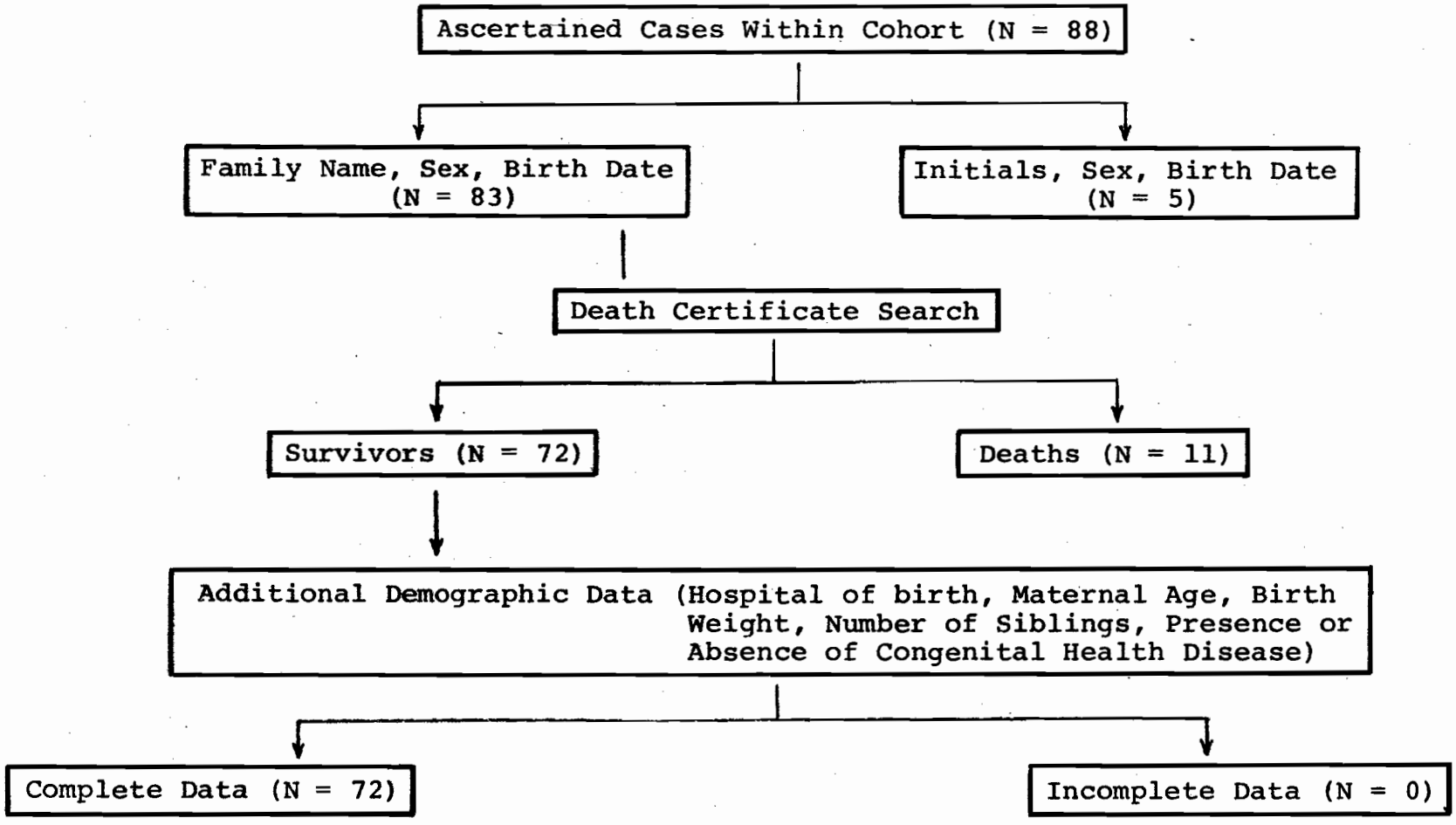

FIGURE 6. Ascertainment of demographic data on cohort of identified cases of Down syndrome.

defined as any heart condition recorded on the medical chart.

(5) Form of residential care being provided, i.e. natural home, foster home or institution.

(6) Hospital of birth, categorized as French or English (see Appendix J).

The selection of the type of demographic data sought centred around four explanations regarding how the sample might differ from the remaining population. These explanations are:

(1) Mothers of the children receiving early intervention services are younger and consequently have had fewer other children than the mothers of children not receiving early intervention services; younger mothers with fewer other children are more able to attend than older mothers with more children. Hence the variables maternal age and number of siblings were selected.

(2) Children receiving early intervention services are "healthier" or less "severely" involved than the children who are not receiving services; healthy children are able to attend versus unhealthy children are too sick to attend. The severity of the child's conditions was evaluated with the two variables, birth weight and congenital heart disease.

(3) Children receiving early intervention services are

more likely to be living in their natural home than those children not receiving early intervention services.

(4) Children receiving early intervention services are more likely to have been born in certain hospitals than those children not receiving early intervention services; certain hospitals may be more aware of the service than other hospitals.

Since no uniform source was available, the above data were collected from a variety of sources. These were:

(1) Parents - for those children receiving early intervention services.

(2) Social service agencies - for those children who were receiving foster or institutional care.

(3) Hospital genetic counseling services - for those children who had received counseling services.

(4) Birth and hospital records - for those children who were not known to any of the above.

In order to abstract data from birth and hospital records, maternity and pediatric hospitals were contacted through a letter addressed to the Director of Professional Services requesting permission to obtain information on those infants known to have been born or treated at each hospital. (See Appendix K.) A form listing each infant's family name, birth date and sex accompanied the request for data. (See Appendix L.) A self-addressed, stamped envelope was provided to stimulate the response rate. Eleven hospitals were approached, with all

providing the requested data. Sixty-three per cent completed and returned the forms; 36% required personal visits to obtain the necessary data.

Some children were known to more than one service which provided a method of validation of the data received. For example, in a case receiving early intervention services and who had also received genetic counseling, the information collected from the parents could be verified with the genetic counseling records. In the case of any discrepancy between the two sources a third source was sought, e.g. birth records.

Data Analysis. Data for both independent and dependent variables were punched on to individual IBM cards for each child in the trial. See Appendix M for a listing of the complete data. Likewise, data collected to assess the representativeness of the sample were handled similarly for each child in the EIP group and the Non-EIP group. (See Appendix N.)

Discriminant analyses were performed to determine: (1) whether the two trial groups, experimental and control, were comparable with regard to the independent variables, (2) whether the two population groups, EIP and Non-EIP differed on any combination of the selected variables, and (3) whether the two trial groups, experimental and control, differed on a set of dependent, outcome, variables.

In general, discriminant analysis attempts to determine the linear combination of the variables, the discriminant function, that best characterizes the differences between the groups.

Variables may be entered into the analysis simultaneously or in a stepwise fashion. When entering simultaneously, the entire set of variables are used to create the discriminant function. In the stepwise mode, variables are entered individually on the basis of their discriminating power. At each step, an F statistic (F-to-enter) is computed to determine which variable should enter next. These F-to-enter values are conditioned on the variables already present in the function. At each step after a variable is entered, the discriminant functions are recomputed to incorporate the effect of the newly entered variable. Moreover, if at any step a variable loses its discriminatory power, it can be removed from the analysis (Nie et al., 1975; Brown, 1977).

All discriminant analyses performed in this thesis were done using the SPSS Discriminant program (Nie et al., 1975). A minimum entry criterion was specified for all stepwise analyses (F-to-enter set at equal to or greater than 1.00). In the event that no variable could satisfy this condition, the criterion was waived. This was done to allow for the possibility that a subset of the variables might be able to significantly differentiate the groups, even though no individual variable could.

Results

Prior to the testing of the main hypothesis dealing with the efficacy of early intervention for infants with Down

syndrome, two subsidiary questions were addressed. First, the comparability of the two groups of children in the trial, experimental and control, was examined. Second, the representativeness of the sample was assessed to determine the generalizability of the results. These two issues will be presented initially, followed by the results of the trial.

Comparability of Trial Groups. The experimental group of Down syndrome infants receiving early intervention treatment and the control group of Down syndrome infants receiving no treatment were compared on a variety of potential confounding variables: initial pre-scores on a developmental measure; quality of the home environment as measured by the HOME Inventory; and a combination of several demographic variables, i.e., sex, chronological age at the time of entry into the trial, birth weight, presence or absence of congenital heart disease, number of siblings, maternal age, and type of residential care.

As listed in Table 27, three stepwise discriminant analyses were conducted to define the linear combination of variables under consideration that best characterized the differences, if any, between the two groups. The first analysis dealt with the pre-Griffiths developmental quotients. The Griffiths Mental Developmental Scale provides developmental quotients for 5 subscales and a composite developmental quotient which is an average of the 5 subscales. The means, ranges, standard deviations and univariate F-ratios for these

TABLE 27

Specific Independent Variables Utilized in Discriminant Analyses to Examine the Comparability of the Experimental and Control Groups

DISCRIMINANT ANALYSIS I	DISCRIMINANT ANALYSIS II	DISCRIMINANT ANALYSIS III
Griffiths Growth Quotients for 5 Subscales	Demographic Variables	HOME Inventory: Six Subscales
1. Total Growth Quotient	1. Chronological age	1. Emotional and verbal responsivity of the mother
2. Locomotor Growth Quotient	2. Birth weight	2. Avoidance of restriction and punishment
3. Personal-Social Quotient	3. Presence or absence of congenital heart disease	3. Organization of the physical and temporal environment.
4. Hearing and Speech Quotient	4. Sex	4. Provision of appropriate play materials
5. Hand and Eye Growth Quotient	5. Number of siblings	5. Maternal involvement with the child
6. Performance Growth Quotient	6. Maternal age	6. Opportunities for variety in daily activities
	7. Type of residential care	

6 pre-scores are presented in Table 28. No significant differences between the two groups on the pre-scores on the Griffiths Mental Development Scales were found.

The second analysis involving the demographic variables similarly failed to discriminate between the two groups. See Table 29 for the means, ranges, standard deviations and univariate F-ratios.

The third analysis was conducted with the six subscale scores from the HOME Inventory. See Table 30 for the means, ranges, standard deviations and univariate F-ratios. The variable with the largest F-ratio, provision of appropriate play materials (PLAY) was the first variable to enter the analysis with an univariate $F = 4.40$. This variable was able to significantly discriminate between the two groups ($p = .043$). No other sub-scale variable provided a significant additional contribution to the discriminate. (See Table 31.)

Finally, a fourth stepwise discriminant analysis was conducted and included all the independent variables: the pre-scores on the Griffiths Mental Development Scale, the demographic variables, and the six subscales on the HOME Inventory. This analysis was performed to determine whether after combining all 19 variables the two groups would differ on any combination of them. As before, however, the only variable to enter the analysis was provision of appropriate play materials (PLAY), which was successful in discriminating between the two groups ($p = .043$).

TABLE 28

Means, Ranges, Standard Deviations and F-Ratios for the Pre-Scores of the Developmental Quotients on the Griffiths Mental Development Scale

Variable	Experimental N = 21	Control N = 16	F-Ratio* df 1,35
Total Quotient			
Mean	79.38	78.88	
Range	65-95	55-118	.01
Standard Deviation	9.67	16.60	
Locomotor Quotient			
Mean	79.05	81.25	
Range	63-106	40-127	.17
Standard Deviation	10.27	21.68	
Personal-Social Quotient			
Mean	84.62	83.56	
Range	63-103	53-121	.04
Standard Deviation	11.95	19.36	
Hearing & Speech Quotient			
Mean	84.57	83.44	
Range	64-110	53-114	.06
Standard Deviation	11.54	15.48	
Hand & Eye Quotient			
Mean	76.24	76.76	
Range	42-103	54-127	.01
Standard Deviation	14.42	18.51	
Performance Quotient			
Mean	72.19	74.75	
Range	48-100	49-109	.23
Standard Deviation	14.88	17.57	

*F-value of at least 4.12 required for $p \leq .05$.

TABLE 29

Means, Ranges, Standard Deviations and F-ratios for Demographic Variables

Variable	Experimental N = 21	Control N = 16	F-Ratio* df 1,35
Chronological Age (Months)			
Mean	9.33	8.43	
Range	2.77-23.80	1.46-17.69	.20
Standard Deviation	6.26	5.78	
Maternal Age (Years)			
Mean	30.43	29.81	
Range	22-47	19-39	.08
Standard Deviation	7.11	6.00	
Number of Siblings			
Mean	0.95	0.81	
Range	0-3	0-3	.19
Standard Deviation	0.97	0.98	
Sex (Male = 1, Female = 2)			
Mean	1.52	1.62	
			.36
Standard Deviation	.51	.50	
Birth Weight (Grams)			
Mean	2,939.10	2,990.00	
Range	2,000-4,500	1,818-4,110	.07
Standard Deviation	607.50	568.25	
Congenital Heart Disease (No = 1, Yes = 2)			
Mean	1.33	1.38	
			.06
Standard Deviation	.48	.50	
Residential Care (Natural = 1, Foster = 2)			
Mean	1.14	1.06	
			.58
Standard Deviation	.36	.25	

*F value of at least 4.12 required for $p \leq .05$.

TABLE 30

Means, Ranges, Standard Deviations and Univariate F-ratios for the Six Subscales on the Home Inventory

Variable	Experimental N = 21	Control N = 16	F-Ratio df 1,35
1. Emotional and Verbal Responsivity of the Mother (11)			
Mean	8.67	7.62	
Range	4-11	1-11	1.41
Standard Deviation	2.42	2.92	
2. Avoidance of Restriction and Punishment (8)			
Mean	6.86	6.69	
Range	5-8	6-8	.46
Standard Deviation	.79	.70	
3. Provision of Appropriate Play Materials (9)			
Mean	5.43	3.62	
Range	1-8	0-8	4.40*
Standard Deviation	2.48	2.73	
4. Organization of the Physical and Temporal Environment (6)			
Mean	4.57	4.50	
Range	3-6	2-6	.03
Standard Deviation	1.12	1.26	
5. Maternal Involvement with the Child (6)			
Mean	3.00	1.94	
Range	0-6	0-6	2.92
Standard Deviation	1.90	1.84	
6. Opportunities for Variety in Daily Activities (5)			
Mean	2.67	2.38	
Range	1-5	1-5	.61
Standard Deviation	1.20	1.02	

*Significant at the 0.05 level.

Numbers in ( ) following name of subscale indicate maximum score possible.

TABLE 31

F Values of Variables Not Yet Entered Into the Stepwise Discriminant Analysis Following the Entrance of Play

Variable	F-to-Enter* df 2,34
Emotional and Verbal Responsivity of the Mother	.03
Avoidance of Restriction and Punishment	.15
Organization of the Physical and Temporal Environment	.73
Maternal Involvement with the Child	.08
Opportunities for Variety in Daily Activities	.002

*F value of at least 3.28 required for $p \leq .05$.

In summary, as a result of the four stepwise discriminant analyses, it was concluded that the two groups of infants did not differ significantly on any of the potential confounding variables with the exception of one HOME Inventory variable, PLAY. With respect to this variable the groups were significantly different ($p = .043$), the experimental group having a significantly higher score on the subscale, provision of appropriate play materials, than the control group. Because this difference in environments might affect the results of the trial, the contribution of this variable is considered separately in later analyses. However, it should be noted that because multiple comparisons were performed, the possibility of detecting a significant difference between the groups on one of the 19 variables was increased. In this situation, it may be that the reported finding involving the PLAY variable has arisen purely by chance and hence, does not reflect a real difference between the two groups.

Representativeness of Sample. To determine the extent to which the results of the trial may be generalized, those Down syndrome infants participating in the Early Intervention Program (EIP Group) were compared with a group of Down syndrome infants who did not so participate (Non-EIP Group) on several factors which might affect development: birth weight, maternal age, number of siblings, presence or absence of congential heart disease, hospital of birth, and type of residential care.

Approximately one-quarter of the 1975-76 birth cohorts, 27.2%, were participating in the Early Intervention Program and were hence allocated to the EIP Group. An additional 60.2% were unknown to the Early Intervention Program and thus made up the Non-EIP Group.* The remaining 12.5% had died within the first year of life and consequently were excluded from this analysis. Data for the variables under consideration were available for 93.5% of all the children allocated to either the EIP or Non-EIP groups. The missing data was confined to five children in the Non-EIP group, who had been born and karyotyped at a hospital unwilling to disclose any identifying information other than sex and date of birth.

One stepwise discriminant analysis was performed to determine which, if any, of the above variables significantly discriminated between the EIP Group and Non-EIP Group. The means, standard deviations and univariate F-ratios for these variables are found in Table 32. The first variable to enter the analysis was Residential Care with an $F = 15.56$ (df 1, 70; $p < .001$) with the second entered variable being Hospital of Birth, F-to-enter = 4.21 (df 2,69; $p = .022$). At this stage the F for the discriminant was 10.24 (df 2,69; $p < .001$).

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*These two groups, EIP and Non-EIP, should not be confused with the two trial groups, experimental and control. As previously stated, the criteria for group placement in the EIP Group were: (1) birth date in 1975-76; (2) participating in the EIP; may or may not be a subject in the trial. Similarly, inclusion in the Non-EIP Group required: (1) birth date in 1975-76; (2) non-participation in the EIP, thereby prohibiting trial membership.

TABLE 32

Means, Standard Deviations, and Univariate F-ratios for the Discriminating Variables Between the EIP and Non-EIP Groups

Variable	EIP N = 24	Non-EIP N = 48	F-Ratio* df 1,70
Birth Weight (grams)			
Mean	2,935.96	2,987.69	.14
Standard Deviation	659.79	502.08	
Maternal Age (Years)			
Mean	29.96	31.46	.84
Standard Deviation	6.11	6.74	
Number of Siblings			
Mean	1.00	1.62	2.13
Standard Deviation	.98	1.97	
Congenital Heart Disease (1=Absence, 2=Presence)			
Mean	1.33	1.27	.30
Standard Deviation	.48	.45	
Hospital of Birth (1=English, 2=French)			
Mean	1.33	1.62	5.74**
Standard Deviation	.48	.49	
Residential Care (1=Natural Home 2=Foster Home 3=Institution)			
Mean	1.17	1.83	15.56***
Standard Deviation	.38	.78	

*F value of at least 3.98 required for $p \leq .05$.

**$p < .025$

***$p < .001$

TABLE 33

Summary of Stepwise Discriminant Analysis for "EIP" and "Non-EIP" Groups

Step Number	Variable	F for Individual Variable Entered	df	p	F for the Total Discriminant	df	p
1.	Residential Care	15.56	1,70	<.001	15.56	1,70	<.001
2.	Hospital of Birth	4.21	2,69	.022	10.24	2,69	<.001
3.	Number of Siblings	1.64	3,68	.139	7.43	3,68	<.001

TABLE 34

F to Enter Values of Variables Not Yet Entered Into the Discriminant Analysis Following the Entrance of Residential Care, Hospital of Birth and Number of Siblings

Variable	F-to-Enter df 3,68
Maternal Age	.0001
Birth Weight	.019
Congenital Heart Disease	.084

The third and final variable to enter the analysis was Number of Siblings with an F to enter of 1.64 (df 3,68; $p = .14$) and an F for the discriminant being 7.43 (df 3,68; $p < .001$). Table 33 summarizes the above steps. The remaining variables failed to contribute significantly to the discriminant. (See Table 34.)

In summary, it is concluded that the EIP and Non-EIP groups differ significantly on the variables Residential Care and Hospital of Birth. The Number of Siblings variable does not contribute additional significance to the analysis. The relevance of these findings to the generalizability of the results of the trial will be considered in the Discussion section.

Outcome of Trial. Several approaches were used to examine the main null hypothesis, there will be no significant differences between the experimental group of Down syndrome infants receiving early intervention treatment and the control group of Down syndrome infants receiving no treatment in the amount of change in development over a six-month period as measured by a developmental measure.

The means, standard deviations, and univariate F-ratios for the six change scores (post-pre score) on the five subscales and total developmental quotient of the Griffiths Mental Development Scales are listed in Table 35. Four of these change scores favoured the control group; two, the experimental group.* None of these were significant at the .05 level.

Initially all six change scores were employed in a

*For example, in the experimental group the TOTAL DQ decreased an average of 7.33 points over the six-month period; the control group, 5.94 points.

TABLE 35

Means, Standard Deviations and Univariate F-Ratios For the Change Scores of the Griffiths Mental Development Scale Quotients

	Experimental N = 21	Control N = 16	F-Ratio* df 1,35
Total Developmental Quotient			
Mean	-7.33	-5.94	.26
Standard Deviation	7.79	8.86	
Locomotor Developmental Quotient			
Mean	-8.81	-2.38	2.68
Standard Deviation	13.31	9.56	
Personal-Social Developmental Quotient			
Mean	-8.19	-7.56	.02
Standard Deviation	14.36	10.15	
Hearing and Speech Developmental Quotient			
Mean	-11.00	-7.56	.51
Standard Deviation	15.64	12.85	
Hand and Eye Development Quotient			
Mean	-2.71	-3.12	.01
Standard Deviation	12.24	16.36	
Performance Developmental Quotient			
Mean	-5.71	-9.56	.57
Standard Deviation	15.00	15.84	

*F value of at least 4.12 required for $p \leq .05$.

discriminate analysis to differentiate between the experimental and control groups. The derived discriminate function had a X^2_6 of 6.057 with an associated p value of .417. It was concluded that the combination of the six change scores failed to discriminate significantly between the two groups.

A stepwise discriminant analysis, allowing only significant discriminators to enter, was then performed. Although the Locomotor subscale entered the analysis (F = 2.68; df 1, 35), it was unable to discriminate significantly between the two groups (p = .11). Following the entrance of the Locomotor variable, all remaining variables failed to satisfy the minimum F to enter criterion. (See Table 36.) Thus this criterion was waived. However, even after this was done, no subset of the variables provided a significant discriminant at any step of the procedure. As a result of these analyses, no significant differences between the two groups on the change scores on the Griffiths Mental Development Scales were found.

A second stepwise discriminant analysis was done to adjust for the initial difference between the two groups on the HOME Inventory PLAY subscale. The PLAY variable was forced into the discriminant analysis on the first step. The next variable to enter after PLAY was the change score for the Locomotor quotient with an F-to-enter of 1.87 (df 2,34; p = .14). (See Table 37.) The F for the discriminant at this stage was 3.19 (df 2,34; p = .05). The remaining variables failed to contribute significantly to the analysis. (See Table 38.)

TABLE 36

F Values of Variables Not Yet Entered Into the Stepwise Discriminant Analysis Following the Entrance of Locomotor

Variable	F-to-Enter* (df 2,34)
Change in Total Developmental Quotient	.05
Change in Personal-Social Quotient	.12
Change in Hearing and Speech Quotient	.03
Change in Hand and Eye Quotient	.02
Change in Performance	.59

*F value of at least 3.28 required for $p \leq .05$.

TABLE 37

F Values of Variables Not Yet Entered Into the Stepwise Discriminant Analysis Following the Entrance of Play

Variable	F-to-Enter* (df 2,34)
Change in Total Quotient	.25
Change in Locomotor Quotient	1.87
Change in Personal-Social Quotient	.05
Change in Hearing and Speech Quotient	.66
Change in Hand and Eye Quotient	.04
Change in Performance Quotient	.40

*F value of at least 3.28 required for $p \leq .05$.

TABLE 38

F Values of Variables Not Yet Entered Into the Stepwise Discriminant Analysis Following the Entrance of Play and Locomotor Developmental Quotient

Variable	F-toEnter* (df 3,33)
Change in Total Quotient	.01
Change in Personal-Social Quotient	.04
Change in Hearing and Speech Quotient	.13
Change in Hand and Eye Quotient	.00
Change in Performance Quotient	.42

*F value of at least 2.89 required for $p \leq .05$.

Although this particular linear combination of PLAY and Locomotor quotient was able to significantly differentiate between the two groups, the primary discriminator was the PLAY variable with an F value of 4.40 (df 1,35) and an associated p value of .04 with the Locomotor change scores detracting from the significance of the analysis. Table 39 summarizes the above analysis.

As a result of these analyses, the null hypothesis that the two groups, experimental and control, are equal in terms of change in development as measured by the Griffiths Mental Scale over a six-month period is supported even after adjusting for initial differences in the home environment. Whether one uses a multivariate analysis, with or without adjusting for the effect of a potentially confounding variable, or employs separate univariate analyses for the six dependent variables, the conclusion is the same. The fact that no statistically significant differences exist, however, does not preclude an examination of the trends. This will be pursued in the discussion section.

Discussion

This section has evaluated the effect of one early intervention program on the remediation of retardation by comparing the change in development of a group of Down syndrome infants receiving treatment over a six-month period with the change in a similar group not receiving care. Consideration was given

TABLE 39

Summary of Stepwise Discriminant Analysis for Experimental and Control Groups

Step Number	Variable	F for Individual Variable Entered	df	p	F for the Total Discrimi-inant	df	p
1.	Play	4.40	1,35	.043	4.40	1,35	.043
2.	Locomotor	1.88	2,34	.140	3.19	2,34	.054

to the initial comparability of the groups, and the infants participating in this program were also compared with those not receiving services to determine whether the sample studied was representative of the eligible population. Each of these areas will be considered separately in this discussion.

Comparability of Trial Groups. As demonstrated, the two groups, experimental and control, differed on only one of nineteen independent variables, provision of play materials, with the experimental group having a significantly higher mean score prior to the trial than the control group. The relevance of such a difference to the development of retarded children has not been well documented. Bradley and Caldwell (1976) reported that increased mental performance in normal infants was related to this subscale. Accordingly, the higher scores for the experimental infants would, if anything, favourably affect the results for these subjects.

The disproportionate number of infants with mosaic chromosomal patterns in the control group is, however, one factor which may have biased the results in favour of this group. Yet, an examination of the developmental scores for these infants does not reveal higher scores than expected. The specific change scores for these three infants are listed in Appendix M.

Aside from the independent variables considered, the fact that the assessment of development for the two groups was not done over the same six-month period must also be recognized.

Infants allocated to the experimental group received intervention throughout the fall and winter months, whereas control subjects were assessed for developmental change occurring during the spring and summer. A seasonal bias may have resulted from this discrepancy in the time of assessment.

Because of Montreal's severe winter, it is possible that the development of infants is different in one season than another. In particular, the experimental infants may have had a disadvantage associated with the timing of their assessments. For example, some minor illnesses, colds, flu, etc., are more prevalent in winter than summer, which in turn may interfere with developmental progress. Moreover, winter in Montreal is not conducive for taking young children out-of-doors, whether for play, shopping, or social visits. This restriction in activity imposed by the weather may have hindered the development of the experimental infants.

Ideally all infants should have been evaluated over the same six-month period. The seasonal bias, unlike the HOME Inventory subscale, PLAY, cannot be considered in the statistical analysis and its effect can only be postulated. However, if a seasonal effect on development exists, it is reasonable to assume that in this trial it would benefit those in the control group.

In summary, an initial comparison of the experimental and control groups revealed a statistically significant difference on only one of nineteen confounding variables. Although it is

extremely difficult to define and measure all the potential variables that might affect the results, the two groups are considered comparable with this one exception. However, the possibility of a seasonal bias in favour of the control group associated with the time of assessment was also raised. The effect of such a bias is impossible to accurately assess and, therefore, must remain conjectural.

Representativeness of Sample. Children participating in the Early Intervention Program (EIP group) differed significantly from those not so participating (Non-EIP group) on two variables, residential status and hospital of birth. Institutionalization or foster home placement was more frequent in the Non-EIP Group than in the EIP group. In addition those Down syndrome children born in English hospitals were more likely to be known to the program than those born in French facilities.

These two findings are not unexpected. Children institutionalized at birth or soon after are generally excluded from participating in the Early Intervention Program. Although institutionalized children fulfill EIP entrance requirements, the fact that they reside in an institution almost always interferes with their participating in the program. Certainly if the institution requested services for a particular child and chose to become actively involved in the treatment regimen, services would be provided. Similarly, foster home placement often impedes enrollment in such programs since most

placement agencies do not compensate foster parents for the added commitment associated with an early intervention regimen.

The association of program involvement with the hospital of birth is also readily explained. Although this particular program provides services to both French and English populations, it is affiliated with an agency that traditionally has been strongly supported by the English sector of Montreal. Hence, the disparate pattern of referrals may merely reflect this historical link with the English community and its hospitals. Yet, it is recognized that the lack of participation by the Non-EIP group does not necessarily denote lack of awareness of the program. It may be that this group of uninvolved families has chosen not to participate in this program after being informed of its existence.

More interesting than the differences are the similarities between the two groups. It has been suggested that children known to the program would be healthier, have fewer siblings and younger mothers than their counterparts. However, none of the variables associated with these hypotheses significantly discriminated between the two groups. Although the effect of Number of Siblings approached significance, its additional contribution to the stepwise discriminant analysis was negligible. Therefore, it is concluded that the Non-EIP and the EIP groups do not differ with regard to health and family composition as measured by the selected variables.

It should be noted that the variables upon which the groups do differ are factors that are both amenable to change and are unlikely to affect the generalizability of the findings. Institutionalization of healthy Down syndrome infants in Quebec is becoming less common since present policies are designed to discourage the institutionalization of any child under three years of age who does not require skilled nursing (Glick, 1977). The demand for foster homes for these healthy infants will most certainly rise as the alternative of institutionalization diminishes. Accordingly, the proportion of affected infants participating in community programs such as the EIP is likely to increase.

The finding relating hospital of birth to involvement in the EIP most probably indicates a lack of knowledge by certain maternity hospitals about programs and services available for these children. Because most Down syndrome cases are identified at birth or shortly thereafter, the task of supporting parents during this initial period of shock and grief is often managed by the staff of the hospital of birth. Whether early intervention is deemed efficacious or not in remediating mental retardation, these children and their families will always need support and care and should be informed about agencies that provide such services. Moreover, given an efficacious treatment regimen, the need to desseminate referral information to appropriate hospitals and facilities becomes even more critical.

The effect of the cited differences between the two groups, EIP and Non-EIP, on the generalizability of the findings of the trial must be examined. Until it can be satisfactorily demonstrated that Down syndrome children reared at home do not differ from those raised in institutions, it will remain unacceptable to consider these two groups as similar. Clearly, in Quebec where healthy mentally retarded infants are no longer being institutionalized, an important difference in terms of severity may exist. Because the EIP group contained no institutionalized infants, the results of this trial cannot be applied to the institutionalized children in the Non-EIP group.

It is more difficult to interpret how the hospital of birth might affect development and the generalizability of the results. If, in fact, older women or multiparous women were more likely to deliver at one hospital than another, it is conceivable that these related factors might influence development. But, because the two groups did not differ on either maternal age or number of siblings, it is concluded that the association between hospital of birth is independent of these potentially confounding variables. It is believed that this difference between the two groups solely represents the dissimilar referral patterns of the two communities.

In summary, had significant differences been found between the two groups either in the health or family structure variables, concern regarding the generalizability of the findings would be warranted since both these factors could affect

development. Instead, it is concluded that the demonstrated differences between the two groups in hospital of birth do not affect the generalizability of the results. Thus, the findings of the trial may be applied to the larger population of Down syndrome infants, with the exception of those institutionalized.

Outcome of Trial. No statistical evidence was found that early intervention, as applied in this trial, was efficacious in remediating retardation during infancy of children with Down syndrome. The performance of the experimental group was not superior to the control group in any of the six areas of development as assessed by the Griffiths Mental Development Scales. Even after the adjustment for the initial difference between the two groups with regard to the environment variable, no significant differences were found.

On only one of the six developmental quotients, Locomotor, did the difference between the two groups approach the conventionally accepted level of statistical significance. Notably, however, this difference in gross motor skills was in favour of the control group (Experimental $\bar{u} = -8.8$; Controls $\bar{u} = -2.4$). This trend may be explained in part by the "seasonal bias" associated with the time of assessment. Locomotor skills may be more readily acquired during the summer than the winter, thus resulting in a beneficial seasonal advantage for the control subjects. Also, it is of particular interest to note that Bidder (1975) found the locomotor area to be the one area of

development least affected by intervention. The fact that Down syndrome children are characteristically hypotonic may counteract attempts to advance the rate of locomotor development.

The initial comparability of the groups lends further support to the conclusion that the children did not differ significantly with respect to change in development over the six-month period. The one home environment variable upon which the groups differed initially, favoured the development of the experimental infants. On the other hand, the "seasonal bias" may have deterred the experimental group's performance. The extent to which the seasonal bias may have influenced the findings is impossible to assess fully. However, because none of the developmental change scores, with the exception of locomotor, even approach the conventionally accepted level of significance, it is unlikely that its removal would influence the findings in favour of the experimental group (see Table 35).

The generally negative findings of this trial are in sharp contrast to most reported in the review of the literature. There are several possible explanations for this discrepancy aside from the methodological limitations in both this study and in others that have been discussed elsewhere and will now be summarized.

Duration of Treatment. The children received treatment for six months, and it is conceivable that a longer period of intervention would have produced different results. Except

for the Aronson and Fallstrom (1977) study, however, all other evaluations were for six months or less. But, because the present trial dealt with infants rather than pre-schoolers, the association between outcome and length of treatment may be different. Perhaps intervention is more efficacious with older children, or perhaps the procedures must be applied for a period greater than six months in infancy to obtain measurable positive results.

Latency Effect. The possibility of a latency effect should be explored. The positive effects of infant intervention may only be detectable with the passing of time and the maturation of the child. Yet, this interpretation differs with the experience cited for culturally disadvantaged children. Bronfenbrenner (1975) found the positive effects of intervention to diminish following the discontinuation of treatment and the aging of the child.

Age. With the decrease of intelligence or developmental quotients over time, the age of the child at the time of intervention may also be a critical factor. Carr (1975) reported the greatest decline in developmental quotients to take place between six and ten months of life. Because the mean age of the infants in this trial was nine months, it is possible that intervention was initiated at a time when the natural decrease in intelligence was occurring at a rapid rate. Arguments can be made for the necessity to either intervene more aggressively or for the futility of treatments during

this period. Regardless of the interpretation, the question about the interaction of chronological age with intervention is still uncertain.

Intensity of Treatment. Similarly, more intensive intervention regardless of age may be necessary. Once again, however, earlier studies reporting positive results do not, in general, include more intensive treatment than the program examined in this study. But, as before, the interaction of amount of treatment with the age of the children may necessitate a different approach for infants than that generally employed with pre-schoolers. An argument for intensive daily treatment for mentally retarded infants can be made based on the findings with culturally deprived infants (Heber and Garber, 1975). If a stimulating environment is truly a prerequisite for altering the mental development of these children, the provision of a consistently high quality learning environment through a structured day-care program may be required to evoke measurable developmental changes in infancy.

Site of Treatment. The site of the treatment may also be an important variable. In this study, infants were brought to the centre where parents were instructed in an activity program to be carried out in the home between treatment sessions. In all other intervention studies, with the exception of Hayden and Haring (1976), the therapist conducted the training sessions in the infant's home. The controversy surrounding home versus centre-based treatment is not new. Systematic home

visiting is not only expensive in time and personnel, but also is often not conducive for teaching (Sandow and Clarke, 1977). Because parents of handicapped children are frequently socially isolated by the constant care of their child, the regular weekly visit can become more social than educational. Although in terms of support this dimension may be of critical importance to a parent, it may also interfere with the productivity of a work session. In contrast, Bronfenbrenner (1975), in his review of early intervention programs for culturally disadvantaged children, strongly advocates frequent home visits by a therapist to encourage the mother's role in the treatment. He emphasizes the critical need for the home visitor to motivate parental interest and involvement in the teaching process. This, it seems, is the crucial variable rather than the site of treatment. It may be, however, that home-based programs facilitate this parent-child interaction more successfully than centre-based approaches. The site of intervention for this study was determined solely by economic considerations. Accordingly, different results might have been obtained had the program been home-based.

Compliance. Compliance with the prescribed home regimens was not measured. The issue of compliance as it pertains to handicapped children is an interesting one. Because immediate gains from treatment are seldom seen, parents may become easily discouraged and discontinue the activities. It may be that, for whatever reason, parents failed to carry out the

demonstrated intervention programs in the home, thereby implicating compliance as the problem rather than the techniques themselves. Nonetheless, because the concern here is not primarily with the intervention techniques *per se* but rather with the effectiveness of the EIP, the problem of compliance is inherent to its evaluation.

Control Experience. In addition, no assessment of the control group's experience during the six-month period was made. Perhaps, some of these families were exposed to intervention techniques from other sources than the program in question. Such exposure would negate the premise that all forms of intervention had been withheld from the control subjects. Because control parents had to wait until the fall to begin treatment, they may have sought information from a variety of sources (books, pediatricians, specialists) to begin their own stimulation program over the summer months. Parents may have made additional efforts to interact with their children as a result of their being deprived of formal treatment. This explanation is an interesting one in view of Bronfenbrenner's (1975) findings which emphasize the importance of parental involvement in early intervention.

Measure Used. The findings of this study pertain only to one specific outcome measure, the Griffiths Mental Development Scales. This developmental measure was selected because it provides developmental quotients for five subscales as well as a general developmental quotient. It may be, however, that

the use of another assessment instrument would have been more sensitive in detecting developmental advances.

In addition the objectives of early intervention programs encompass other areas apart from the remediation of a child's retardation. The acceptance of the child into the family structure, the resolution of guilt feelings, and the establishment of realistic expectations are additional reasonable goals of therapy for these children. The focus of this study, however, was limited solely to the effect of early intervention on mental retardation. The selection of this specific outcome measure by no means denies the possible benefits of other components of this or other infant stimulation programs.

Sample Size. The failure to reject the null hypothesis may be a result of the small sample size employed in this trial; that is, the probability of "accepting" the null hypothesis is larger than desired. However, because the direction of the difference between the experimental and control groups on the majority of the change scores favoured the control group, it is doubtful that a larger sample size would have resulted in significant findings favouring the experimental group.

The failure to demonstrate differences between the two groups in this study is disappointing for those seeking a means to minimize the retardation seen in Down syndrome. Although other possible explanations exist for these results, the findings clearly suggest that the efficacy of early intervention with these infants must be questioned. It is concluded, with

appropriate reservations, that the particular early intervention regimen investigated was not efficacious in changing the pattern of mental development in those Down syndrome infants participating in the program, and that these findings may be generalized to other non-institutionalized Down syndrome infants in Montreal.

PART III: SUMMARY

CHAPTER 5

OVERVIEW AND IMPLICATIONS

Statement of Originality

This thesis has studied the effect of both preventive and remediative procedures on the incidence and impact of Down syndrome in Montreal. Prior investigations have been confined either to the subject of prevention or to the issue of remediation. This thesis has assessed the contributions made by both procedures to the problem of Down syndrome. Maternal age-specific incidence rates for five-year and single-year intervals were computed and examined for two time periods. No study to date has furnished these rates for childbearing women in Montreal. In addition, a study designed to evaluate the effect of a remediative procedure for infants with Down syndrome was conducted. No previous trial has investigated the outcome of early intervention for Down syndrome children under two years of age. Likewise, the attention to the issue regarding the representativeness of the study sample to the population from which it was derived is an original contribution to the field of early intervention.

Summary

Down syndrome continues to be a major form of mental retardation in Montreal despite a decline in maternal age and

the ability to detect cases prenatally. Unquestionably, the total number of Down syndrome births has decreased from 148 cases in 1965-66 to 88 in 1975-76. This apparent reduction in the size of the problem is deceptive, for the crude incidence rate for all child-bearing women has declined minimally from 2.02/1,000 livebirths to 1.85/1,000 livebirths. This slight decrease is less than that predicted for the observed decline in the maternal age structure. A rise in certain age-specific rates and the lack of utilization of prenatal diagnosis have resulted in a situation that is disappointing for those committed to the primary prevention of mental retardation.

Moreover, the prospects for remediating or minimizing the associated mental retardation through postnatal intervention are not encouraging. The results of this study failed to support the notion that the pattern of mental development of children receiving early intervention could be altered.

Several possible explanations for these discouraging findings have been presented. It is a well known principle that the most efficacious procedure must be utilized or applied in order to be effective. Amniocentesis for prenatal diagnosis suffers from underutilization and, for this reason, has failed in this study to significantly affect the incidence of Down syndrome. Less than 5% of the potential cases were prevented through prenatal diagnosis. The reason for the underutilization of this primary preventive procedure is uncertain.

Physicians may not be offering the procedure to women at risk, or women may be refusing the service after being informed of its availability. Whatever the explanation, it is obvious that this particular method of prevention has as yet had little impact on the incidence of Down syndrome in Montreal.

Perhaps more disconcerting is the finding that although the mean maternal age declined, the age-specific rates for both middle-aged and older women in Montreal increased. These noted increases may not represent a trend, but the fact remains that the age-specific rates for these women in 1975-76 are generally higher than those computed for 1965-66.

An explanation for the increase in rates was beyond the scope of this thesis. Since similar findings have been reported in Canada and elsewhere (Jones and Lowry, 1975; Mikkelsen et al., 1976; Holloway and Emery, 1977; Evans et al., 1978), several hypotheses were advanced, including better methods of ascertainment in the later cohort and the possibility of environmental or social factors causing a true biological increase.

More importantly, this study has suggested the necessity of combining the preventive technology with current age-specific rates for a particular geographic area. This, it seems, will only be possible through continuous monitoring of these rates in a defined community. Today the screening of all pregnant women aged 35 years and over in Montreal would detect a smaller proportion of all cases than ten years ago. Both the

decrease in maternal age and the possible rise in the age-specific rates for younger women account for this finding. The most efficient use of prenatal diagnosis is, therefore, dependent on the accurate definition of women "at risk". Because of limited resources and the uncertainty surrounding the feasibility of universal screening, prevention of Down syndrome will become a reality only if those most likely to give birth to an affected infant either deter from conceiving or avail themselves of prenatal diagnosis.

The failure to confirm the findings of previous investigations, and hence, demonstrate the efficacy of early intervention, is disturbing. Limitations of the trial have been discussed elsewhere and include the possibility that a different approach, in terms of intensity, duration, place of treatment, and age of the population may produce differing results.

This study focused on Down syndrome infants over a six-month period of development. The regimen consisted of an hour of bi-weekly instruction at the centre with therapist, parent and child and a home program to be followed between sessions. While this particular approach for this particular population did not prove efficacious, this finding should not be interpreted to imply that all programs classified as early intervention for Down syndrome children do not influence development. It may be that a dissimilar approach will in fact produce more positive findings. Until, however, credible investigations present such results, the efficacy of early intervention for

infants with Down syndrome will remain unproven.

But, because the Down syndrome infants participating in the study were not shown to be a unique group when compared with those not involved in the trial, it was concluded that the results of this investigation could be generalized to other non-institutionalized Down syndrome infants at least in Montreal. Had the two groups exhibited major differences, it might have been argued that the Non-EIP children would have responded differently to treatment, suggesting that these children are more in need of stimulation, and thus more amenable to change than those who voluntarily enroll in an intervention program. Because this argument cannot be supported, the possibility of early intervention, as described in this study, being efficacious for a different group of Down syndrome infants is questionable.

Implications

Because the problem of Down syndrome has not disappeared, the challenge of finding future solutions remains. At best, the eradication of the problem as it now exists will occur either by deterring conception in high risk women and terminating prenatally diagnosed pregnancies or by discovering the means to ameliorate the mental retardation associated with the syndrome. At present, the prevention of the birth of all new cases seems unlikely, even with the advent of universal screening, due to the moral and ethical issues associated with

selective abortions. Thus, the search for an efficacious method of remediating the mental retardation must continue. Theoretically, the combination of both preventive and remediative measures will not only help alleviate the dilemma of Down syndrome but also will offer a viable alternative to couples unwilling to accept selective pregnancy termination as a method of prevention.

What then are the necessary initial steps in developing an effective combination of these two approaches in Montreal? With regard to primary prevention through amniocentesis for prenatal diagnosis, the following suggestions are offered:

1. The continued monitoring of the age-specific incidence rates of livebirths with Down syndrome is essential to accurately define the women "at risk" in Montreal. This monitoring could be accomplished by maintaining the reporting system established in this study. The computation of single year age-specific rates is critical, for if the age criterion for prenatal screening is to be altered it will most likely be done by the gradual addition of single years to the inclusion criterion. Such additions of certain women are warranted if the "risk" of giving birth to an affected child for women aged 34, 33, etc. is equal to or greater than that for women aged 35 or over. For example, based on the 1975-76 rates, a strong argument can be made for monitoring Montreal women aged 34 years. Because their rate was strikingly similar to that for 35 year-old women, the rationale for excluding 34 year-old

women from the service must be carefully evaluated.

The ongoing computation of age-specific rates in Montreal will also provide genetic counselors with the most recent data available. Since age-specific rates in this study, as well as from other North American investigations (Hook, 1976; Christianson, 1976) demonstrate marked differences from those computed by Collmann and Stoller (1962), the replacement of the five year age-specific Australian rates presently employed in counselling of Canadian women with more appropriate rates should be considered.

Moreover, continuous monitoring of age-specific rates may be helpful in the identification of causative factors of the chromosomal anomaly of Down syndrome. The role of either environmental exposures or sociological trends can be more readily identified if rates are monitored over time.

2. Efforts must be taken to make prenatal diagnosis a more effective procedure. The reasons for underutilization of this service should be determined and when possible corrected. It has been demonstrated that women of lower socioeconomic status are grossly underrepresented among the minority being tested (Bannerman et al., 1977) even in Canada where the financial cost of the test is not an issue (Simpson et al., 1976). Explanations of the underuse of prenatal diagnosis by this particular group of women are only conjectural, but include the possibilities that they may be less well informed and therefore do not demand the procedure, that they may be

less accepting of selective abortion and therefore refuse when offered, or that they may seek obstetric care too late in pregnancy to qualify for prenatal diagnosis (Forster and Davison, 1977). Research is required to document the barriers to the delivery and use of this preventive service so that appropriate methods of intervention can be applied.

At present Montreal women aged 35 years and over are eligible for amniocentesis for prenatal diagnosis and should continue to qualify for this procedure. Within this group of women a concentrated effort to monitor women aged 40 years and over should be made as the logical first step in meeting the goal of primary prevention in Montreal. This relatively small group of women still contributes 15% of the cases and has the highest risk of having an affected child. Furthermore, the noted rise in their 1975-76 age-specific rate makes them prime candidates for screening. Physicians should be informed of the prenatal diagnostic services available and the risks associated with pregnancies in older women. Unless the women themselves are refusing the service, the failure to effectively prevent Down syndrome in these high risk women must be evaluated carefully in terms of the feasibility of increasing the effectiveness of prenatal diagnosis by extending services to women under 35 years of age.

The remediation or amelioration of the mental retardation of Down syndrome is, at present, a more difficult goal since, unlike primary prevention, an efficacious method has yet to

be established. Obviously, there are no easy solutions to this problem. The importance of ongoing evaluation of any treatment regimen purporting to affect development must be recognized. The difficulties encountered in such evaluations are not easily resolved, as the "seasonal bias" present in this study demonstrates. Yet, until such investigations are initiated and perfected, the effect of treatment approaches will remain ill-defined. The following proposals are offered as possible methods to delineate the critical variables which may contribute to the eventual remediation of Down syndrome.

1. The focus of this study was limited to the effects of short-term intervention on the development of Down syndrome infants. It is possible that the extension of the treatment into the pre-school years might produce different results than those reported here. Because it is difficult to withhold treatment in this program for a period longer than six months, prospective developmental measures at specific chronological ages, as defined by Carr (1970), during the first five years of life on all children participating in the Early Intervention Program will be collected. These scores could then be compared with control data collected for the same aged children being raised in the home but not receiving intervention.

2. Because the efficacy of early intervention may be dependent on a combination of variables, a multi-centre trial is suggested to help determine which factors under which circumstances are necessary to affect a positive change in the

developmental pattern of Down syndrome children. This design has been selected to increase the number of potential subjects and to obtain an answer to the question more quickly than if only one centre was involved. Several Canadian early intervention facilities for Down syndrome infants would be enlisted to follow a well defined protocol to evaluate the contributions of age at the time of intervention, intensity and site of treatment.

3. A pilot day-care program, similar to the Heber and Garber (1975) curriculum for culturally deprived infants, is proposed to evaluate the efficacy of intensive early intervention for Down syndrome infants. Consistency in the learning environment may provide the best means for altering the development of these children. As a substitute to institutionalization, this method of intervention would also offer an alternative form of care to parents that combines the benefits of home care while relieving some of the burden associated with the continuous care of a handicapped child. It may be that the application of early intervention as defined in this study lacked the intensity and consistency of a stimulating environment that an optimal day-care setting offers. Due to the findings with children "at risk" for retardation, the provision and evaluation of an intensive optimal learning environment for a select sample of mentally retarded infants seems warranted.

Treatment regimens for handicapped children have often

been based on subjective impressions and unproven theories rather than on the results of rigorous investigations. This lack of informative data has resulted in controversy and confusion surrounding the establishment of services for these children. Extensive and often expensive, both in terms of financial and parental commitment, treatment programs have been launched. The discontinuation of operational programs is always difficult. However, continued financial support for any treatment program should be contingent upon the establishment of an ongoing evaluation of outcome. And, the financial support for the initiation of new approaches should be restricted to those that have been demonstrated efficacious.

Two approaches to solving the problem of Down syndrome in Montreal have been presented in this thesis: the primary prevention through prenatal diagnosis and selective pregnancy termination and the remediation of the mental retardation of those children born alive. Neither approach, in isolation, offers the complete solution to the situation. Prenatal diagnosis, an efficacious method of primary prevention, suffers from underutilization; early intervention as a form of remediation has not, as yet, been proven efficacious. Given the effective delivery of amniocentesis for the purpose of prenatal diagnosis and an efficacious method of remediating mental retardation, the existing difficulties surrounding the

conception and subsequent birth of a Down syndrome child should be alleviated. Until that time, however, the search for both the means to improve the utilization of prenatal diagnosis and a proven method of postnatal remediation must continue. The necessity for combining the two processes is dictated by the rejection of a preventive technique dependent on elective abortion by certain individuals. Consequently, the combination of preventive and remediative procedures provides the most acceptable means of minimizing the impact of Down syndrome in a community.

McGill University

Department of Epidemiology and Health

APPENDIX A-1

LETTER TO CYTOGENETIC LABORATORIES

Dear Dr. :

I am a Ph.D. graduate student in the Department of Epidemiology and Health at McGill University and am presently involved in research with Down's syndrome infants. I am writing to you to request information concerning the identification of a birth cohort of Down's syndrome infants born alive in Montreal between January 1, 1975 through December 31, 1976. I am interested in identifying this birth cohort in order to ascertain (1) the type of care, i.e. natural home, foster home or institutional that is presently being provided for these children, and (2) the present incidence of Down's syndrome in Montreal. I would like to identify this birth cohort through records kept by the cytogenetic laboratories which provide karyotyping services for infants suspected of having Down's syndrome. It is for this reason that I am seeking your assistance.

I would be very grateful if you could provide the following information concerning all the children who were positively karyotyped as having Down's syndrome in your laboratory and who were born alive in Montreal between January 1, 1975 through December 31, 1976. The information requested includes: (1) The initials of both the first and the last name of the infant, (2) Date of birth of the infant, and (3) Sex of the infant. This identifying information is essential in order to prevent counting the same child more than once. Enclosed please find a form to report the above information and a self-addressed envelope. If your laboratory has not identified any Down's syndrome infants during this specific time period, please indicate this information and return the form in the envelope provided. Please accept my assurances that all information received will remain confidential and reporting of the data compiled will never be done by individual hospitals.

If you have any questions concerning the study or how the data will be used please feel free to contact me at 392-4297 or my supervisor Dr. I. Barry Pless, Director of Community Pediatric Research at The Montreal Children's Hospital, 937-8511, Local 466.

Thank you for you assistance.

Sincerely yours,

(Mrs.) Martha Piper

Postal address: 3775 University Street, Montreal, PQ, Canada H3A 2B4

McGill University

Department of Epidemiology and Health

APPENDIX A-2

Dr. :

Comme candidate au Ph.D. dans le département d'épidémiologie et santé de l'université McGill, je poursuis présentement des recherches sur les nourrissons affectés du syndrome de Down.

Je vous serais obligée de me fournir les renseignements, dont j'ai besoin, sur l'identité des bébés affectés du syndrome de Down et nés vivants à Montréal entre le 1er janvier 1975 et le 31 décembre 1976, c'est à dire, les initiales des nom et prénom(s); la date de naissance; et le sexe de l'enfant, ainsi que (1) le type de soins, soit en foyer naturel, nourricier ou établissement, dont bénéficient présentement ces enfants et (2) l'incidence actuelle du syndrome de Down à Montréal. Je pense que le moyen le plus efficace pour obtenir ces renseignements serait les dossiers tenus par les laboratoires de cytogénétique qui rendent les services de caryotypie aux enfants que l'on soupçonne d'être atteints du syndrome de Down.

Veuillez trouver ci-joint, la formule pour les renseignements, ainsi qu'une enveloppe déjà affranchie.

Si au cours de la période de temps spécifiée aucun bébé atteint du syndrome de Down ne s'est présente à votre laboratoire, veuillez l'indiquer sur la formule et me la retourner ainsi remplie. Soyez assuré(e) que tous les renseignements fournis resteront confidentiels et que le rapport sur la compilation des données ne sera jamais effectué par hôpital.

Si vous désirez de plus amples renseignements sur l'étude ou sur l'utilisation qui sera faite des données, n'hésitez pas à communiquer avec moi (392-4297) ou avec mon supérieur, le Dr. I. Barry Pless, directeur des recherches en pédiatrie communautaire à l'hôpital Montreal Children's (937-8511, poste 466).

En vous remerciant d'avance de votre aimable collaboration, je vous prie d'agréer, Docteur, l'expression de mes sentiments distingués.

(Mme) Martha Piper

Postal address: 3775 University Street, Montreal, PQ, Canada H3A 2B4

APPENDIX B-1

REPORTING FORM FOR DOWN SYNDROME CASES

DOWN'S SYNDROME INFANTS
(Born between January 1, 1975
through December 31, 1976)

If no positive karyotypes were performed please indicate and return this form.

INITIALS of Child's Name Family Name	SEX	DATE OF BIRTH

Responding Pathologist: _____ Date: _____

Hospital: _____

APPENDIX B-2

DEPARTEMENT D'EPIDEMIOLOGIE ET DE SANTE, UNIVERSITE MCGILL

BEBES ATTEINTS DU SYNDROME DE DOWN
(nés entre le 1er janvier 1975
et le 31 décembre 1976)

Si aucun bébé n'a reçu le caryotype, prière de l'indiquer et de retourner le formulaire.

INITIALES de l'enfant Prénom(s) Nom	SEXE	DATE OF NAISSANCE

Pathologiste: _____ Date: _____

Hôpital: _____

APPENDIX C-1

EXAMPLES OF INFANT ACTIVITIES. ADAPTED FROM THE CAROLINA INFANT CURRICULUM, FRANK PORTER GRAHAM CHILD DEVELOPMENT CENTER

PROPPING THE BABY SO HE CAN SEE BETTER

HOW

ADULT: Place the infant on the pillow so he is on his chest. Be sure his arms are in front of the pillow. Watch him carefully and help him if he slips. Rest him by turning him onto his back. Put some toys in front of him for him to see and play with. Or put him in front of a mirror so he can see himself. Talk about the things he can see.

INFANT: At first the infant will not hold his head up very long and will need to rest after a short time. Later he will hold it up longer. He will push with his legs at the same time and roll over sideways.

EQUIPMENT: Rolled blanket or prop pillow

WHY

GOAL: To help the baby hold his head up so he can see more. To help him use his hands better when he is on his stomach.

USES: The baby will be happier if he is able to look around and see more things. Later, he will need to have good head balance when he is on his stomach so he can crawl.

APPENDIX C-2

HELPING THE BABY TO SEE TALKING

HOW

ADULT: Hold your baby with his head cupped in your hands so he can see your face and lips. Lean toward him and make some sounds like "ahh - ahh", "oo", "eee", "m-m-m-m", "p-p-p-p". Give him time to make his own sounds. When he makes a sound by accident or intention laugh, pat, and praise him. When he is older hold him on your lap facing you.

INFANT: The baby will watch your face and lips, may smile and will enjoy the game but may not at first make any sounds. Eventually he will begin to imitate. He will be able to accurately repeat the sounds. He will be pleased with your attention and will smile at your praise.

WHY

GOAL: To teach the baby that sounds and mouth movement can go together. To get him to watch your face when you talk.

USES: The baby will need to know how to make mouth noises so he can talk.

APPENDIX D

DETAILS OF THE GRIFFITHS LOCOMOTOR SCALE (SCALE A)

FIRST YEAR

Items

First Three Months

The baby:

1. Lifts his chin up slightly when lying in the prone position.
2. Pushes with both feet against the examiner's hands.
3. Holds his head erect for a few seconds.
4. Lifts his head well up when lying prone.
5. Kicks his feet vigorously when put to lie down.
6. Is active in his bath, kicking his feet, etc.
7. Lifts his head up slightly when in the dorsal position.
8. Can roll from side to back.

Second Three Months

9. His back is firm when held in the sitting position.
10. Lifts his head and chest up when lying prone.
11. Holds his head erect continuously.
12. Lifts his head and shoulders when in dorsal position.
13. Can roll from one side right over to the other.
14. Plays with his toes.
15. First crawling reaction: Pushes on hands, draws up knees, etc.
16. Sits with slight support, e.g. can be left sitting among pillows in pram or cot.

Third Three Months

17. Can roll over from back to stomach or from stomach to back.
18. First stepping reaction (a): Moves feet alternately as if dancing when held up.
19. Tries vigorously to crawl, using both hands and feet (Crawling II).
20. Sits alone for a short while.
21. Stepping reaction (b): Feet now go definitely one in front of the other.
22. Can turn himself around when left lying on the floor (Crawling III).
23. Can be left sitting on the floor.
24. Crawling IV: Makes some progress, forwards or backwards.

Fourth Three Months

25. Stands when held up.
26. Sits well in a chair.
27. Can pull himself up from crawling or sitting, by grasping the furniture.
28. Can stand holding on to furniture.
29. Crawling V: Creeps on hands and knees, or gets about freely by some other method, e.g. bear walk.
30. Side-steps around inside cot or play-pen, holding on to railings, etc.
31. Can walk when led, adult holding one or both hands.

SECOND YEAR

First Three Months

The baby:

32. Climbs on to a ledge or step when crawling.
33. Can stand alone.
34. Walks alone, at first unsteadily.
35. Can kneel on floor or chair. Balances in this position.
36. Climbs the stairs, climbing up but not yet down.
37. Likes to walk pushing a pram, or toy horse, or other wheeled toy.

Second Three Months

38. He now trots about well.
39. Can stoop to pick up a toy without over-balancing.
40. Climbs into a low chair.
41. Can walk backwards.
42. Likes to walk pulling a toy on a string.

Third Three Months

43. Can climb stairs, up and down.
44. Can jump. Child gives a little jump when standing if pleased, etc., with both feet off floor together.
45. Runs. This is not a trot now, but a definite running.
46. Can now walk upstairs, no longer on hands and knees, but holding adult's hand, etc.
47. Climbs and stands up on a chair.

Fourth Three Months

48. Can jump off a step, both feet off the ground together.
49. Can seat himself at table, placing chair first.
50. Walks up and down stairs; has abandoned climbing, but still holds adult's hand or banisters.
51. Can kick a ball.
52. Can be trusted on stairs alone.

APPENDIX E

DETAILS OF THE GRIFFITHS PERSONAL-SOCIAL SCALE (SCALE)

FIRST YEAR

Items

First Three Months

The baby:

1. Regards persons--momentarily.
2. Is quieted if crying by being picked up.
3. Enjoys his bath.
4. Smiles.
5. Recognizes mother visually.
6. Vocalises when talked to.
7. Follows moving persons, especially the mother, with his eyes.
8. Returns the examiner's glance with smiling back or cooing.

Second Three Months

9. He is friendly to strangers.
10. He resists when the examiner tries playfully to take the ring or toy; he tries to hold on to it.
11. He frolics happily when played with.
12. He stops crying when talked to.
13. He now turns his head deliberately to a person talking or calling to him.
14. Makes anticipatory movements when mother goes to lift him up.
15. Holds on to a spoon.
16. Stretches his arms to be taken up.

Third Three Months

17. Drinks from a cup.
18. Manipulates spoon or cup in play.
19. Reacts to his own mirror image (I): Looks at it thoughtfully.
20. Knows strangers from familiar friends.
21. Shows prompt reaction to situations, e.g. at table.
22. Shows displeasure if toy is taken away.
23. Helps to hold cup for drinking (hands go round cup).
24. Pulls off his hat.

Fourth Three Months

25. Reacts to his own mirror image (II): smiles at or plays with it.
26. Waves bye-bye.
27. Shows affection. That is, gives back a show of affection.
28. Finger feeds, using fine prehension. Picks up small pieces of food.
29. Plays with cup, spoon and saucer in a way consistent with some understanding of function.
30. Obeys simple requests: "Give me the cup (toy, etc.)."
31. Plays "Pat-a-cake" (clapping).
32. Puts small objects in and out of cup or box in play.

SECOND YEAR

First Three Months

The baby:

33. Tries to help dressing, puts arm ready for coat, etc.
34. Can now hold cup for drinking (but is liable to spill a little).
35. Uses a spoon himself, but is not yet very efficient.
36. Shows shoes on request.

Second Three Months

37. Tries to turn a door-knob.
38. Cleanliness--asks when he needs attention.
39. Manages cup well--half full.
40. Can take off shoes and socks (if unfastened for him).
41. Likes adult to sit and show picture-book.

Third Three Months

42. Parts of body (I): Can indicate eyes, or nose, or hands, etc.
43. Cleanliness--bowel control complete.
44. Uses a spoon well, feeds himself.
45. Has complete bladder control by day, but not yet at night.
46. Tries to tell experiences.

Fourth Three Months

47. Asks for things at table in words--at least two articles.
48. Knows two parts of body by name.
49. Knows three parts of body by name.
50. Knows four parts of body by name.

APPENDIX F

DETAILS OF THE GRIFFITHS HEARING AND SPEECH SCALE (SCALE C)

FIRST YEAR

Items

First Three Months

The baby:

1. Is startled by sounds.
2. Is quieted by his mother's voice.
3. (Vocalization other than crying.) Makes murmured sounds.
4. Listens to a soft bell note near him.
5. Makes definite cooing noises, one syllable.
6. Searches for sounds with eye movements.
7. Listens to music.
8. Makes two or more different sounds.

Second Three Months

9. Searches for sound with head movements.
10. Laughs aloud.
11. Turns his head deliberately to the bells.
12. Listens to tuning-fork.
13. Coos or stops crying on hearing music.
14. Talks (babbles) to persons.
15. Manipulates the handbell.
16. Makes four or more different sounds. (Separate single sounds or syllables.)

Third Three Months

17. Responds when called.
18. Uses two-syllable babble.
19. Shouts for attention.
20. Listens to conversations.
21. Uses singing tones.
22. Uses babbled phrases of four or more syllables.
23. Says "Mama", or "Dada", etc. One word clear.
24. Listens to a stop-watch.

Fourth Three Months

25. Shakes head for "No!"
26. Now says two clear words. Two words clear.
27. Uses short babbled sentences. (Meaningful babble.)
28. Rings the bell.
29. Reacts to music vocally.
30. Babbled monologue when alone.
31. Says three clear words.

SECOND YEAR

First Three Months

The baby:

32. Tries to sing.
33. Looks at pictures for a short while.
34. Knows his own name.
35. Likes nursery rhymes and jingles.
36. Uses four or five clear words.

Second Three Months

37. One object in the box is identified when named by the examiner.
38. Uses six or seven clear words.
39. Makes long babbled conversations, with some words clear.
40. Enjoys a picture-book.
41. Two objects in the box are identified.
42. Uses nine clear words.
43. Four objects in the box are identified.
44. Vocabulary--twelve clear words.
45. Picture vocabulary--one picture named.
46. Uses word combinations.
47. Picture vocabulary--two pictures named.

Fourth Three Months

48. Listens to stories.
49. Vocabulary--twenty words clear.
50. Identifies eight objects in the box when named by the examiner.
51. Names four toys.
52. Uses sentences of four or more syllables.

APPENDIX G

DETAILS OF THE GRIFFITHS HAND AND EYE SCALE (SCALE D)

FIRST YEAR

Items

First Three Months

The baby:

1. Follows a moving light with the eyes.
2. Looks at the ring or toy momentarily when it is held up in front of him.
3. Looks steadily at the ring held still.
4. Follows the moving ring when swung horizontally.
5. Follows the ring vertically.
6. Glances from one object to another.
7. Follows the moving object in a circle.
8. Watches an object pulled along on the table surface by a string.

Second Three Months

9. Grasps a ring when given it.
10. Visually explores a new environment.
11. Reaches for ring and grasps when offered.
12. Carries the ring to his mouth.
13. Clutches at the dangling ring.
14. Secures the dangling ring.
15. His hands explore the table surface when he is held sitting near the table.
16. Plays with the ring after he has secured it, waving it or banging on table, etc.

Third Three Months

17. Reaches for and picks up the string tied to the moving object.
18. Looks for a dropped toy.
19. Strikes one object or surface with another.
20. Watches examiner scribble on paper.
21. Secures the ring or toy by means of the string.
22. Forefinger and thumb are partly specialized.
23. Fine prehension.
24. Having secured the ring or toy, he dangles it by the string.

Fourth Three Months

25. Plays pulling the ring or toy along by the string.
26. Throws objects. (This is a deliberate throw, not just dropping.)
27. Thumb opposition is complete.
28. Child can point with the index finger.
29. Interested in toy motor-car. Goes after it, picks it up, etc.
30. Can hold a pencil as if to mark on paper.
31. Uses a pencil on paper a little. Makes some kind of mark.

SECOND YEAR

First Three Months

The baby:

32. Likes holding little toys continuously in his hands.
33. Shows preference for one hand. Right- or left-handed.
34. Plays rolling a ball.
35. Can hold four cubes at once, two in each hand.
36. Plays pushing little cars around.

Second Three Months

37. Places one lid, box or brick upon another.
38. Scribbles more freely.
39. Pulls paper or cloth to get toy.
40. Enjoys constructive play with boxes, lids and cubes.
41. Builds a tower of three bricks.

Third Three Months

42. Can throw a ball.
43. Builds a tower of four bricks.
44. Enjoys vigorous straight scribble.
45. Can pour water from one cup to another. (No spilling.)
46. Uses a pencil freely, circular scribble. (May be shown this.)
47. Builds a tower of five or more bricks.

Fourth Three Months

48. Makes a perpendicular stroke with the pencil, after shown.
49. Makes a train of three or more bricks.
50. Throws a ball into a basket. (Waste-paper basket, box or bucket.)
51. Makes a brick or toy walk. (Imitation.)
52. Makes a horizontal stroke with the pencil.

APPENDIX H

DETAILS OF THE GRIFFITHS PERFORMANCE SCALE (SCALE E)

FIRST YEAR

Items — First Three Months

The baby:

1. Grasps examiner's finger and holds on for a short time.
2. Reacts to paper on face--I: Generalized physical movements.
3. Hand goes to mouth, sucks fingers, etc.
4. Waves arms energetically.
5. Reacts to paper on face--II: Vigorous head turning.
6. Holds doll.
7. Plays with own fingers.
8. Looks at box on table.

Second Three Months

9. Resists examiner who tries gently to take the doll away.
10. Clasps a cube that is put into his hand, and holds on to it.
11. Drops the first cube when a second one is offered.
12. Reacts to paper on face--III; Pulls it away.
13. Shows interest in box, tries to take hold of it, etc. (Test box.)
14. Picks up a toy from the table.
15. Holds two objects, one in each hand.
16. Grasps the box when given. (Test box.)

Third Three Months

17. Manipulates cube or toy, puts in mouth, etc.
18. Reacts to paper--IV: Reaches for paper held out in front of him, and secures it.
19. Passes toy from one hand to the other.
20. Drops one cube or toy when a third one is offered.
21. Manipulates two objects at once--two toys, one in each hand.
22. Plays with paper--V: Observed by examiner.
23. Lifts inverted box in search of toy.
24. Rattles the box.

Fourth Three Months

25. Clicks two bricks together. (Imitation.)
26. Takes the lid off the box.
27. Finds the toy under the box.
28. Tries to take the cubes out of the box.
29. Takes the third cube, when offered, without dropping the others.
30. Removes both cubes from the box. (Second one shown if necessary.)
31. Manipulates the box, lid and cubes.

SECOND YEAR

First Three Months

The baby:

32. Upwraps and finds toy.
33. Puts one circle into circle board. Two trials allowed.
34. Opens two boxes.
35. Puts two cubes back into the box when encouraged to do so.
36. Two-circle board. One circle in. Two trials.
37. Puts cubes in and out of boxes in play.

Second Three Months

38. Puts square into the square board. Two trials.
39. Two-circle board. Puts both circles in. Two trials.
40. Can put the lid back on the test box.
41. Three-hole board. One inset placed correctly. Two trials.
42. Puts two cubes into any one test box, lid on, all complete.

Third Three Months

43. Does circle and square board together. Two trials.
44. Three-hole board. Two insets correctly placed. Two trials.
45. Three-hole board. Three in. Two trials.
46. Two-circle board, rotated. Two trials.

Fourth Three Months

47.
48. Circle and square boards rotated. (Credit 2 points.)

49. Assembles three boxes, lids on, all complete, but not yet
50. for colour. (Credit 2 points.)

51.
52. Can open screw-toy. (Credit 2 points.)

APPENDIX I

HOME OBSERVATION FOR MEASUREMENT OF THE ENVIRONMENT (HOME) INVENTORY

		YES	NO
I.	**EMOTIONAL AND VERBAL RESPONSIVITY OF MOTHER**		
1.	Mother spontaneously vocalized to child at least twice during visit (excluding scolding)	___	___
2.	Mother responds to child's vocalizations with a verbal response.	___	___
3.	Mother tells child the name of some object during visit or says name of person or object in a "teaching" style.	___	___
4.	Mother's speech is distinct, clear, and audible.	___	___
5.	Mother initiates verbal interchanges with observer--asks questions, makes spontaneous comments.	___	___
6.	Mother expresses ideas freely and easily, and uses statements of appropriate length for conversation (e.g., gives more than brief answers).	___	___
7.	Mother permits child occasionally to engage in "messy" types of play.	___	___
8.	Mother spontaneously praises child's qualities or behavior twice during visit.	___	___
9.	When speaking of or to child, mother's voice conveys positive feeling.	___	___
10.	Mother caresses or kisses child at least once during visit.	___	___
11.	Mother shows some positive emotional responses to praise of child offered by visitor.	___	___
	SUBSCORE		

	YES	NO

II. AVOIDANCE OF RESTRICTION AND PUNISHMENT

12.	Mother does not shout at child during visit.	___	___
13.	Mother does not express overt annoyance with or hostility toward child.	___	___
14.	Mother neither slaps nor spanks child during visit.	___	___
15.	Mother reports that no more than one instance of physical punishment occurred during the past week. When do you use physical punishment, and how often do you use it.	___	___
16.	Mother does not scold or derogate child during visit.	___	___
17.	Mother does not interfere with child's actions or restrict child's movements more than three times during visit.	___	___
18.	At least ten books are present and visible.	___	___
19.	Family has a pet.	___	___

SUBSCORE

III. ORGANIZATION OF PHYSICAL AND TEMPORAL ENVIRONMENT

20.	When mother is away, care is provided by one of three regular substitutes.	___	___
21.	Someone takes child into grocery store at least one time a week. "Do you take the child shopping with you?"	___	___
22.	Child gets out of house at least four times a week.	___	___
23.	Child is taken regularly to doctor's office or clinic.	___	___
24.	Child has a special place in which to keep his toys and "treasures".	___	___
25.	Child's play environment appears safe and free of hazards. Crib--Where does child play most of the time. Is he left alone, and where.	___	___

SUBSCORE

		YES	NO
	IV. PROVISION OF APPROPRIATE PLAY MATERIALS		
26.	Child has some muscle activity toys or equipment. "What kind of toys does your child have?"	___	___
27.	Child has push or pull toys.	___	___
28.	Child has stroller or walker, kiddie car, scooter or tricyle.	___	___
29.	Mother provides toys or interesting activities for child during interview.	___	___
30.	Provides learning equipment appropriate to age--cuddly toy? or role-playing toys.	___	___
31.	Provides learning equipment appropriate to age--mobile, table and chairs, high chair, play pen.	___	___
32.	Provides eye-hand coordination toys--items to go in and out of receptacle, fit together toys, beads.	___	___
33.	Provides eye-hand coordination toys that permit combinations--stacking or nesting toys, blocks or building toys.	___	___
34.	Provides toys for literature and music.	___	___
	Does your child like to listen or look at books.	___	___
	SUBSCORE		
	V. MATERNAL INVOLVEMENT WITH CHILD		
35.	Mother tends to keep child within visual range and to look at him often.	___	___
36.	Mother "talks" to child while doing her work.	___	___
37.	Mother consciously encourages developmental advance.	___	___
	What do you think your child should be doing next?	___	___
38.	Mother invests "maturing" toys with value via her attention.	___	___
39.	Mother structures child's play periods.	___	___
	Do you have a special time set aside to play with your child.	___	___
40.	Mother provides toys that challenge child to develop new skills.	___	___
	Select a toy and ask mother purpose of toy.	___	___
	SUBSCORE		

VI. OPPORTUNITIES FOR VARIETY IN DAILY STIMULATION	YES	NO
41. Father provides some caretaking every day.	___	___
"Does your husband bathe the baby, feed the baby, etc."	___	___
42. Mother reads stories at least three times weekly.	___	___
How often do you read to your child or show your child pictures in a book.	___	___
43. Is your child present when the family eats.	___	___
Child eats at least one meal per day with mother and father.	___	___
44. Family visits or receives visits from relatives.	___	___
Do you have family in Montreal?	___	___
Do they visit you, or visit them.	___	___
45. Child has three or more books of his own.	___	___
SUBSCORE		

APPENDIX J

CATEGORIZATION OF MATERNITY HOSPITALS AS FRENCH OR ENGLISH

French

(1) Centre Hospitalier de Lachine
(2) Centre Hospitalier de Lasalle
(3) Centre Hospitalier de Maisonneuve-Rosement
(4) Centre Hospitalier Sainte Jeanne d'Arc
(5) Centre Hospitalier de Verdun
(6) Hôpital Bellechase
(7) Hôpital Jean-Talon
(8) Hôpital Général Fleury Inc.
(9) Hôpital Notre Dame
(10) Hôpital du Sacré-Couer
(11) Hôpital Sainte-Justine
(12) Hôpital Saint-Luc
(13) Hôpital Saint-Michel
(14) Hôpital Santa Cabrini

English

(1) Jewish General Hospital
(2) Lachine General Hospital Centre
(3) Lakeshore General Hospital
(4) Montreal General Hospital
(5) Royal Victoria Hospital
(6) St. Mary's Hospital

McGill University

Department of Epidemiology and Health

APPENDIX K-1

LETTER TO DIRECTOR OF PROFESSIONAL SERVICES

May 9, 1978

Dear Dr. _____:

I am a Ph.D. graduate student in the Department of Epidemiology and Health at McGill University and am presently involved in research with Down syndrome infants. One aspect of the research is the evaluation of the efficacy of an early intervention program for these children. I have recently identified those Down syndrome children who were born on the Island of Montreal between January 1, 1975 and December 31, 1976. I am now collecting demographic data on these children in order to compare two groups of children within the cohort: those children who are receiving an early intervention program and those children who are not receiving such a program. The demographic factors upon which the comparision is being made are:

1. Maternal birth date/age at the time of the birth of the infant
2. Birth weight
3. Gestational age
4. Presence or absence of congenital heart disease
5. Number of sibs

I am writing to you to request permission to obtain the above information from medical records on those children who have been identified as having been born at _____. Please accept my assurances that all information received will remain confidential and reporting of the data compiled will never be done by individual child or hospital.

I have enclosed a form with a self addressed envelope listing the individual child's family name, sex and birth date. I would be most grateful if your hospital could provide me with this data. If it would be more convenient for you, I would be willing to come to the hospital to collect the data.

If you have any questions concerning the study or how the data will be used please feel free to contact me at 392-8053 or my supervisor Dr. I. Barry Pless, Director of Community Pediatric Research at The Montreal Children's Hospital, 937-8511, Local 466.

Thank you for your assistance.

Yours very truly,

(Mrs.) Martha Piper

Postal address: 3775 University Street, Montreal, PQ, Canada H3A 2B4

McGill University

Department of Epidemiology and Health

APPENDIX K-2

Le 22 mai 1978

Dr.

En tant qu'étudiante de doctorat au département d'épidémiologie et de la santé de l'université McGill, je pursuis actuellement des recherches sur le syndrome de Down chez les jeunes enfants. Un des aspects de la recherche consiste à évaluer l'efficacité d'un programme d'intervention appliqué à un stade précoce chez ces enfants. J'ai récemment relevé le nom de tous les enfants atteints du syndrome de Down et nés sur l'Ile de Montréal entre le ler janvier 1975 et le 31 décembre 1976. Je m'efforce actuellement de réunit des données démographiques sur ces mêmes enfants afin d'établir des comparaisons entre deux groupes d' enfants appartenant à l'ensemble, soit un premier groupe où les enfants bénéficient d'un programme d'intervention précoce et un deuxième groupe où les enfants ne bénéficient pas de ce programme. Les données démographiques servant de base àl'établissement des comparaisons sont les suivantes:

(1) Date de naissance/âge de la mère au moment de la naissance de l'enfant
(2) Poids à la naissance
(3) Durée de la gestation
(4) Présence ou absence de maladie cardiaque congénitale
(5) Nombre de frères et soeurs

Le but de ma lettre est de vous demander l'autorisation d'avoir accès aux dossiers médicaux des enfants nés a Hôpital du Sacré-Couer, afin de réunir les renseignements mentionnés. Soyez assuré que tous ces renseignements resteront strictment confidentiels et que jamais le nom de l'enfant ou de l'hôpital ne figurera dans les rapports utilisant les données rassemblées.

Vous trouverez ci-joint une formule comportant le nom de famille de chaque enfant, son sexe et sa date de naissance et accompagnée d'une enveloppe préadressée. Je vous serais très reconnaissante si votre hôpital pouvait me fournir ces informations. Je suis toute disposée à venir chercher ces renseigne,ents à l'hôpital même, si cela peut vous faciliter les choses.

Si vous souhaitez me poser des questions sur cette étude ou sur la façon dont les données seront traitées, je reste à votre

Postal address: 3775 University Street, Montreal, PQ, Canada H3A 2B4

entière disposition pour y répondre; veuillez à cette fin me téléphoner au 392-8053 ou contacter mon directeur de recherche, le docteur I. Barry Pless, directeur de la recherche pédiatrique communautaire àl'hôpital Montreal Children's, 937-8511 poste 466.

Je vous remercie de votre aimable collaboration et vous prie de croire, Docteur, en l'assurance de ma considèration.

(Mme) Martha Piper

APPENDIX L-1

DEMOGRAPHIC DATA - DOWN SYNDROME CASES

Name	Birth Date	Sex	Maternal Birth Date/ Age	Birth Weight	Gestational Age	No. of Sibs (Prior to Case)	Congenital Heart Disease (Yes or No)

APPENDIX L-2

DONNEES DEMOGRAPHIQUES - SYNDROME DE DOWN

Nom	Date de naissance	Sexe	Date de naissance âge de la mère	Poids à la naissance	Durée de la gestation	Nbre de frères et soeurs (nés avant le sujet étudié)	Maladie cardiaque congénitale (OUI ou NON)

APPENDIX M

DATA FOR TRIAL SUBJECTS ON BOTH INDEPENDENT AND DEPENDENT VARIABLES

Patient No.	Sex	Maternal Age	Birth Weight (grams)	Number of Sibs	Congenital Heart Disease	Residential Care	Chronological Age (months)	Home - Total	Home - Emotional	Home - Punish	Home - Environment	Home - Play	Home - Involve	Home - Variety	Pre-Total	Pre-Locomotor	Pre-Personal Social	Pre-Speech	Pre-Hand & Eye	Pre-Performance	Change - Total	Change - Locomotor	Change Personal - Social	Change Speech	Change Hand & Eye	Change Performance
EXPERIMENTALS																										
1	1	41	2579	3	1	1	15.00	30	10	8	3	5	2	2	70	71	80	85	61	51	-06	-15	-13	-15	+03	+14
2	1	27	2800	2	2	1	3.90	19	6	6	4	2	0	1	86	89	96	110	75	61	-04	-27	-03	-44	+18	+25
3	2	41	2557	3	2	1	13.62	44	10	8	6	9	6	5	91	92	93	109	90	71	-03	-09	+09	-20	-01	+06
4	1	28	2438	0	1	1	5.69	29	5	7	5	8	3	1	72	75	80	70	70	65	-17	-11	-28	-41	+04	-10
5	2	32	2700	1	2	1	7.23	35	10	8	4	7	5	1	81	80	80	93	80	72	-22	-21	-30	-20	-16	-24
6	1	38	4090	1	1	1	4.69	36	9	7	4	8	6	2	83	70	100	82	82	82	+03	+05	-05	+05	-02	+13
7	2	28	2000	1	1	1	4.69	32	10	7	5	4	3	3	77	76	82	88	70	70	+01	-20	+05	+03	+09	+09
8	2	27	4500	1	1	1	6.23	38	11	6	6	7	4	4	69	74	71	82	59	59	-02	+03	+08	+02	-08	-12
9	2	23	3330	0	1	1	13.69	28	5	6	4	8	1	4	74	65	81	83	71	71	-09	-11	-18	-09	+05	-14
10	1	41	3590	1	1	1	10.85	33	7	7	4	8	4	3	72	64	64	88	74	71	-12	-07	-03	-16	-19	-16
11	2	29	2850	0	1	2	20.00	34	11	7	5	5	3	3	65	71	68	74	63	48	-12	-13	-10	-16	-10	-10
12	1	30	2500	2	1	1	4.23	21	7	7	3	1	1	2	94	95	95	88	95	95	-12	+18	-25	-22	-12	-18
13	2	26	2955	1	1	1	17.00	28	11	6	4	2	2	3	71	65	79	75	72	63	-04	-01	-11	-10	+04	00
14	1	23	2841	1	2	1	6.92	23	5	8	4	2	1	3	84	78	87	87	96	74	-06	-17	+01	-05	-17	+08
15	1	22	2610	0	1	1	2.77	30	9	5	6	5	2	3	95	90	106	90	90	98	-01	+16	-08	+08	-04	-17
16	2	26	3515	0	1	1	3.60	35	11	7	6	5	4	2	95	96	103	82	103	89	-15	-20	-27	+09	-16	-21
17	2	27	3027	2	2	1	5.31	16	4	6	3	2	0	1	85	85	90	90	85	74	-17	-19	-14	-07	-19	-24

APPENDIX M
(CONTINUED)

18	2	31	2386	1	1	1	3.46	41	11	7	6	6	6	5	88	85	85	85	85	100	+10	+14	+26	+10	+07	-05
19	1	30	3170	0	2	2	9.70	33	10	7	3	8	2	3	76	91	95	64	71	106	-12	-21	-25	-04	-06	-03
20	1	47	2215	0	1	2	23.80	38	11	7	6	7	5	2	66	70	71	65	67	56	-01	-07	+01	-04	-04	+09
21	1	22	2306	0	2	1	3.46	32	9	7	5	5	3	3	73	78	71	86	42	86	-13	-22	-02	-35	+27	-30
CONTROLS																										
1	1	29	2863	1	2	1	6.23	17	5	7	3	0	1	1	80	85	80	75	90	70	-06	+08	-13	-02	-20	-03
2	2	25	3239	0	1	1	4.23	32	9	7	6	5	2	3	118	127	121	114	127	101	-24	-12	-21	-18	-39	-32
3	2	29	4110	3	1	1	6.87	16	4	7	2	0	1	2	72	74	72	81	68	66	-04	+11	-07	-11	-05	-07
4	1	38	3775	2	1	1	2.46	27	8	8	4	3	2	2	91	100	109	91	72	81	+03	-14	-14	+14	+23	+09
5	2	28	2860	1	1	2	11.69	34	11	7	5	5	3	3	54	53	53	53	60	53	+11	+16	+12	+20	+02	+05
6*	1	27	1818	0	2	1	15.00	38	11	6	6	8	6	1	68	74	77	78	62	51	-01	-06	+03	-08	+03	00
7	1	31	2890	0	1	1	6.23	37	10	7	5	7	3	5	81	80	94	85	75	70	-03	-06	-04	-08	+08	-06
8	2	24	2841	0	1	1	2.31	17	5	7	3	1	0	1	89	100	82	90	82	90	-04	-07	+03	+03	+03	+07
9	2	24	2500	1	2	1	22.00	26	8	6	6	2	1	3	72	75	74	72	77	64	+02	+05	-01	-01	00	+05
10*	2	29	2600	2	2	1	1.46	27	8	6	5	4	1	3	102	109	109	98	87	109	-19	-17	-25	-14	-03	-38
11	1	36	3125	1	1	1	5.77	22	7	7	4	2	0	2	59	40	60	60	70	65	-15	+08	-16	-33	-15	-21
12	2	38	3120	2	1	1	8.77	41	11	8	6	7	6	3	84	92	79	88	88	75	-03	-03	-00	-05	-15	+04
13	1	36	3409	0	2	1	7.70	32	9	6	4	8	2	3	96	87	105	97	97	93	-12	-02	-20	-12	-15	-08
14*	2	25	2610	0	2	1	3.20	17	1	6	5	2	1	2	78	78	86	86	54	86	-03	-04	-03	-12	+25	-21
15	2	19	2440	0	1	1	10.00	25	10	6	3	2	2	2	66	62	62	69	62	73	-14	-03	-11	-13	-14	-27
16	2	39	3640	0	1	1	10.90	20	5	6	5	2	0	2	68	64	74	98	57	49	-03	-12	-04	-21	+08	+13

*Mosaic Infants

APPENDIX N

DATA TO ASSESS REPRESENTATIVENESS OF SAMPLE

Patient Number	Hospital of Birth	Maternal Age	Birth Weight (Grams)	Congenital Heart Disease	Number of Sibs	Resi-dential Care	Sex
EIP GROUP							
1	1	28	2810	1	1	1	1
2	2	41	2579	1	3	1	1
3	1	27	2727	2	1	1	1
4	2	29	4110	1	3	1	2
5	2	27	4500	1	1	1	2
6	1	27	1814	2	0	2	1
7	1	23	3330	1	0	1	2
8	1	41	3450	1	1	1	1
9	1	27	4090	1	3	1	1
10	1	29	2850	1	0	2	2
11	2	24	2500	2	1	1	2
12	1	21	3272	2	1	1	1
13	1	27	2800	2	2	1	1
14	1	28	2438	1	0	1	1
15	1	32	2700	2	1	1	2
16	1	29	2863	2	1	1	1
17	1	28	2860	1	1	2	2
18	2	38	3540	1	1	1	1
19	2	28	2000	1	1	1	2
20	1	25	3239	1	0	1	2
21	2	47	2215	1	0	2	1
22	1	30	2500	1	2	1	1
23	2	32	2386	2	0	1	2
24	1	31	2890	1	0	1	1

APPENDIX N
(CONTINUED)

Patient Number	Hospital of Birth	Maternal Age	Birth Weight (Grams)	Congenital Heart Disease	Number of Sibs	Resi-dential Care	Sex
NON-EIP GROUP							
1	2	21	2080	2	2	3	1
2	1	40	3990	1	9	2	2
3	2	38	3543	1	3	3	1
4	2	29	2580	1	0	1	2
5	1	42	2350	1	1	2	2
6	1	30	2770	2	3	1	1
7	2	19	3061	1	0	1	1
8	1	28	3720	1	1	3	1
9	2	38	2970	2	2	1	1
10	2	26	3147	1	2	3	1
11	2	28	2693	1	0	1	1
12	1	25	2805	1	1	3	1
13	2	29	1430	1	1	2	1
14	2	44	3110	1	6	1	1
15	2	34	3895	1	1	2	1
16	1	40	3300	2	2	1	1
17	2	36	2977	2	3	1	1
18	1	24	3300	1	0	1	2
19	2	43	2780	1	1	2	1
20	1	29	2350	2	1	1	2
21	1	27	2770	2	0	1	1
22	1	23	2700	2	0	3	1
23	1	24	2550	1	0	2	2
24	2	34	3790	1	1	2	1
25	1	32	2300	1	4	2	1
26	1	35	3210	1	1	1	2

APPENDIX N
(CONTINUED)

Patient Number	Hospital of Birth	Maternal Age	Birth Weight (Grams)	Congenital Heart Disease	Number of Sibs	Residential Care	Sex
27	2	27	3080	1	2	1	2
28	2	38	3270	1	2	1	1
29	1	30	3180	1	2	3	2
30	2	34	2750	1	3	2	1
31	2	30	3430	1	2	2	2
32	2	43	2825	2	9	2	1
33	2	43	2910	2	2	3	1
34	2	29	3260	1	1	2	2
35	2	29	3380	1	2	1	1
36	2	17	1920	1	0	2	1
37	2	43	2780	1	1	1	2
38	2	30	3040	1	1	3	2
39	2	28	2570	1	0	2	1
40	2	29	3050	2	0	2	1
41	2	32	3190	2	1	3	1
42	2	35	3523	1	1	2	1
43	1	23	2650	1	0	1	1
44	1	28	3090	1	2	1	2
45	2	35	3250	1	1	1	1
46	2	25	3380	1	0	3	1
47	1	30	3530	2	0	2	2
48	1	34	3180	1	1	2	2

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