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ARTICLE

Trends in maternal age distribution and the live birth prevalence of Down's syndrome in England and Wales: 1938–2010

This article has been corrected since online publication and a corrigendum is also printed in this issue

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There have been concerns about the effects of increases in maternal age since the 1980s on the prevalence of Down's syndrome. This study examined changes in the distribution of maternal age in England and Wales from 1938 to 2010. The live birth prevalence of Down's syndrome in the absence of screening and subsequent termination was estimated using the numbers of babies born in England and Wales according to maternal age and the maternal age-related risk of a birth with Down's syndrome. The proportion of women age 35 years or older at the time of giving birth reached a peak of 20% in 1945, declined to 5.5% in 1977 and rose to 20% in 2007. In the absence of screening and subsequent termination, the estimated live birth prevalence of Down's syndrome would have mirrored these changes (2.3 per 1000 births in 1945, 1.2 per 1000 in 1976 and 2.2 per 1000 in 2007). The observed live birth prevalence (recorded by the National Down Syndrome Cytogenetic Register) was1.0 per 1000 from 1989 to 2010, due to screening and subsequent termination. In conclusion since the 1980s there has been an increase in the mean maternal age and in the expected prevalence of Down's syndrome. When put in a longer historical context the current expected live birth prevalence is similar to that in the 1940s and the observed live birth prevalence is about 54% less than expected, due to screening and subsequent termination, and has remained reasonably constant since 1989 at 1.0 per 1000 births.
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Keywords: Down's syndrome; maternal age; live birth prevalence

INTRODUCTION

There has been considerable interest in couples deciding to delay having children for financial or career reasons, with concern about the effects of this on the prevalence of Down's syndrome. However, the increases in maternal age have generally been compared only since the 1980s.[1,2] This paper aims to examine changes in maternal age and the associated live birth prevalence of Down's syndrome in England and Wales from 1938 to 2010.

METHODS

The numbers of live births in England and Wales between 1938 and 2010 were extracted from Birth Statistics and Characteristics of Birth 2010, where they are stratified into 5-year maternal age groups.[3,4]Maternal age is the strongest risk factor for Down's syndrome and the maternal age-specific risk of having a baby with Down's syndrome has been accurately estimated using the following equation: risk $= 1/(1+\exp(7.330-4.211/(1+\exp(-0.282\times(\text{age}-37.23)))))$.[5,6] The average age-specific risk was calculated for each age group (it was 0.66 per 1000 for under 20 years of age; 0.70 per 1000 for ages 20–24; 0.84 per 1000 for ages 25–29; 1.48 per 1000 for ages 30–34; 4.72 per 1000 for ages 35–39; 15.22 per 1000 for ages 40–44 and 30.71 per 1000 for 45 years and older). For each year of birth the number of live births with Down's syndrome was estimated by multiplying these risks by the number of live births in that age group and summing across all age groups.

The number of babies born with Down's syndrome has been reported annually since the National Down Syndrome Cytogenetic Register (NDSCR) started to collect details of antenatal and postnatal diagnoses of Down's syndrome in England and Wales in 1989,[7–9] and such data were extracted from the 2010 NDSCR annual report.[8]

A χ^2 test was used to examine differences in maternal age distribution at three different time points. Poison regression was conducted to investigate the trend of observed and expected live birth prevalence between 1989 and 2010.

RESULTS

Figure 1 shows how the maternal age distribution has changed since 1940. The maternal age distribution was significantly different between 1940 and 1980 ($P=0.0001$) and between 1980 and 2010 ($P<0.0001$), but not different between 1940 and 2010 ($P=0.46$). In particular, the proportion of mothers who are aged under 25 increased dramatically to 1970 and then decreased to the level in 1940s.

Figure 2 shows the proportion of mothers 35 years of age or older reached a peak of 19.7% in 1945, declined to 5.5% in 1977 before rising to a new peak of 20.4% in 2007. In the absence of prenatal diagnosis and subsequent terminations the estimated live birth prevalence of Down's syndrome mirrored these changes, with a peak of 2.27 per 1000 births in 1945 down to 1.22 per 1000 in 1976 and then up to 2.18 per 1000 in 2007.

Figure 3 and Table 1 shows the estimated live birth prevalence of Down's syndrome in the absence of prenatal diagnosis and subsequent terminations compared with the observed live birth prevalence of

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Down's syndrome in England and Wales. The difference between the two curves was due to prenatal diagnosis and subsequent terminations being performed. Poisson regression for data between 1989 and 2010 shows an increase of 2.8% (95% CI: 2.6–3.0%) per annum in the estimated live birth prevalence, but only a very small annual increase of 0.3% (95% CI: 0.1–0.5%) in the observed live birth prevalence. The percentage reduction between the observed and expected live birth prevalence increased since 1989 (Table 1). In 2010, the observed live birth prevalence of Down's syndrome was 0.99 per 1000 births, 54% lower than expected due to prenatal diagnosis and subsequent terminations being performed.

DISCUSSION

Figure 1 demonstrates that the recent proportions of older women having children are in fact similar to the proportions in the 1940s, even though the births to older mothers in the past would have been to women having large families, whereas the births now are likely to be either first or second children to mothers who have delayed having children. Birth order is not associated with the prevalence of Down's syndrome, it is only the age of the mothers that is important.[5,6] Figure 2 shows how the prevalence of Down's syndrome is predicted by maternal age. Although the use of infertility treatments using donated eggs is increasing, their use is still too infrequent to make a detectable change in the population prevalence of Down's syndrome.

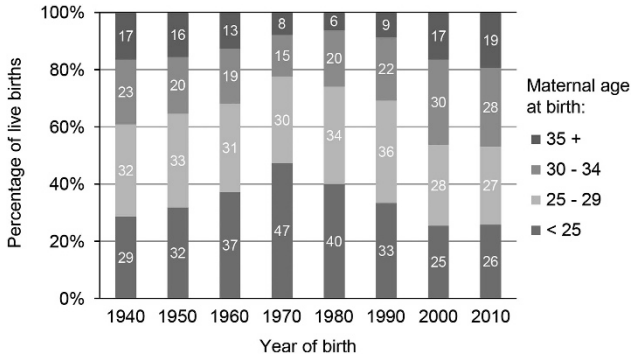

Figure 1 Distribution of maternal ages according to year of birth in England and Wales from 1940 to 2010.

Other studies in Europe and the rest of the world have also observed increases in the proportion of mothers aged 35 and over since the 1980s.[2,10–13] As the changes in the live birth prevalence of Down's syndrome are also dependant on the proportion of Down's syndrome cases diagnosed prenatally and the proportion of subsequent terminations being performed, the birth prevalence of Down's syndrome only increased slightly in the United States,[11] stayed stable in Singapore and Europe,[2,12,13] and decreased in Australia.[10] In developing countries, such as China,[14] with a lower availability of prenatal diagnosis and subsequent termination, the increase in the proportion of mothers aged 35 and over had a bigger impact on the birth prevalence of Down's syndrome.

With the increasing availability of more powerful screening tests, such as the combined test, a higher proportion of Down's syndrome fetuses are being detected prenatally particularly among younger mothers (the proportion of mothers under 35 with Down's syndrome diagnosed prenatally increased from 10% to nearly 60% in England and Wales from 1989 to 2010, Figure 2 in NDSCR report[8]). The result of this increased detection rate and subsequent terminations in younger mothers has been to increase the maternal age of mothers with Down's syndrome births from 30 to 35 years of age (Figure 4 in NDSCR report[8]). This 5 year increase is important when considering the implications for the long-term care of these children and subsequently adults with Down's syndrome. The introduction of new techniques, such as sequencing fetal DNA in maternal blood,[15,16] would be expected to increase these trends in increasing detection rates. However, the birth prevalence of Down's syndrome will continue to be highly influenced by any increases in maternal age and women should be made aware of these increased risks.

One of the weakness of this study is that before 1989 we do not know how many babies are born with Down's syndrome. Data on the

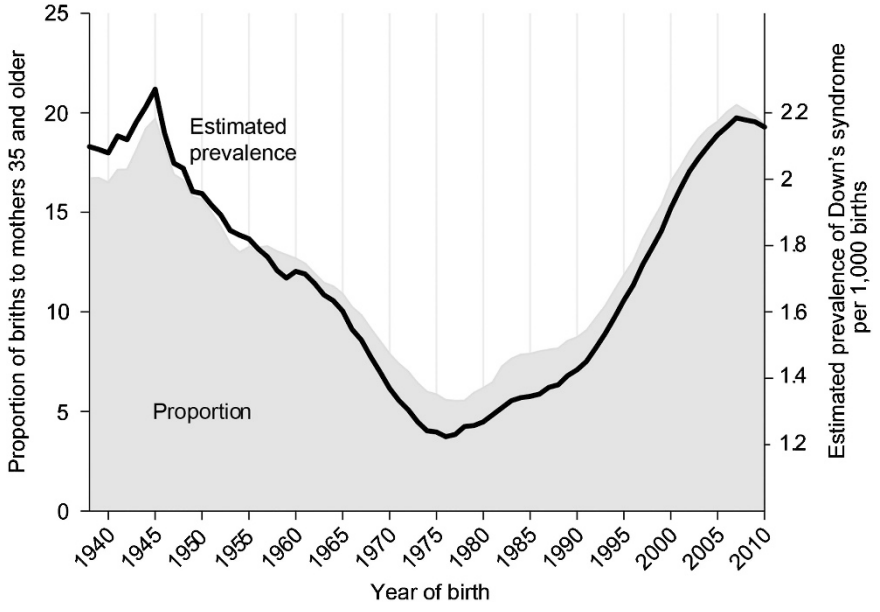

Figure 2 Live birth prevalence of Down's syndrome and proportion of mothers 35 and older according to year of birth in England and Wales from 1938 to 2010.

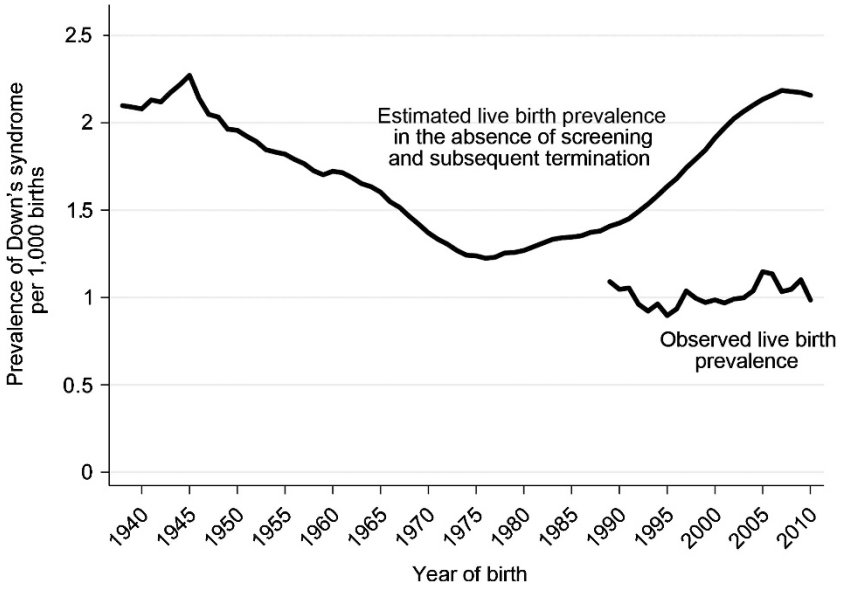

Figure 3 Live birth prevalence of Down's syndrome estimated in the absence of screening and subsequent termination (1938–2010) and observed in England and Wales (1989–2010).

Table 1 Number of all births and births with Down's syndrome estimated in absence of screening and selective termination and number recorded by the NDSCR in England and Wales: 1938–2010

		Down's syndrome live births				
		Estimated in absence of screening and subsequent termination		*Recorded in NDSCR (from 1989)*		*Percentage reduction of observed compared with expected prevalence (per 1000 births; %)*
Year of birth	*Number of live births in population*	*Number*	*Prevalence (per 1000 births)*	*Number*	*Prevalence (per 1000 births)*	
1938	621 204	1303	2.10			
1939	614 479	1284	2.09			
1940	590 120	1227	2.08			
1941	579 091	1234	2.13			
1942	651 503	1381	2.12			
1943	684 334	1487	2.17			
1944	751 478	1667	2.22			
1945	679 937	1544	2.27			
1946	820 719	1756	2.14			
1947	881 026	1805	2.05			
1948	775 306	1576	2.03			
1949	730 518	1434	1.96			
1950	697 097	1364	1.96			
1951	677 529	1302	1.92			
1952	673 735	1275	1.89			
1953	684 372	1263	1.85			
1954	673 651	1234	1.83			
1955	667 811	1216	1.82			
1956	700 335	1254	1.79			
1957	723 381	1277	1.77			
1958	740 715	1278	1.73			
1959	748 501	1274	1.70			
1960	785 005	1352	1.72			
1961	811 281	1391	1.71			
1962	838 736	1414	1.69			
1963	854 055	1411	1.65			
1964	875 972	1431	1.63			
1965	862 725	1383	1.60			
1966	849 823	1315	1.55			
1967	832 164	1261	1.52			
1968	819 272	1200	1.46			
1969	797 538	1131	1.42			

Table 1 (Continued)

		Down's syndrome live births				
		Estimated in absence of screening and subsequent termination		Recorded in NDSCR (from 1989)		Percentage reduction of observed compared with expected prevalence (per 1000 births; %)
Year of birth	Number of live births in population	Number	Prevalence (per 1000 births)	Number	Prevalence (per 1000 births)	
1970	784 486	1075	1.37			
1971	783 155	1044	1.33			
1972	725 440	947	1.31			
1973	675 953	858	1.27			
1974	639 885	795	1.24			
1975	603 445	747	1.24			
1976	584 270	715	1.22			
1977	569 259	701	1.23			
1978	596 418	773	1.25			
1979	638 028	802	1.26			
1980	656 234	833	1.27			
1981	634 492	819	1.29			
1982	625 931	821	1.31			
1983	629 134	838	1.33			
1984	636 818	854	1.34			
1985	656 417	883	1.35			
1986	661 018	894	1.35			
1987	681 511	936	1.37			
1988	693 577	958	1.38			
1989	687 725	968	1.41	750	1.09	23
1990	706 140	1007	1.43	739	1.05	27
1991	699 217	1014	1.45	737	1.05	27
1992	689 656	1029	1.49	663	0.96	36
1993	673 467	1034	1.53	621	0.92	40
1994	664 726	1052	1.58	640	0.96	39
1995	648 138	1060	1.63	581	0.90	45
1996	649 485	1092	1.68	607	0.93	44
1997	643 095	1120	1.74	667	1.04	40
1998	635 901	1140	1.79	633	1.00	44
1999	621 872	1147	1.84	604	0.97	47
2000	604 441	1156	1.91	596	0.99	48
2001	594 634	1172	1.97	576	0.97	51
2002	596 122	1207	2.02	591	0.99	51
2003	621 469	1283	2.06	620	1.00	52
2004	639 721	1344	2.10	664	1.04	51
2005	645 835	1378	2.13	741	1.15	46
2006	669 601	1445	2.16	760	1.14	47
2007	690 013	1508	2.18	713	1.03	53
2008	708 711	1544	2.18	742	1.05	52
2009	698 324	1517	2.17	769	1.10	49
2010	715 467	1565	2.16	715	0.99	54

Abbreviation: NDSCR, National Down Syndrome Cytogenetic Register.
The width of the 95% confidence interval of prevalence rates is about 0.2 per 1000 births due to the stable live birth population since 1938.

numbers of babies born with Down's syndrome was collected by the National Congenital Anomaly Service (NCAS), and published annually by the Office for National Statistics from 1971 to 2008.[17] However, both the NDSCR and other regional congenital anomaly registers demonstrated that the NCAS system had a significantly lower ascertainment rate.[18,19] Therefore, we have chosen not to use the data from NCAS for 1971–1989. The data on population births is only available in 5 year age bands, which will produce a small amount of inaccuracy.

In conclusion, this paper demonstrates that recent increases in maternal age mirror the decreases that occurred from the 1940s and that the live birth prevalence of babies with Down's syndrome has remained reasonably constant since the introduction of prenatal diagnosis in the 1980s.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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