Advances in Medical Technology and Creation of Disparities: The Case of Down Syndrome

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Objectives. We assessed socioeconomic differences in probabilities of prenatal diagnoses of Down syndrome and continuation of pregnancies after such diagnoses, along with the effects of these differences on disparities in live-birth prevalences of Down syndrome.

Methods. Using population-based data derived from 1433 cases of Down syndrome and 3731 control births, we assessed age-adjusted effects of maternal occupation and geographic origin on prenatal diagnoses, as well as overall and live-birth odds, of Down syndrome.

Results. Maternal occupation and geographic origin had significant effects on the probability of a prenatal diagnosis of Down syndrome and on continuation of pregnancy after such a diagnosis. Women in lower-status occupational categories had higher odds of delivering a live-born infant with Down syndrome. In comparison with women in the highest-status occupational category, the age-adjusted odds ratio for a Down syndrome live birth among women without an occupation was 2.4 (95% confidence interval [CI] = 1.7, 3.3). By contrast, there were no disparities in age-adjusted overall likelihood of Down syndrome.

Conclusions. Socioeconomic differences in use of prenatal testing have created disparities in the live-birth prevalence of Down syndrome. Overall Down syndrome risk does not vary according to socioeconomic status. (*Am J Public Health.* 2006;96:2139–2144. doi:10.2105/AJPH.2005.069377)

Prenatal testing designed to detect congenital malformations has progressed considerably over the past 30 years. Particular advancements have been made in the case of Down syndrome,[1,2] the foremost known genetic cause of mental retardation.[3] Prenatal screening techniques for Down syndrome include assessment of ultrasonographic markers, particularly measurement of nuchal translucency in the first trimester of pregnancy and maternal serum screening during both the first and second trimesters. Techniques used in making definitive prenatal diagnoses include amniocentesis and chorionic villus sampling. In addition, a noninvasive method of prenatal diagnosis involving molecular detection of fetal DNA in maternal blood is being developed.[4]

An extensive literature has documented socioeconomic disparities in use of medical services,[5–8] particularly prenatal testing,[9–13] in several countries. For example, socioeconomic differences in use of prenatal testing persist in France[14,15] despite an active national policy aimed at increasing access to prenatal testing[16] and an accompanying reduction in the live-birth prevalence of Down syndrome.[17] The mechanisms underlying socioeconomic differences in the use of prenatal testing[11,18] are not completely understood. However, disparities may be related more to barriers to access and information than to differences in women's preferences.[15] Moreover, previous data suggest that different socioeconomic factors have distinct and partially independent effects on use of prenatal testing.[15]

The extent to which documented socioeconomic differences in use of prenatal testing have resulted in disparities in the actual proportions of Down syndrome cases diagnosed prenatally is not known. Population-based data have not been used to evaluate socioeconomic differences in the probability of continuation of pregnancy after a prenatal diagnosis of Down syndrome. Moreover, few population-based studies have assessed the impact of socioeconomic differences in use of prenatal testing on the birth prevalence of Down syndrome.[12,13,19]

Studies conducted in the United States have relied on vital statistics data, which are likely to underestimate the true birth prevalence of Down syndrome. Furthermore, vital statistics do not include cases of Down syndrome in which mothers opt for pregnancy termination. Hence, they do not allow for a complete assessment of socioeconomic differences in the probability of prenatal diagnoses of Down syndrome or the probability of continuation of pregnancy after such diagnoses.

Using population-based data, we assessed the effects of 2 socioeconomic factors, maternal occupation and geographic origin, on the probability of a prenatal diagnosis of Down syndrome and on continuation of pregnancy after such a diagnosis. Also, we examined the effects of these factors on overall and live-birth odds of Down syndrome. We hypothesized that differences in use of prenatal testing might result in mothers in lower-socioeconomic-status groups having higher age-adjusted odds than women in higher-socioeconomic-status groups of delivering a live-born infant with Down syndrome.

METHODS

We used data from the population-based Paris Registry of Congenital Malformations for the period 1983 to 2002. The registry includes women who resided in Greater Paris (Paris and Petite Couronne) and gave birth or terminated their pregnancy in Parisian maternity units (approximately 38 000 births per year) during that time period.

The registry follows the methodology of the European network of registries for congenital malformations (EUROCAT), and data quality is routinely monitored by both the registry and the EUROCAT central registry. In addition, data collection and storage procedures and data quality are examined on a regular basis by France's National Committee of Registries. Data are collected from

multiple sources, including maternity units, neonatology services, and cytogenetic and pathology services, to allow high levels of case ascertainment.

We conducted 2 sets of analyses. The first set involved cases of Down syndrome only. We examined the effects of maternal occupation and geographic origin on the probability of (1) prenatal diagnoses of Down syndrome and (2) continuation of pregnancy after such diagnoses. We estimated probabilities and age-adjusted odds of prenatal diagnosis in relation to maternal occupation and geographic origin for all cases of Down syndrome included in the registry. We then assessed probabilities and age-adjusted odds of continuation of pregnancy among all cases of Down syndrome that had been diagnosed prenatally.

Second, we used a case–control design to assess the effects of maternal occupation and geographic origin on the odds of a delivery involving Down syndrome. Our working hypothesis was that there are no significant socioeconomic disparities in overall maternal age-adjusted odds of Down syndrome. Hence, any observed disparities in the live-birth odds of a Down syndrome delivery would be those created ("de novo") as a result of unequal use of prenatal testing. To test this hypothesis, we examined both overall and live-birth odds of Down syndrome in relation to maternal occupation and geographic origin.

Cases were defined as live births, pregnancy terminations, and stillbirths involving Down syndrome (in analyses assessing overall odds) or as live births involving Down syndrome. Several a priori criteria were used in selecting control births from the list of malformations included in the registry. The first requirement was that there be no evidence of the prevalence of the malformation in question being associated with socioeconomic factors (e.g., neural tube defects were not included because their prevalence is known to be associated with socioeconomic factors[20]). Second, selected anomalies were required not to be subject to prenatal diagnosis on a routine basis (e.g., cases of congenital heart disease and gastrointestinal abnormalities were not included). Finally, malformations selected as controls were required to involve a relatively high frequency of occurrence.

Our initial study population included 1698 cases of Down syndrome (live births, pregnancy terminations, and stillbirths combined) and 4005 controls. The control group comprised the following set of isolated anomalies: congenital dislocation of the hip (n=1562), cleft palate (n=166), syndactyly (n=172), clubfoot (n=966), angioma (n=593), congenital abnormalities of the integument (n=450), and anorectal anomalies (n=96).

The registry includes information on maternal occupation and geographic origin. Data on paternal occupation are collected, but a considerable proportion of this information is missing. Data on other socioeconomic factors, including education and marital status, are not currently available. It should also be noted that French law prohibits collection of data on religious beliefs and ethnic origin.

We classified maternal occupation using the categories defined by the French National Institute of Statistics and Economic Studies. We used the following categories, which generally represent the order of highest to lowest occupational classifications in France: professional (n=1246), intermediate (n=1199), administrative/public service (n=1199), "other" (n=363), and none (n=1244). The "other" group included several subcategories comprising a relatively small number of women: artisan/small business owner, shopkeeper/shop assistant, service worker, skilled worker, and unskilled worker. We classified mother's geographic origin using 4 categories representing the major groups in France: French (n=3560), North African (n=603), other African (n=320), and other (n=1007).

Data on occupation were missing for 420 (7.4%) women, and data on geographic origin were missing for 213 (3.7%) women. We found no significant differences in the frequency of missing data for maternal geographic origin between cases and controls (3.7% vs 3.8%). Missing data on maternal occupation were more frequent for cases (14.7%) than for controls (4.3%). In addition, the prenatal diagnosis rate was somewhat higher among women with missing data on occupation (79.0%) than in the overall group of women with complete data on occupation (70.6%). However, when women with missing information on occupation were excluded, the prenatal diagnosis rate for the overall sample did not change appreciably (71.8% vs 70.6%).

Cases with missing data on maternal occupation and geographic origin were excluded from the study population. The final sample included 1433 cases of Down syndrome (461 live births) and 3731 controls (3713 live births). Data on maternal age were missing for 11 (0.2%) cases, which were excluded from the age-adjusted analyses.

Data on prenatal diagnosis were missing for 5 cases (0.3%) of Down syndrome, and information regarding continuation of pregnancy after a prenatal diagnosis was missing for 24 cases (2.4%). These cases were excluded from the analyses of the effects of maternal occupation and geographic origin on prenatal diagnoses of Down syndrome (n=1428; Table 1) and continuation of pregnancy after such diagnoses (n=984).

Amounts of missing prenatal diagnosis information did not differ significantly across the maternal occupation and geographic origin categories. In comparison with women in the highest occupational category (the "professional" group; n=3; 1.0%), more women in the intermediate (n=5; 2.0%), administrative/public service (n=8; 4.4%), other (N=4, 6.0%), and no occupation (n=4; 2.0%) categories had missing data on continuation of pregnancy after a prenatal diagnosis of Down syndrome. Also, more women of North African (n=3; 3.3%) and African (n=5; 10.6%) origin than women from France (n=13; 1.9%) had missing data on continuation of pregnancy.

Given increasing frequencies of delayed childbearing among women in higher socioeconomic groups and the strong effect of maternal age on the risk of fetal Down syndrome, adequate adjustment for maternal age is crucial in studies of the relation between socioeconomic factors and overall or live-birth prevalence of Down syndrome. We used 2 alternative strategies of adjusting for maternal age.

First, we used the cumulative sum (cusum) model for binary variables,[21] a nonparametric technique designed to assess alternative strategies for adjustment of a continuous variable (e.g., maternal age) in logistic regression models. Second, we used fractional polynomials[22] to determine the optimal strategy for adjusting for maternal age. These 2 strategies produced similar results in terms of estimates of

TABLE 1—Socioeconomic Differences in Prenatal Diagnoses of Down Syndrome and Continuation of Pregnancy After Prenatal Diagnoses: Paris, France, 1983–2002

	Prenatal Diagnosis		Continuation of Pregnancy After Prenatal Diagnosis	
	No.[a]	% (95% CI)	No.[b]	% (95% CI)
Occupational category[c]				
Professional	375	84.0 (79.9, 87.6)	312	3.2 (1.5, 5.8)
Intermediate	330	75.5 (70.4, 80.0)	244	2.9 (1.2, 5.8)
Administrative, public service	279	64.5 (58.6, 70.1)	172	5.8 (2.8, 10.4)
Other[d]	102	65.7 (55.6, 74.8)	63	7.9 (2.6, 17.6)
No occupation	342	57.6 (52.2, 62.9)	193	11.4 (7.3, 16.7)
Geographic origin[c]				
France	916	73.9 (70.9, 76.7)	664	2.9 (1.7, 4.4)
North Africa	165	55.2 (47.2, 62.9)	88	15.9 (9.0, 25.3)
Other Africa	79	59.5 (47.9, 70.4)	42	21.4 (10.3, 36.8)
Other	268	72.0 (66.2, 77.3)	190	6.3 (3.3, 10.8)
All regions	1428	70.6 (68.1, 72.9)	984	5.5 (4.1, 7.1)

Note. CI = confidence interval.
[a]Total number of Down syndrome cases.
[b]Total number of prenatally diagnosed cases of Down syndrome.
[c]$P < .001$ (χ^2 test of significance) for both prenatal diagnosis and continuation of pregnancy.
[d]Artisan, small business owner, shopkeeper, shop assistant, service worker, skilled worker, or unskilled worker.

the age-adjusted effects of maternal occupation and geographic origin on overall and live-birth odds of Down syndrome. Here we present the results of analyses in which fractional polynomials were used.

RESULTS

Of the 1428 cases of Down syndrome, 1008 (70.6%; 95% confidence interval [CI]= 68.1%, 72.9%) were diagnosed prenatally. In the case of both maternal occupation and geographic origin, there was a substantial socioeconomic gradient in the probability of a prenatal diagnosis of Down syndrome (Table 1). Probabilities of prenatal diagnoses were significantly higher among women from more advanced occupational categories than among women in the other categories. Also, probabilities were higher among women of French origin than among women of African origin. Differences in the odds of prenatal diagnoses across occupational categories and between women of North African origin and those of French origin were independently significant and remained so after adjustment for maternal age (Table 2).

Among the women in the sample, 5.5% (95% CI=4.1%, 7.1%) continued their pregnancy after a prenatal diagnosis of Down syndrome (Table 1). There was a tendency for women from lower occupational categories (vs those from the highest category) and women of African origin (vs those of French origin) to be more likely to continue their pregnancy after such a diagnosis. Differences in the probability of continuation of pregnancy across occupational categories were no longer significant, however, after adjustment for maternal age and geographic origin (Table 2). By contrast, odds of continuation of pregnancy remained significantly higher among women of African origin after adjustment for maternal age and occupation.

Table 3 shows the results of the logistic regression analyses assessing socioeconomic differences in overall and live-birth odds of Down syndrome. Overall odds of Down syndrome were reduced among women in lower occupational categories (vs those in the highest category), suggesting a lower overall prevalence for these women. This difference disappeared after adjustment for maternal age. We found no significant differences in odds among women of different geographic origins, suggesting that the overall prevalence of Down syndrome was similar among these women.

Conversely, there were substantial socioeconomic differences in the odds of a Down syndrome live birth. Women in lower occupational categories had higher odds of delivering a live-born infant with Down syndrome both before and after adjustment for maternal

TABLE 2—Socioeconomic Differences in Odds of Prenatal Diagnoses of Down Syndrome and Continuation of Pregnancy After Prenatal Diagnoses: Paris, France, 1983–2002

	Prenatal Diagnosis, Adjusted OR[a] (95% CI)	Continuation of Pregnancy After Prenatal Diagnosis, Adjusted OR[a] (95% CI)
Occupational category[b]		
Professional	1.0	1.0
Intermediate	0.7 (0.4, 1.0)	0.8 (0.3, 2.2)
Administrative, public service	0.4 (0.3, 0.7)	1.2 (0.5, 3.0)
Other[c]	0.3 (0.2, 0.6)	1.5 (0.5, 4.8)
No occupation	0.3 (0.2, 0.5)	1.7 (0.7, 4.1)
Geographic origin[d]		
France	1.0	1.0
North Africa	0.5 (0.3, 0.7)	5.0 (2.3, 11.1)
Other Africa	0.8 (0.5, 1.4)	6.3 (2.5, 16.2)
Other	1.2 (0.8, 1.7)	1.7 (0.8, 3.8)

Note. OR = odds ratio; CI = confidence interval.
[a]Adjusted for maternal age, occupation, and geographic origin. Fractional polynomials were used to adjust for maternal age.
[b]$P < .001$ (Wald test of significance) for prenatal diagnosis; $P = .54$ (Wald test of significance) for continuation of pregnancy.
[c]Artisan, small business owner, shopkeeper, shop assistant, service worker, skilled worker, or unskilled worker.
[d]$P < .001$ (Wald test of significance) for both prenatal diagnosis and continuation of pregnancy.

TABLE 3—Results of Case–Control Logistic Regression Analysis of Socioeconomic Differences in Overall and Live-Birth Odds of Down Syndrome: Paris, France, 1983–2002

	Total Births[a]		Total Births[a]		Live Births		Live Births	
	Unadjusted OR (95% CI)	P^b	Adjusted OR[c] (95% CI)	P^b	Unadjusted OR (95% CI)	P^b	Adjusted OR[c] (95% CI)	P^b
Occupational category		.01		.70		<.001		<.001
Professional	1.0		1.0		1.0		1.0	
Intermediate	0.9 (0.7, 1.1)		1.1 (0.9, 1.3)		1.3 (1.0, 1.9)		1.5 (1.1, 2.1)	
Administrative, public service	0.7 (0.6, 0.9)		1.0 (0.8, 1.2)		1.6 (1.2, 2.2)		1.9 (1.3, 2.6)	
Other[d]	0.9 (0.7, 1.2)		1.0 (0.7, 1.4)		2.0 (1.3, 3.1)		2.0 (1.3, 3.1)	
No occupation	0.9 (0.7, 1.0)		1.1 (0.9, 1.4)		2.3 (1.7, 3.1)		2.4 (1.7, 3.3)	
Geographic origin		.71		.76		<.001		<.001
France	1.0		1.0		1.0		1.0	
North Africa	1.1 (0.9, 1.4)		0.9 (0.7, 1.2)		2.2 (1.7, 2.8)		1.5 (1.1, 2.0)	
Other Africa	1.0 (0.7, 1.3)		1.1 (0.8, 1.6)		1.7 (1.2, 2.5)		1.3 (0.9, 2.0)	
Other	1.0 (0.9, 1.2)		1.0 (0.9, 1.3)		1.1 (0.9, 1.5)		1.0 (0.7, 1.3)	

Note. OR = odds ratio; CI = confidence interval. Odds ratios refer to odds of a Down syndrome birth (cases) relative to a birth involving one of the following anomalies (controls): congenital dislocation of the hip, cleft palate, syndactyly, clubfoot, angioma, congenital abnormalities of the integument, or anorectal anomalies.
[a]Live births, pregnancy terminations, and stillbirths.
[b]Wald tests of significance of the overall effect of maternal occupation or geographic origin.
[c]Adjusted for maternal age, profession, and geographic origin. Fractional polynomials were used in adjusting for maternal age.
[d]Artisan, small business owner, shopkeeper, shop assistant, service worker, skilled worker, or unskilled worker.

age and geographic origin. For example, relative to women in the highest occupational category, odds ratios were 1.5 (95% CI=1.1, 2.1) for women in the intermediate category and 2.4 (95% CI=1.7, 3.3) for women with no profession after adjustment for maternal age and geographic origin. In addition, women of North African origin had higher odds (OR=1.5; 95% CI=1.1, 2.0) of delivering a live-born infant with Down syndrome than women of French origin after adjustment for maternal age and occupation.

DISCUSSION

Our results suggest considerable disparities in prenatal diagnoses of Down syndrome and, therefore, in women's odds of delivering a live-born infant with this condition. This was particularly the case across maternal occupational groups, with increasingly higher odds of Down syndrome live births among women in lower occupational groups. Women with no occupation were at more than 2-fold risk of delivering a live-born infant with Down syndrome than women in the highest occupational category. These disparities in prenatal diagnoses and live-birth prevalences of Down syndrome persisted in the context of a prenatal testing policy that has egalitarian intentions and provides reimbursed access to prenatal testing.[16,23]

By contrast, we did not find any evidence of socioeconomic differences in the overall odds of Down syndrome after adjustment for maternal age. Together, these results suggest that the increasing use of prenatal testing accompanied by persistent differences in its use has created disparities in the live-birth prevalence of Down syndrome, a congenital anomaly whose overall risk does not seem to vary according to socioeconomic status after socioeconomic differences in frequency of delayed childbearing have been taken into account.[24,25]

We also found differences in the probability of continuation of pregnancy after a prenatal diagnosis of Down syndrome among women of different geographic origins, suggesting that women's own preferences may also contribute to socioeconomic differences in the live-birth prevalence of Down syndrome. Such differences in preferences with respect to prenatal testing and pregnancy termination have been observed in France[14,15] and other countries[26,27] and, in particular, in a recent US study[18] conducted by Kuppermann and colleagues that involved a socioeconomically diverse sample and included a comprehensive evaluation of women's preferences.

It should be noted, however, that previous data[28,29] and the results of our study suggest that by far the majority of women across different socioeconomic groups do not continue their pregnancy after a prenatal diagnosis of Down syndrome. Moreover, differences in use of prenatal testing appear to be for the most part because of barriers to access and information rather than differences in women's preferences or informed decision-making.[15] It is also possible that the apparent differences in preferences are related in part to factors associated with health providers, particularly miscommunication between providers and pregnant women from different cultural backgrounds.[27]

Limitations

Interpretation of our results is subject to several caveats and limitations. In our case–control analysis of differences in overall and live-birth odds of Down syndrome, we used a selective set of malformations from the Paris registry as controls. The limitations and

advantages of the use of such controls in epidemiological studies of congenital malformations have been discussed elsewhere.[30–33] The main issue of concern has been the possibility of selection bias. As mentioned earlier, we sought to minimize such bias by setting a priori criteria for selection of controls.

Our results indicating an absence of socioeconomic differences in age-adjusted overall odds of Down syndrome are consistent with the findings of previous studies.[34] In addition, the fact that we found no significant disparities in the maternal age-adjusted overall odds of Down syndrome suggests that any bias related to socioeconomic differences in the malformations used as controls was negligible. That is, such selection bias would need to exactly balance the differences we found regarding live-birth odds of Down syndrome to result in an absence of socioeconomic effects on overall odds, which does not seem very likely. Moreover, the socioeconomic differences we found in odds of live birth were consistent with our findings on disparities in prenatal diagnoses and continuation of pregnancy after such diagnoses.

Missing data on maternal profession were more frequent for Down syndrome cases than for controls. However, we found no significant differences in prenatal diagnosis rates between cases of Down syndrome initially included in the study and those included in the final study population, which excluded cases with missing data on maternal occupation. Also, we are not aware of any a priori reason or empirical evidence suggesting differences in reporting of maternal occupation in cases of Down syndrome vis-à-vis the malformations included here as controls.

Women in the "no occupation" and "other" occupational groups were more likely than women in the remaining occupational groups to have missing data on continuation of pregnancy after a prenatal diagnosis of Down syndrome, and women of African origin were more likely than women of French origin not to have complete information on this variable. However, only a small number of cases involved missing continuation of pregnancy data, and any differences in misclassification because of missing data were unlikely to have had a substantial impact on our estimates.

We examined the effects of only 2 socioeconomic factors, maternal occupation and geographic origin, because data on other socioeconomic variables were not available from the Paris registry. Clearly, women's socioeconomic status and its possible effects on prenatal testing cannot be comprehensively represented by occupation and geographic origin alone. Indeed, previous studies have shown that other socioeconomic factors also affect use of prenatal testing[13–15,35] and that they do so in ways that are, at least to some extent, independent of maternal occupation and geographic origin.

We did not examine time trends in disparities, which merit their own separate analysis. A previous study[17] revealed substantial age-specific increases in overall proportions of Down syndrome cases diagnosed prenatally in the Parisian population during the period 1983 through 2000. Trends in prenatal diagnoses showed substantial increases, particularly among younger women, until the early 1990s; thereafter, increases were less pronounced. That study also revealed an overall trend of decreases in live-birth prevalences of Down syndrome despite increases in its overall prevalence as a result of delayed childbearing.

The estimates offered here can be considered "average" effects over the study period. However, because of the much faster rate of increase in prenatal Down syndrome diagnoses in the 1980s and early 1990s compared with the more recent period (after 1996), our estimates reflect much more closely current rates of prenatal diagnosis, particularly among younger women, than 1980s rates. In addition, prenatal Down syndrome diagnosis rates tend to be higher in the Paris registry than in most other European registries.[36] Therefore, the available data suggest that the prenatal diagnosis rate reported for our overall study period is fairly representative of current rates in several European countries.

Conclusions

Preferences and cultural values should clearly be considered in evaluations of prenatal testing policies.[37–39] At the same time, socioeconomic differences in prenatal testing that result from barriers to access and information should be addressed. Otherwise, as a result of the increasing use of prenatal testing, a new set of disparities in live-birth prevalences of severe types of congenital anomalies are likely to emerge. Moreover, in situations in which prenatal diagnoses substantially improve outcomes among newborns with congenital anomalies,[40–42] disparities in mortality, morbidity, and neurodevelopmental outcomes may begin to be observed.

Our results suggest that the increasing use of prenatal testing, accompanied by persistent socioeconomic differences in its use, has created disparities in the live-birth prevalence of Down syndrome, a congenital malformation whose overall risk does not vary according to socioeconomic status. Thus, socioeconomic differences in the live-birth prevalence of Down syndrome constitute an example of the creation of disparities in health outcomes for which socioeconomic inequalities did not exist initially. Such disparities come about as a result of advances in, and the increasing use of, medical care technology (e.g., prenatal testing), along with socioeconomic differences in its use.[8] In the case of congenital anomalies, disparities in prenatal testing imply that families with fewer resources may become disproportionately responsible for the care of infants born with the more severe types of anomalies. ■

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Contributors

B. Khoshnood, C. De Vigan, and B. Blondel originated the study. B. Khoshnood conducted the statistical analyses and wrote the first draft. C. De Vigan and B. Blondel contributed to the conceptualization of ideas and made suggestions about the required analyses. All of the authors contributed to the interpretation of findings and revisions of the article.

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Human Participation Protection

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