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Birth Prevalence of Down Syndrome in Singapore from 1993 to 1998

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ABSTRACT

Objective: To examine the livebirth prevalence rate of Down Syndrome in Singapore from 1993 to 1998.

Design: Index cases for the National Birth Defects Register were obtained from all neonatal nurseries in Singapore, all hospital discharge summaries, cytogenetic and pathology reports from all pathology laboratories in Singapore and from the compulsory reporting of all termination of pregnancy cases and stillbirths delivered.

Setting: Information for the Register was obtained from case notes retrieved from the medical record offices, antenatal clinics, cytogenetic laboratories, pathology departments and the Registry of Births and Deaths.

Subjects: All foetuses with Trisomy 21 diagnosed prenatally together with livebirths and stillbirths with Down Syndrome diagnosed at or after birth were identified from the Registry database.

Main outcome measures: Prevalence of Down Syndrome

Results: From 1993 to 1998, there were 295 Down Syndrome livebirths, four stillbirths and 197 Down Syndrome foetuses aborted. There has been an increasing number of Down Syndrome foetuses diagnosed antenatally ending in termination and this is accompanied by a falling trend in the Down Syndrome livebirth rate in the same years from 1.17 to 0.89 per 1000 total live births. This is despite an expected increase in Down Syndrome livebirth rate obtained by modelling maternal Down Syndrome age-related risks on the maternal age distribution over the years.

Conclusions: The livebirth prevalence of Down Syndrome in Singapore has fallen over the years from 1.17/1000 livebirths in 1993 to 0.89/1000 livebirths in 1998 due to antenatal diagnosis and selective termination.

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INTRODUCTION

Down syndrome is one of the most serious and most frequently reported major congenital abnormalities among liveborn children and accounts for 25 to 35 percent of severe mental retardation[1,2]. A number of studies have noted a decline in the birth prevalence of Down Syndrome due to prenatal diagnosis and selective terminations or other factors, such as changes in environmental exposures, health behaviour and demographic characteristic of the population[3]. However, several other studies[4,5] have reported that it has increased or has remained steady since the early 1980's. This increase may be due to the expected increase in the number of Down syndrome births due to delayed childbearing in women[6]. However, an increase in elective terminations of pregnancies in foetuses with Down syndrome may be counteracting this natural increase. The advancing maternal age effect has also been supported by the findings that the live birth prevalence of Down Syndrome would have been higher than observed without prenatal diagnosis and subsequent elective abortions[7-9].

POPULATION AND VITAL STATISTICS

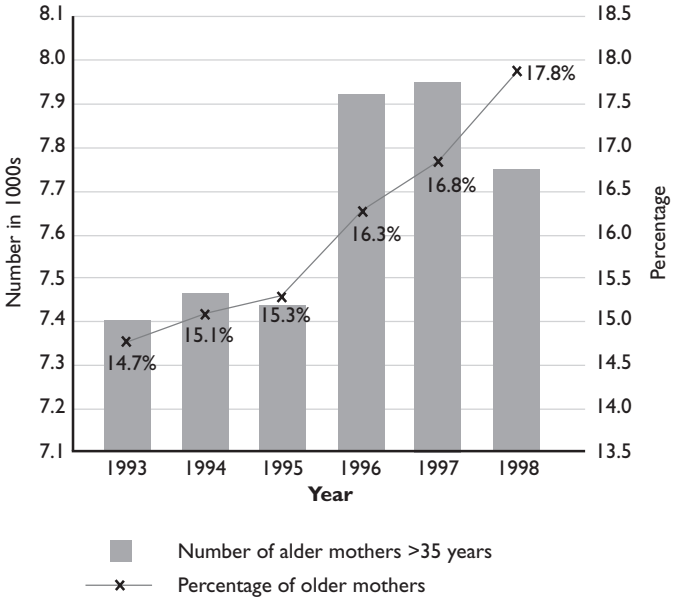
Singapore is an island republic with a resident population of 3.1 million spread over 647.8 square kilometres, of which 77.0% are Chinese, 14.0% Malays, 7.6% Indians and the remaining 1.4% of other origin (Singapore Department of Statistics, 1998). The infant mortality rate, one of the most important indicators of health has declined sharply from 82.2 per 1,000 live births in 1950 to 4.1 per 1,000 in 1998 due to the dramatic changes in socio-economic development and educational level. Today, congenital anomalies and perinatal diseases are the leading causes of death in infants and toddlers[10].

The age distribution of mothers has changed dramatically in Singapore over time, with a greater proportion of births now among older mothers. Data

from the Registry of Births and Deaths[11] show that 8.3% of mothers were 35 years or older at delivery in 1985, rising to 14.7% in 1993, and increasing steadily to 16.8% in 1997 and 17.8% in 1998[11] (Fig. 1).

The proportion of mothers 35 years or older at delivery in Singapore is much higher than those reported from the United Kingdom 9.2%[12] or the USA 12.2%[13]. This delay in childbearing is similarly reflected in the rising median age of mothers, from 28.0 years in 1985, to 29.9 in 1993 and 30.5 years in 1998.

Fig. 1 (Number and Percent of mothers aged 35 years and above in Singapore, 1993-1998).



MATERIALS AND METHODS

National Birth Defects Registry

The National Birth Defects Registry (NBDR) records all confirmed birth defects diagnosed antenatally or postnatally up to 18 years after delivery or detected by postmortem in Singapore regardless of citizenship, place of domicile, outcome (livebirth, foetal demise, or elective termination) or the gestational age of the foetus at the time of delivery/ termination. In addition to the diagnosed birth defect(s) and the demographic characteristics of the parents, any significant medical or family history of the mother, significant obstetric history, use of serum screening, results of karyotyping analysis and details of antenatal ultrasound scan(s) are recorded as well.

To ensure a high level of completeness of registration, the NBDR ascertainment is based on multiple sources of information. This includes all hospital discharge diagnoses index, cytogenetic and pathology reports from all pathology laboratories in Singapore and data from the Ministry of Health.

Hospital Discharge Summary forms are submitted by all government and private hospitals in Singapore to a computerised database system at the Ministry of Health. The System captures the principal diagnosis and additional diagnoses at the time of discharge, which are coded using the International Classification of Diseases, Ninth Revision (ICD 9)(World Health Organisation). A list of all cases with congenital birth defects codes is provided to the NDBR staff every month. This is cross-checked with the existing NBDR database and the staff nurses then routinely visit all relevant hospitals, clinics and laboratories island-wide to review medical records and to extract important information requested by the registry for all confirmed cases. Records reviewed include the antenatal notes, neonatal and paediatric notes, stillbirth and ultrasound reports, cytogenetic laboratory and pathology-autopsy reports.

A system of double-reporting is ensured by systematically collecting and reviewing all relevant laboratory reports from hospitals, private clinics or medical laboratories that perform prenatal diagnostic screening, testing or follow-up counselling to a foetus with anomalies. Incomplete demographic information for cases identified with birth defects is supplemented by the Registry of Births and Deaths database .

In Singapore, all induced abortion cases due to medical reasons or otherwise and clinically recognised spontaneously aborted foetuses after 28 weeks gestation are notified to the Ministry of Health by all relevant hospitals and clinics island-wide provided for under the statute law (Termination of Pregnancy Act, 1987). A list of all abortion cases done for a medical reason or due to a birth defect is given to the NBDR to verify by retrieving and reviewing all relevant case notes. In this way, a good ascertainment of abortion cases with foetal anomaly as the indication is ensured.

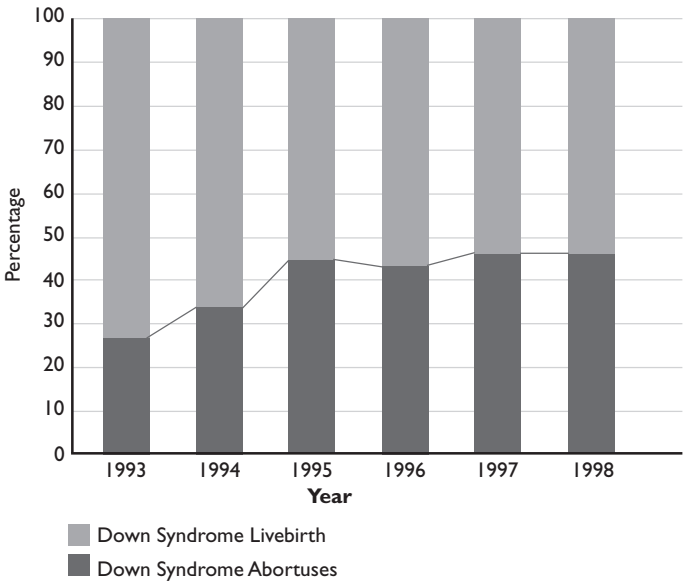
To ensure a high quality of information provided to the Registry, a number of quality control checks are conducted. NBDR staff actively follows up any birth defect registration with health professionals and hospitals' records for incomplete, inconsistent and uncertain information. In addition, the identifiers, the mother's National Registration Identity Card (NRIC) for Singapore citizens and permanent residents (or Foreign Identification Number for foreigners), date of birth or abortion, number of foetuses, and order of foetus for multiple pregnancy, are incorporated into the data management system to check for duplicate reporting. Given the smallness in size of the country, the multiple sources of ascertainment, strict quality control procedures, and the NBDR database on prenatal diagnosis and elective terminations, the ascertainment of birth defects in Singapore is comprehensive and accurate.

Table I. Down Syndrome livebirths, stillbirths and abortions, and actual and expected Down Syndrome livebirth rates, Singapore 1993 to 1998.

	Year						
	1993	1994	1995	1996	1997	1998	Total (93-98)
Down Syndrome Livebirth	59	53	54	44	46	39	295
Down Syndrome Stillbirth	2	1	0	0	0	1	4
Down Syndrome Abortuses	22	28	43	34	38	32	197
Total	83	82	97	78	84	72	496
Total Livebirths 1	50225	49554	48635	48577	47333	43664	287988
Down Syndrome rate /1000 livebirths	1.17	1.07	1.11	0.91	0.97	0.89	1.02
Down Syndrome to livebirths ratio	1:851	1:935	1:901	1:1104	1:1029	1:1120	1:976
Expected Down Syndrome Livebirths in the absence of induced abortions	76	75	87	70	75	64	447
Expected Down Syndrome rate/1000 livebirths in absence of induced abortions	1.51	1.50	1.79	1.44	1.59	1.46	1.55
Expected Down Syndrome to livebirths ratio in absence of induced abortions	1:661	1:665	1:558	1:692	1:629	1:686	1:645

1 Report on Registration of Births and Deaths 1998, Singapore Immigration and Registration

Fig. 2 Trend of Down Syndrome Livebirths vs Abortions 1993-1998.



Definitions and assumptions

The expected livebirth prevalence rates in the absence of selective termination are corrected for by factoring the probability that an aborted Down Syndrome pregnancy would have survived to term (taken to be 0.77)[14]. The predicted livebirth prevalence rates in the absence of selective termination are modelled by using the total number of maternities stratified at one-year intervals multiplied by various age-specific risk models for livebirth prevalence of Down Syndrome to predict the number of Down Syndrome liveborns. These rates, which have been derived from populations from Europe or primarily of European origin, are assumed to be the same for the local population[15].

Additional audit of completeness of data set was therefore obtained by comparing it to the predicted Down Syndrome livebirth prevalence rate derived by modeling.

The maternal age structure in one-year intervals from 1993 to 1998 was obtained from the report of the Registry of Births and Deaths published yearly. For each one-year maternal age interval, the predicted number of Down Syndrome livebirths was obtained by multiplying the number of mothers in each age group (in individual years) by the age-specific risk algorithms published[14,16,17]. This assumes that the age-related risks that were derived from predominantly Caucasian populations are the same for Asian populations. Eight risk algorithms were used to derive the predicted number of Down Syndrome livebirths for each age maternal group for the years 1993 to 1998. Stillbirths were excluded as the numbers were small and were not expected to significantly affect the results[18].

RESULTS

Down Syndrome livebirths, stillbirths and abortions in Singapore 1993 to 1998 (Table I)

Table I shows the number of Down Syndrome livebirths, stillbirths and abortions identified in the NBDR. The number of Down Syndrome livebirths has decreased steadily over the years from 59 in 1993 to 39 in 1998. This has taken place in the background of decreasing numbers of births over the same period. The livebirth prevalence of Down Syndrome has decreased over the years, from 1.17/1000 livebirths (1 in 851 livebirths) in 1993 to 0.89/1000 livebirths (1 in 686 livebirths) in 1998. In the absence of intervention, it is assumed that

Table II. Down Syndrome livebirths, stillbirths and abortions by ethnic group in Singapore 1993-1998.

	1993-98			
	Chinese	Malay	Indians	Others
Live births	195	73	16	11
Abortions	174	11	10	2
Stillbirths	4	0	0	0
Expected live births	329	81	24	13
Maternities (in 1000s)	373	84	26	13
Expected rate /1000 live births	1.68	1.42	1.14	0.96
Total Livebirths	195871	54392	23159	14566

Table III. BPA classification (3-digit code) of cases of birth anomalies, 1993 to 1998, among Down Syndrome livebirths, stillbirths and abortions

	BPA Code	1993	1994	1995	1996	1997	1998	Total 1993-98	Total 1994-97
Nervous system anomalies	740-742	0	0	0	2	1	2	5	3
Eye anomalies	743	0	0	0	0	1	0	1	1
Ear, face and neck anomalies	744	0	0	0	0	0	1	1	0
Heart anomalies	745-747	2	6	12	7	26	31	84	51
Bulbus cordis/cardiac septal closure anomalies	745	2	5	9	7	19	27	69	40
Other heart anomalies	746	0	1	1	1	1	1	5	4
Other circulatory system anomalies	747	1	3	6	4	18	22	54	31
Respiratory system anomalies	748	0	0	1	0	0	0	1	1
Cleft palate and cleft lip	749	0	0	0	0	0	1	1	0
Gut system anomalies	750-751	3	6	1	0	7	7	24	14
Genital organ anomalies	752	0	1	0	2	2	4	9	5
Urinary system anomalies	753	1	0	1	0	1	1	4	2
Musculoskeletal anomalies	754-756	0	1	1	1	4	4	11	7
Integument anomalies	757	0	0	2	3	1	0	6	6
Other congenital anomalies	759	1	0	0	0	0	0	1	0
Maternal related anomailes	760-761	0	0	0	0	0	0	0	0

Table IV. BPA classification (3-digit code) of cases of birth anomalies, 1993-1998, among Down Syndrome livebirths and stillbirths

	BPA Code	1993	1994	1995	1996	1997	1998	Total 1993-98	Total 1994-97
Nervous system anomalies	740-742	0	0	0	2	0	0	2	2
Eye anomalies	743	0	0	0	0	1	0	1	1
Ear, face and neck anomalies	744	0	0	0	0	0	1	1	0
Heart anomalies	745-747	2	6	12	7	24	29	80	49
Bulbus cordis/cardiac septal closure anomalies	745	2	5	9	7	17	25	65	38
Other heart anomalies	746	0	1	1	1	1	1	5	4
Other circulatory system anomalies	747	1	3	6	4	17	22	53	30
Respiratory system anomalies	748	0	0	0	0	0	0	0	0
Cleft palate and cleft lip	749	0	0	0	0	0	1	1	0
Gut system anomalies	750-751	3	6	1	0	7	7	24	14
Genital organ anomalies	752	0	1	0	1	2	3	7	4
Urinary system anomalies	753	1	0	0	0	1	1	3	1
Musculoskeletal anomalies	754-756	0	1	0	1	4	3	9	6
Integument anomalies	757	0	0	2	0	0	0	2	2
Other congenital anomalies	759	1	0	0	0	0	0	1	0
Maternal related anomailes	760-761	0	0	0	0	0	0	0	0

Table V. BPA classification (3-digit code) of cases of birth anomalies, 1993-1998, among abortions.

	BPA Code	1993	1994	1995	1996	1997	1998	Total 1993-98	Total 1994-97
Nervous system anomalies	740-742	0	0	0	0	1	2	3	1
Eye anomalies	743	0	0	0	0	0	0	0	0
Ear, face and neck anomalies	744	0	0	0	0	0	0	0	0
Heart anomalies	745-747	0	0	0	0	2	2	4	2
Bulbus cordis/cardiac septal closure anomalies	745	0	0	0	0	2	2	4	2
Other heart anomalies	746	0	0	0	0	0	0	0	0
Other circulatory system anomalies	747	0	0	0	0	1	0	1	1
Respiratory system anomalies	748	0	0	1	0	0	0	1	1
Cleft palate and cleft lip	749	0	0	0	0	0	0	0	0
Gut system anomalies	750-751	0	0	0	0	0	0	0	0
Genital organ anomalies	752	0	0	0	1	0	1	2	1
Urinary system anomalies	753	0	0	1	0	0	0	1	1
Musculoskeletal anomalies	754-756	0	0	1	0	0	1	2	1
Integument anomalies	757	0	0	0	3	1	0	4	4
Other congenital anomalies	759	0	0	0	0	0	0	0	0
Maternal related anomailes	760-761	0	0	0	0	0	0	0	0

77% of abortuses[14,19] would have resulted in livebirths. There would have been a total of 447 Down Syndrome livebirths expected, had there not been terminations for this period. For the period 1993 to 1998 an expected Down Syndrome livebirth prevalence of 1 in 645 livebirths would have occurred in the absence of selective termination. The decreasing birth prevalence over the period has been brought about by an increase in the abortion rate of affected pregnancies throughout this period (Fig. 2).

Demographics of mothers with Down Syndrome

The median age of mothers having foetuses with Down Syndrome was 35.0 years and the mean age 34.3 years (range 18 to 45 years). 45-60% of Down Syndrome cases were born to mothers 35 years or older at delivery. The percentage of Down Syndrome livebirths in older mothers has decreased and the percentage of Down Syndrome pregnancies terminated has increased in mothers younger than 35 years from 1993 to 1998. (Fig. 3). The maternal age of 35 years is normally used as a cut-off by care-providers in offering routine pre-natal diagnosis based on age-risk. Chinese had the highest expected livebirth prevalence rate (1.68/1000 livebirths) followed by the Malays (1.42/1000 livebirths), Indians (1.14/ 1000 livebirths) then other races (0.96/1000 livebirths) (Table II).

Main structural abnormalities found in Down Syndrome livebirths, stillbirths and abortions

Tables III, IV and V show the main structural abnormalities reported in Down Syndrome livebirths, stillbirths and abortions. Cardiac anomalies contributed the majority of foetal anomalies, followed by gastrointestinal and musculoskeletal anomalies. There is likely to be an under-ascertainment of birth defects in abortions (Table III). Firstly, prior to 1999, antenatal details in reporting of foetuses with birth defects were not included in the reporting format. Secondly, Down Syndrome pregnancies diagnosed through karyotyping from amniocentesis at around 16 weeks (for maternal age indication) may not have had a subsequent screening ultrasound scan or post-mortem to look for structural anomalies. Lastly, in foetuses with foetal anomalies found on ultrasound screening, karyotyping may not have been done prior to a second trimester termination of pregnancy. Data from the NBDR reveal that only 57% of foetuses aborted for cardiac anomalies had karyotyping done.

Comparison with expected number of Down Syndrome prevalence by modeling

The minimum and maximum predicted Down Syndrome livebirth prevalence for each year is shown in Table VI.

From the NBDR registry, the expected Down Syndrome prevalence in the absence of selective termination was expected to be 1.6/1000 livebirths over the six-year period. The predicted Down Syndrome prevalence from models was 1.4/1000 to 1.6/ 1000 livebirths for the same period (Table VI). Except for 1995, the expected Down Syndrome prevalence rate in the absence of selective termination in each year was lower than the minimum Down Syndrome livebirth prevalence rate predicted from modeling (Fig. 4).

Table VI. Expected versus predicted Down Syndrome livebirth rates.

	Year						
	1993	1994	1995	1996	1997	1998	Total (93-98)
Expected Down Syndrome/1000 livebirths in absence of induced abortions	1.5	1.5	1.8	1.4	1.6	1.5	1.6
Predicted Down Syndrome/1000 livebirths in absence of induced abortions (minimum) using models	1.6	1.7	1.7	1.7	1.8	1.9	1.4
Predicted Down Syndrome/1000 livebirths in absence of induced abortions (maximum) using models	1.8	1.8	1.8	1.9	1.9	2.1	1.6

The Down Syndrome livebirth rates for Chinese, Malays and Indians were found to be different. As the livebirth prevalence rate is confounded by abortions and the maternal age population structure (there are more older Chinese mothers than Malay or Indian mothers), the predicted livebirth prevalence rates for the various ethnic groups were modeled for the maternal population for 1993-1998 for comparison. The predicted livebirth prevalence rate for Down Syndrome obtained was 1.8-1.9/1000, 1.6-1.7/1000, 1.5-1.7/1000 and 1.8-2.0/1000 livebirths for Chinese, Malays, Indians and other races respectively.

DISCUSSION

The livebirth prevalence rate for Down Syndrome in Singapore has fallen steadily over the years 1993-1998. This fall is due to the increasing abortion rate resulting from increased awareness of antenatal diagnosis. This downward trend continues despite the predicted increase in Down Syndrome livebirth prevalence rate obtained by modeling the age distribution maternal population that has seen a steady rise in the median age of mothers.

The expected Down Syndrome livebirth prevalence rate, which is the assumed livebirth rate in the absence of selective termination in each year (with the exception of 1995) is consistently below the lower range of the predicted prevalence rate. This apparent difference could be due to the confounding factor of under-reporting or under-ascertainment of Down Syndrome foetuses aborted. It is likely that there were some Down Syndrome foetuses with foetal anomalies that were aborted without karyotyping done. The apparent difference found in most years is likely to be a Type 1 or ∝ error due to relatively small number of Down Syndrome cases in each year. On combining the data from six years, the expected livebirth prevalence rate is 1.6/1000 livebirths, which is within the predicted livebirth rate of 1.4 -1.6/1000 livebirths.

The expected livebirth prevalence rate for Down Syndrome was similar to the predicted livebirth prevalence rate among the Chinese (1.91/1000 and 1.8-1.9/1000 livebirths respectively). However, it was

Fig. 3 Down Syndrome pregnancies by maternal age.

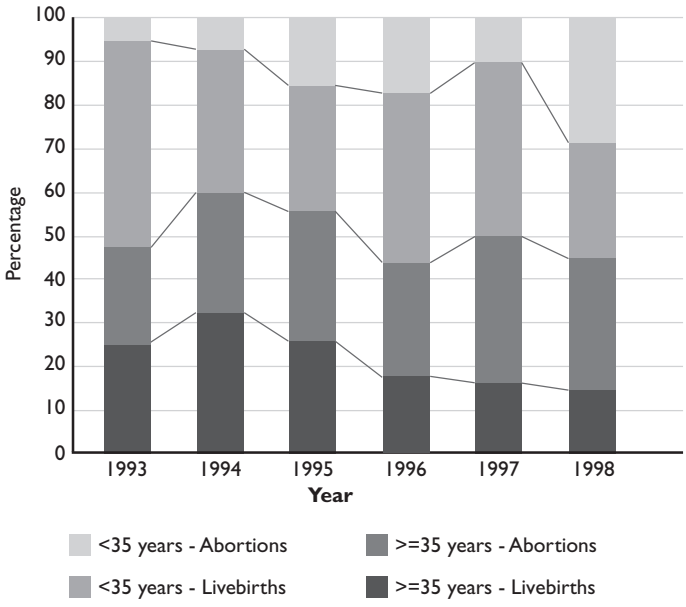
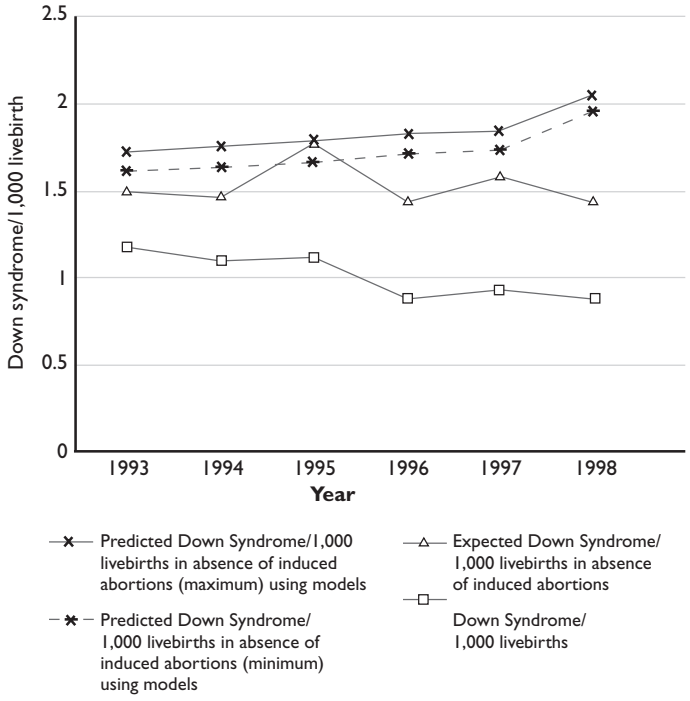


Fig. 4 Down Syndrome/1,000 livebirths in Singapore 1993 to 1998.



lower for Malays (1.42/1000 vs. 1.6-1.7/1000 livebirths), Indians (1.14/1000 vs. 1.5-1.7/1000 livebirths) and other races (0.96/1000 vs. 1.8-2.0/1000 livebirths) respectively. This discrepancy could be due to the lower postmortem and karyotyping rate of Malay foetuses aborted with structural fetal anomalies.

The main structural abnormalities in Down Syndrome livebirths were cardiac anomalies. However, it can be seen that the associated anomalies are under-reported especially in the first few years of the Registry. With the changes in database structure and new notification forms, these details have been captured in the later years.

The increasing proportion of younger mothers having Down Syndrome foetuses diagnosed antenatally resulting in terminations is likely to be due to increasing detection of structural anomalies by antenatal screening ultrasound scans and the increasing use of serum screening since the 1990's.

A full work-up of foetal anomalies detected antenatally is important from the point of accurate diagnosis and management of subsequent pregnancies. Karyotyping and post-mortem of foetuses with congenital foetal anomalies should be encouraged.

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