The Preventability of Down's Syndrome

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DOWN'S syndrome (mongolism) presents a problem of growing magnitude in developed countries. The syndrome accounts for at least one-fifth, and probably as much as one-third, of the prevalence of severe mental retardation among children and young adults (*1,2*). Fifty years ago the proportion was more like one-tenth (3).

The estimated rise in prevalence cannot be attributed to a rise in the incidence of Down's syndrome at birth since incidence at birth appears to be remarkably stable through time and across countries. There is reason to think that a predictable number of affected infants will be born each year in populations as disparate as those of Great Britain, Israel, Japan, Australia, and the black and white populations of the United States (*4–8*).

In part, the rise in the prevalence of Down's syndrome is relative to other causes of mental retardation and can probably be attributed to a decline in the incidence of other causes (*1,9*). There has been, however, an absolute rise over time in the prevalence of the syndrome among successive birth cohorts because of an increased expectation of life in the persons affected (*10, 11*). Between 1940 and 1960, the life expectancy at birth of persons with Down's syndrome is estimated to have risen from about 12 to about 16 years in England and in Australia. Surveys elsewhere indicate that approximately one-half of the infants with the syndrome now survive through childhood. After the age of 15, mortality rates are far lower than before that age.

Many persons with Down's syndrome now survive the respiratory diseases to which they were particularly likely to succumb in the past (*3*). Excepting certain malformations, and leukemia (from which about 1 percent of the persons with Down's syndrome die), the once-fatal hazards which are common among children with the syndrome are becoming amenable to treatment. Surgery corrects congenital abnormalities, vaccines protect against a growing number of infectious diseases, and better designed environments reduce accidents. By contrast, no available treatment will modify the organic brain impairment and the severe intellectual disability that accompanies Down's syndrome. Medical advances over the next decade may further increase the prevalence of the syndrome.

It is true that within the limits imposed by organic impairment, favorable circumstances can alleviate the social handicaps of survivors with Down's syndrome, lessen the degree of their social dependency, and help them to avoid the intellectual retardation fostered by poor institutional environments (*12–14*). But whatever is done, the survivors continue in a state of permanent dependence that imposes a severe burden on their families and on existing forms of social organization.

The goal of public health in such a situation must be prevention, and preferably primary pre-

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vention, that is, reduction of the incidence of the disorder by action taken before it becomes manifest. In a rational preventive approach, special attention is paid to groups that are at high risk. The only outstanding and well-established variation in Down's syndrome occurs in relation to maternal age at birth. Until the age of about 30, the risk that a woman will bear a liveborn child with Down's syndrome remains at a uniformly low level (less than 1 per 1,000). At 35 years, the risk is of the order of 3.5 per 1,000; at 40 years, 10 per 1,000; and after 45 years, 20 per 1,000, or 1 chance in 50. Women over 35 years of age are clearly a high-risk group.

The Contribution of Maternal Age

We have estimated the extent to which a program aimed at preventing births to the high-risk group of older mothers can be expected to reduce the frequency of Down's syndrome. In this effort, a model was developed, step by step, from the actual population trends of New York City over the preceding 15 years. Wherever assumptions are made in this model, they are supported by epidemiologic studies, albeit at other times and places. We used available demographic data for New York City from 1953 through 1967, including unpublished estimates of the city's population in the periods 1953–59 and 1961–67 provided us by the New York State Department of Health and publications of the Department of Health of New York City (*15*) and of the U.S. Bureau of the Census (*16*).

In the calculation on which figure 1 is based, the risk of bearing an affected child in each maternal age group was applied to all the births in New York City for each maternal age group. The incidence rates for the maternal age groups used in the calculations are taken from an Australian series of persons with Down's syndrome born in the period 1942–57. This series of 1,119 cases is the largest reported in the world literature for which the maternal age at birth is known, and the rates are consistent with most other series (*17, 18*). Penrose and Smith pointed out that, in the reliable reports available to them, the incidence of Down's syndrome at birth for each maternal age group had a high degree of stability. We believe, therefore, that our estimates give a reasonable representation of actuality. They were obtained by the application of the reliable Australian rates and were preferred to the rates from a series of births of infants with Down's syndrome reported in New York City (*19*). The New York data were taken from birth certificates and, although the expected trend in respect to maternal age was present, reporting is known to have been incomplete.

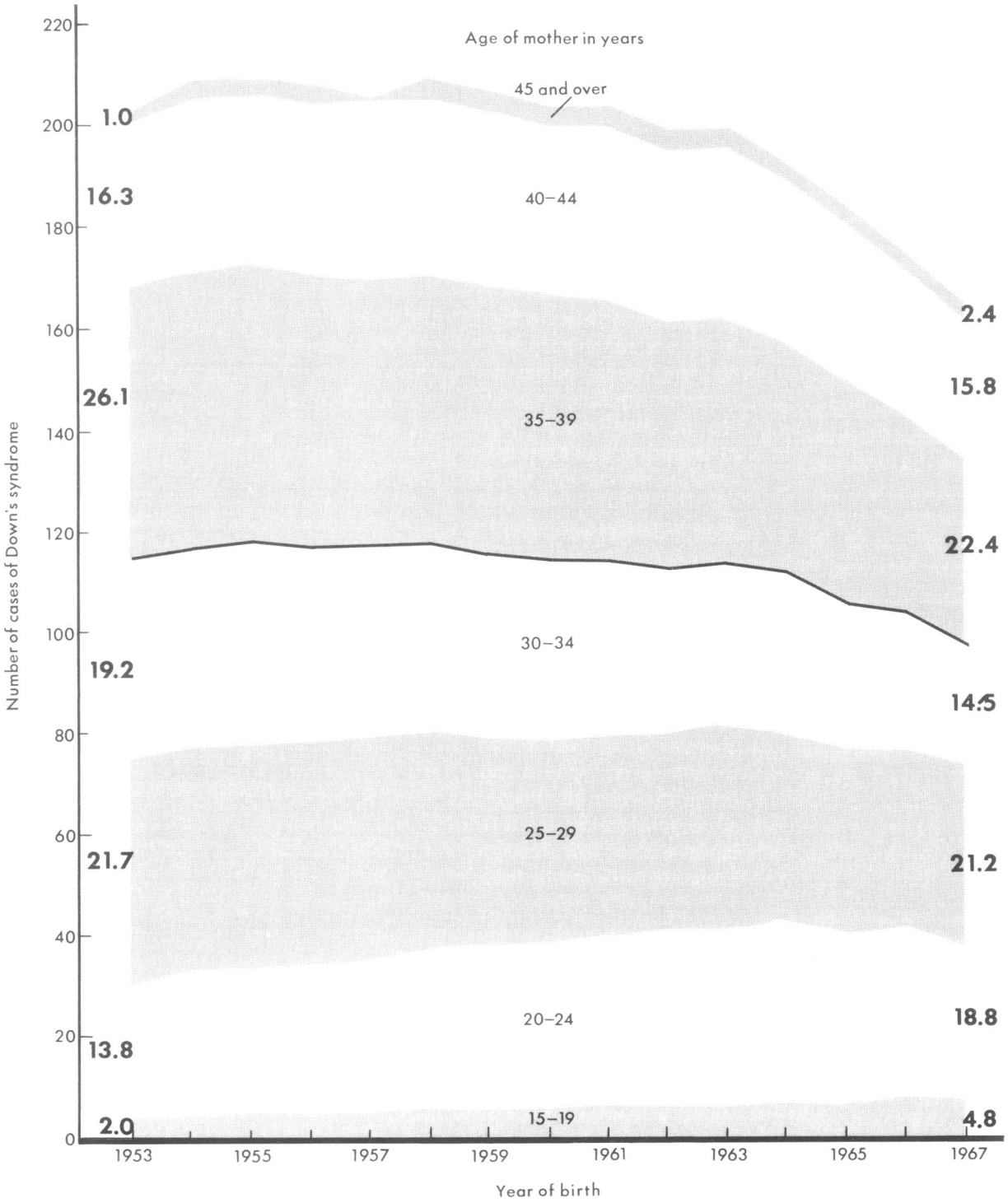
Incidence. We began with published data. From these data we could calculate the annual expected numbers of infants with Down's syndrome that would be born in New York City by maternal age. Figure 1 shows the estimated contribution made by women in each age group from 1953 through 1967. Figure 2 shows, in contrast, the contribution of each age group to total births and the much smaller contribution of older women. In 1953, women 40 years of age and over contributed an estimated 17 percent of the cases of Down's syndrome and only 2 percent of all births; in 1967, women of this age group still contributed 18 percent of cases and 2 percent of all births. In 1953, women 35 years of age and over contributed an estimated 43 percent of the cases of Down's syndrome and 11 percent of all births. In 1967, they still contributed 41 percent of the cases of Down's syndrome and 9 percent of all births.

Figures 1 and 2 emphasize the known contribution of high maternal age to the incidence of Down's syndrome at birth. To predict the ultimate effect of preventive action founded on this risk factor, however, we needed to know more. Other demographic factors, less malleable than the fertility rates of older women, could have affected the proportions of women in each maternal age group who bore children with the syndrome.

The following table shows that in New York City from 1953 to 1967 the estimated incidence rate of Down's syndrome per 1,000 live births fell about 10 percent. Was this fall the result of a decline in the fertility rates of older women?

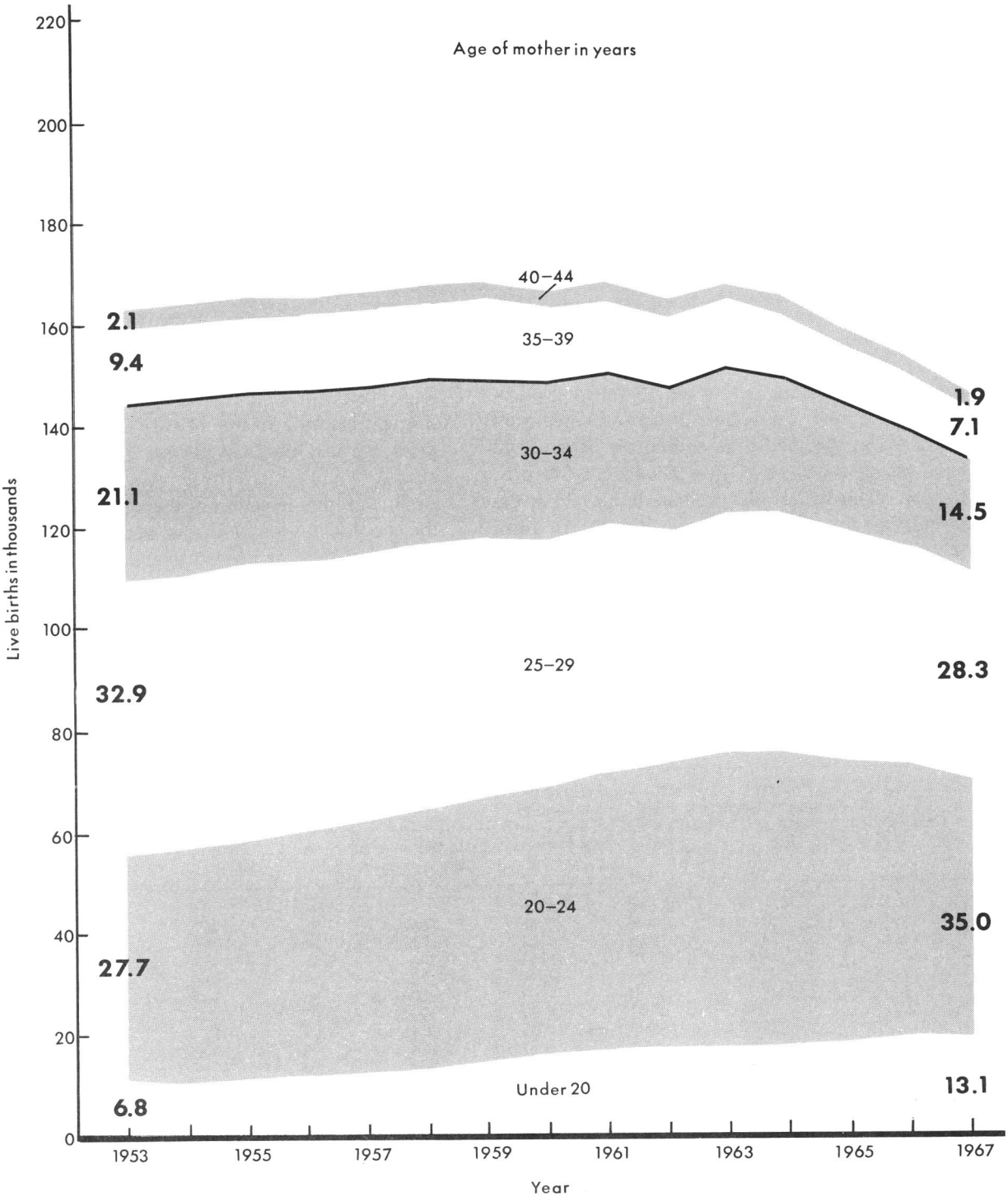
Year	*Rate*
1953	1.25
1954	1.27
1955	1.27
1956	1.26
1957	1.23
1958	1.25
1959	1.23
1960	1.23
1961	1.21
1962	1.20
1963	1.19
1964	1.16
1965	1.16
1966	1.13
1967	1.13

Figure 1. Contribution in numbers and percent of each maternal age group to total cases of Down's syndrome at birth in New York City, 1953–67



NOTE: Data are estimated from New York City births 1953–67 (*15*) and maternal age-specific incidence in Victoria, Australia, 1942–57 (*7*). Percentages are in boldface.

Figure 2. Contribution in numbers and percent of each maternal age group to total live births in New York City, 1953–67



NOTE: The age group 45 years and over is not shown separately because of its insignificant size. Percentages are in boldface.

SOURCE: Reference 15.

The preceding incidence rates per 1,000 live births are estimated from data on births at each maternal age in New York City in the period 1953–67 and from data shown in the following tabulation on the incidence at each successive maternal age in Victoria, Australia, in the period 1942–57.

Maternal age group (years)	*Rate*
15–19	0.43
20–24	.62
25–29	.83
30–34	1.15
35–39	3.50
40–44	9.93
45 and over	22.00

We assumed that the incidence of Down's syndrome at birth in New York City for each maternal age was constant during the 15-year period of study. Therefore, the decline in the estimated total incidence of the syndrome among all births could have been caused only by a decline in the proportion of births to older women and a rise in the proportion to younger women (fig. 2). In turn, the changed proportions of all births by maternal age could have been determined by either or both of two factors—the distribution of fecund (potentially fertile) women by age and the rates, by age, at which these women give birth (fertility rates).

To examine this question, we had to seek out unpublished data. Figure 3 shows the trends for the first factor, the age distribution of fecund women. Among women of child-bearing age in New York City, the proportion aged 35 through 44 years declined 6 percent from 1953 to 1967, while the proportion 15 through 24 years rose 10 percent. If constant fertility rates are assumed, the change in the distribution of fecund women by age could have brought about a decline of 8.8 percent in the incidence of Down's syndrome at birth.

Figure 4 shows the trends for the second factor, fertility rates. To our surprise, we found that the fertility rates of women 35 years and over had changed little in the period 1953–67. Among women under 25 years of age, however, there was an appreciable rise in fertility rates, followed by a fall. If the distribution of fecund women by age had been constant, these changes could have brought about a decline of only 2.4 percent in the incidence of Down's syndrome at birth. Thus the effect of changes in fertility rates on incidence was small and but a fraction of the effect of changes in the age-distribution of fecund women.

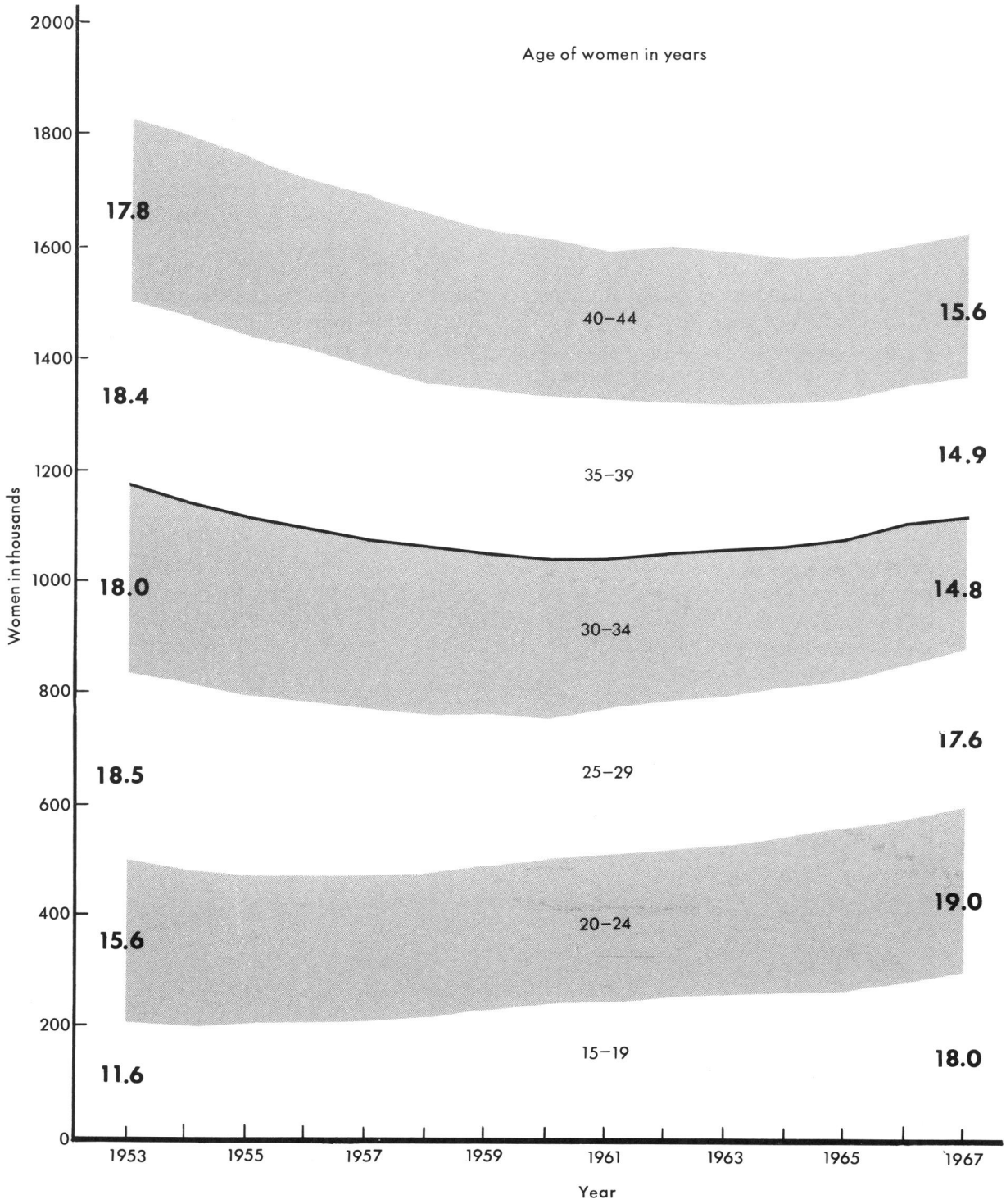
The 10 percent decline in the incidence rate of Down's syndrome accounts for part of the estimated 19 percent decline in the total number of births of infants with the syndrome in New York City, from 203 in 1953 to 165 in 1967 (fig. 1).

Numbers and proportions of children born with Down's syndrome in New York City, 1953–67, and surviving in 1969

Year of life	Percent dying during year of life	Percent surviving during year of life	Estimated probability of surviving x years	Estimated total number born with syndrome			Estimated number born to women 35 and over	
				Born per year	Surviving in 1969	Birth cohort	Born per year	Surviving in 1969
1	[1]0.3114	0.6886	0.6886					
2	.1594	.8406	.5788	165	96	1967	67	39
3	.0664	.9336	.5404	174	94	1966	70	38
4	.0482	.9518	.5144	184	95	1965	78	40
5	.0396	.9604	.4940	192	95	1964	80	40
6	.0070	.9930	.4905	200	98	1963	86	42
7	.0249	.9751	.4783	199	95	1962	86	41
8	.0097	.9903	.4737	204	97	1961	89	42
9	.0116	.9884	.4682	204	96	1960	89	42
10	.0144	.9856	.4614	207	96	1959	91	42
11	[2].0135	.9856	.4552	209	95	1958	91	41
12	.0135	.9856	.4490	205	92	1957	88	40
13	.0135	.9856	.4429	208	92	1956	91	40
14	.0135	.9856	.4369	209	91	1955	91	40
15	.0135	.9856	.4310	209	90	1954	92	40
16	.0135	.9856	.4252	203	86	1953	88	37
Total				2,972	1,408		1,277	604

[1] Observed age-specific mortality rates.
[2] Estimated age-specific mortality rates (average of observed mortality rates for survivors 6–10 years of age).
NOTE: The data were estimated from New York City births and from life tables for Victoria, Australia, 1942–57.

Figure 3. Contribution in numbers and percent of each age group to total women in New York City aged 15–44 years, 1953–67



NOTE: The age group 45 years and over is not included because of its insignificant contribution to the birth rate. Percentages are in boldface.

SOURCE: References 16 and 17.

The estimated decline in the numbers of births of infants with Down's syndrome was a consequence also of another demographic trend, a decline in the total number of fecund women in New York City (fig. 3). This decline resulted in a parallel decline in the total number of live births.

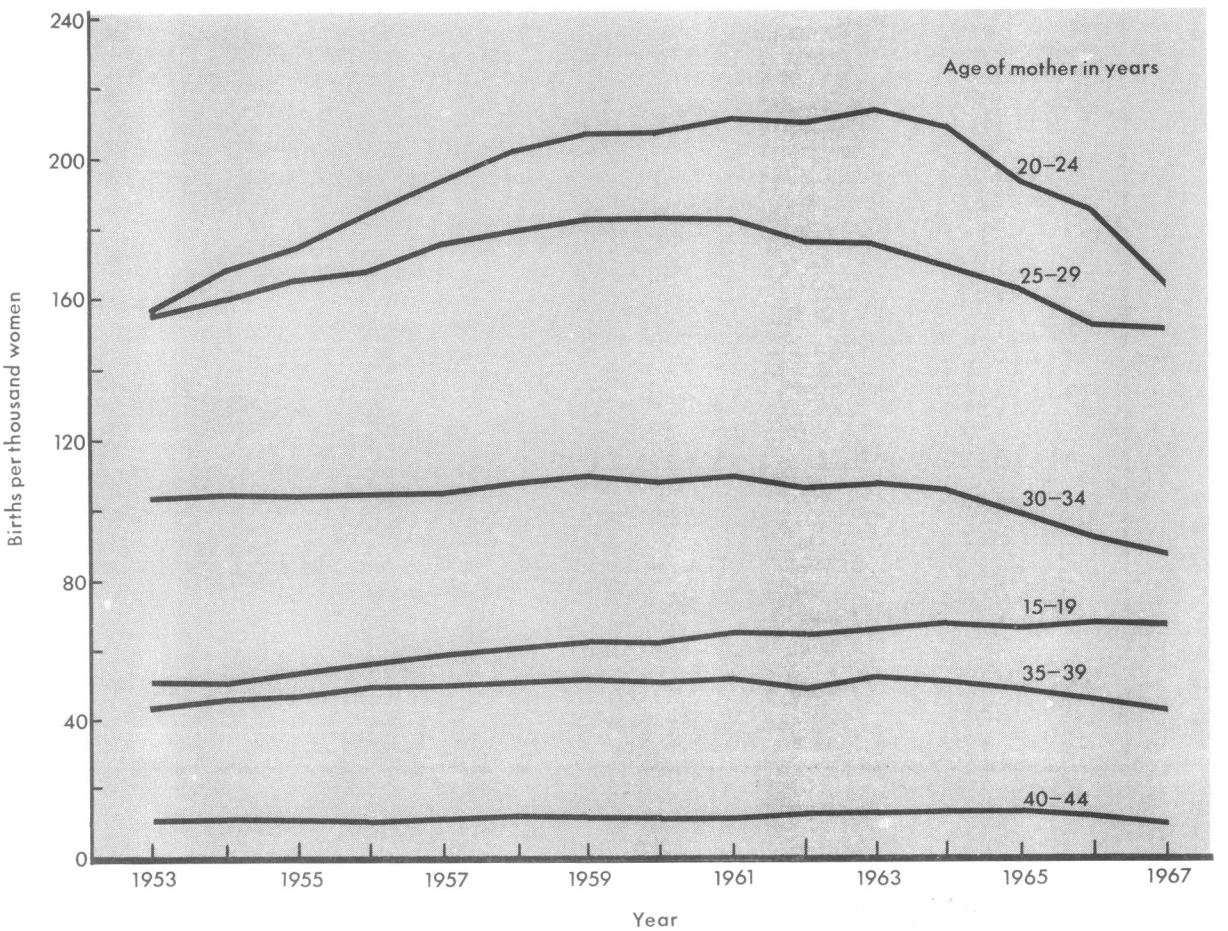
If we consider the experience of 1953 as unity, then in 1967 the incidence at birth of Down's syndrome was 0.9 and the total number of live births was likewise 0.9. The product of these figures, 0.81, is the number of births of infants with the syndrome. In other words, the decline in incidence rates and the decline in total live births contributed equally to the 19 percent (1 minus 0.81) decline in the numbers of births of infants with the syndrome in New York City.

In sum, the estimated decline in the number of cases and in the incidence of Down's syndrome at birth in New York City from 1953 through 1967 resulted from changes in the distribution of fecund women by age, from changes in fertility rates, and from a decline in the number of fecund women. Changes in fertility rates, the only factor that is realistically subject to control, contributed least to the estimated decline.

Prevalence. The existing need for health care created by a chronic condition is best measured by prevalence, which in the case of Down's syndrome is the product of incidence and survival. To estimate the contribution of births, at each maternal age, to the prevalence of Down's syndrome in a population, we therefore constructed life tables.

The table on page 654 shows the expected numbers of persons with Down's syndrome surviving in 1969 from the 1953–67 birth cohorts in New York City. These numbers also were calculated from New York City births and from the Australian life tables for Down's syndrome in the period 1942–59. (The chance of error in the esti-

Figure 4. Live births per 1,000 women, by age of mother, New York City, 1953–67



SOURCE: References 15–17.

mates of survival based on the life tables is likely to be larger than in the estimate of births.) The life table shows that about half of those born with the syndrome since 1953 would be expected to have been living in 1969. We estimate that 2,972 infants were born with Down's syndrome in the relevant period, of whom 1,408 survived to 1969. Women 35 years and over would have contributed 43 percent of the births among the survivors.

Implications

The data we have presented suggest that the prevention of births in New York City among women 35 years of age and over in the period 1953–67 would have had a major effect on the prevalence of Down's syndrome. Changes in the fertility rates of older women were small and contributed little to the 19 percent decline in the estimated numbers of births of infants with Down's syndrome. Prevention of births among these women would have reduced both the incidence of the syndrome at birth and its prevalence in the population at large by an estimated 43 percent.

The prevention of births among these older women would also have had a smaller, but no less significant, effect on the total prevalence of severe mental retardation (I.Q. less than 50). Current prevalence surveys indicate that at 10 years of age Down's syndrome may comprise from 16 to 28 percent of all cases of severe mental retardation. These estimates mean that a reduction of 43 percent in Down's syndrome would reduce the prevalence of severe mental retardation by 9 to 14 percent. By contrast, genetic counseling for couples who have had a child affected by this syndrome would have a trivial effect on prevalence, since genetically transmitted causes of the condition are rare (*20*).

The rising expectation of life for persons with Down's syndrome makes it all the more important to focus on prevention. Fecund women in their later years are clearly a salient target group for a preventive program. The problem is ripe for attack. Public attitudes and laws about contraception and abortion are changing, and methods for prenatal diagnosis of Down's syndrome have been developed.

We advocate four specific preventive measures to reduce the incidence of Down's syndrome at birth, namely, education, birth control, prenatal diagnostic testing, and elective termination of pregnancy.

Education. The hazard to offspring of older women should be made widely known. Some women may prefer to face the risk of having an infant with Down's syndrome, just as some cigarette smokers prefer to face the risk of disease and premature death. Many other women would undoubtedly choose to modify their fertility. Couples should be given the knowledge that will allow them to make informed choices about childbearing. The argument might be advanced that to inform the public of the risk of a rare event would induce unnecessary anxiety. This argument is no more sound in regard to older parents and Down's syndrome than it is in regard to smoking and lung cancer or fast motoring and traffic accidents. In the case of Down's syndrome, an uninformed family can pay a high price.

It is a principle of effective health education, however, that a health message which specifies a risk should also specify a solution. Birth control, prenatal diagnostic testing, and elective termination of pregnancy are measures that seek to meet this requirement.

Birth control. Contraceptive advice and methods should be fully available to older couples. These might include procedures to insure permanent and complete protection, like tube ligation and vasectomy, as well as the usual temporary devices.

Prenatal diagnostic testing. Where primary prevention fails, secondary prevention may avert the full development of a condition. For older women who become pregnant, whether by accident or design, prenatal diagnosis could make an important contribution to a preventive program.

It has been reported that the existence of a fetus with Down's syndrome can be diagnosed by amniocentesis, with reasonable accuracy and apparent safety, 14 to 16 weeks after conception (*21,22*). Prenatal diagnosis needs further development and research. Techniques such as automated recognition of chromosome patterns with computers could greatly facilitate the procedures. Facilities for prenatal diagnosis should be extended once the criteria for safety are satisfied.

Elective termination of pregnancy. Abortion should be freely offered to any older woman who desires it. Should a diagnosis of Down's syndrome have been made by intrauterine aspiration, it should be mandatory to offer the mother the choice of a therapeutic abortion.

Knowledge and techniques are available with which to reduce significantly the prevalence of the

largest single cause of severe mental retardation. It seems to us that health professionals have a duty to pursue this goal.

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The contribution of Down's syndrome to the prevalence of severe mental retardation is rising. Because of the known association of Down's syndrome with maternal age, a model was developed to analyze the extent to which the control of fertility in older women would reduce the prevalence of the syndrome in an actual population. Estimates of incidence at birth and of survival were made for the birth cohorts 1953–67 in New York City. These estimates indicate that the prevention of the syndrome in the offspring of women aged 35 years and over could have led to a reduction of 9 to 14 percent in the prevalence of severe mental retardation.

In New York City, during the period under study, there was a decline in the estimated number of infants born with Down's syndrome. This estimated decline was a result of shifts in the proportions of fecund women in each age group and a decline in the absolute numbers of fecund women. By contrast, fertility rates in older women gave little sign of declining. These older women are a salient target group for a preventive program. Such a program is made feasible and opportune by the changing attitudes and laws about contraception and abortion and advances in prenatal diagnosis.