HAL
open science

Advances in medical technology and creation of disparities: the case of Down syndrome.

Babak Khoshnood, Catherine de Vigan, Véronique Vodovar, Gérard Bréart, François Goffinet, Béatrice Blondel

To cite this version:

Babak Khoshnood, Catherine de Vigan, Véronique Vodovar, Gérard Bréart, François Goffinet, et al.. Advances in medical technology and creation of disparities: the case of Down syndrome.. American Journal of Public Health, 2006, 96 (12), pp.2139-44. 10.2105/AJPH.2005.069377 . inserm-00119020

HAL Id: inserm-00119020

https://inserm.hal.science/inserm-00119020v1

Submitted on 11 Apr 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Hal author manuscript

Am J Public Health 12/2006; 96(12): 2139-44

Hal author manuscript inserm-00119020, version 1

Advances in medical technology and creation of disparities: The case of Down syndrome

Babak Khoshnood, MD, PhD, Catherine De Vigan, MD, Véronique Vodovar, RN, Gérard Bréart, MD, François Goffinet, MD, PhD, Béatrice Blondel, PhD

Correspondence, proofs and reprint requests to:

Babak Khoshnood, Inserm U149, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, France
Tel: (33 1) 45 59 50 09
Fax: (33 1) 45 59 50 89
Email: khoshnood@vjf.inserm.fr

Hal author manuscript inserm-00119020, version 1

Abstract

Objectives: To assess: i) socioeconomic differences in the probability of prenatal diagnosis, and continuation of pregnancy after prenatal diagnosis of Down syndrome (DS) and ii) their impact on disparities in live birth prevalence of DS.

Methods: Based on population-based data for 1,433 cases of DS and 3,731 malformed controls, we assessed maternal age-adjusted effects of maternal profession and geographic origin on prenatal diagnosis, total and live birth odds of DS. Statistical analyses included fractional polynomials for optimal adjustment of maternal age.

Results: Maternal profession and geographic origin had significant effects on the probability of prenatal diagnosis, and continuation of pregnancy after prenatal diagnosis of DS. Lower maternal professions were associated with higher odds of a DS live birth. Women without a profession had an age-adjusted odds of 2.4 (95%CI,1.7–3.3) for a DS live birth as compared with women in the highest professional category. In contrast, there were no disparities in the age-adjusted odds of total DS.

Conclusion: Socioeconomic differences in prenatal testing have apparently created disparities in live birth prevalence of DS, whose overall risk does not vary by socioeconomic status.

Hal author manuscript inserm-00119020, version 1

Introduction

Prenatal testing for congenital malformations has progressed considerably over the past thirty years. This has been particularly the case for Down syndrome[1,2], the foremost known cause of mental retardation of genetic origin[3]. Prenatal screening techniques for Down syndrome include assessment of ultrasonographic markers, in particular first trimester measurement of nuchal translucency, and maternal serum screening during the first and second trimesters of pregnancy. Techniques for definitive prenatal diagnosis include amniocentesis and chorionic villus sampling. In addition, non-invasive prenatal diagnosis of Down syndrome using molecular techniques for 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] and in particular prenatal testing[9-13] in several countries. 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], which has been accompanied by a reduction in the live birth prevalence of Down syndrome[17]. The underlying mechanisms for socioeconomic differences in use of prenatal testing[11,18] are incompletely understood. However, disparities may be related more to barriers to access and information rather than differences in women's preferences[15]. Moreover, previous data suggest differential and partially independent effects across various socioeconomic factors in their relation to use of prenatal testing[15].

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

Hal author manuscript inserm-00119020, version 1

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

Using population-based data, we assessed the effects of two socioeconomic factors, maternal profession and geographic origin, on the probability of: i) prenatal diagnosis, ii) continuation of pregnancy after a prenatal diagnosis of Down syndrome, and iii) the total and live birth odds of Down syndrome. We hypothesized that differences in prenatal testing may have resulted in higher maternal age-adjusted odds of a live birth with Down syndrome for lower socioeconomic groups.

Hal author manuscript inserm-00119020, version 1

Materials and Methods

We used data from the Paris Registry of Congenital Malformations ("Registry") for the period 1983 to 2002. The Registry is population-based, and a member of the European network of registries of congenital malformations (EUROCAT), and of the International Clearinghouse for Birth Defects Surveillance and Research. The Registry population comprise women who reside in Greater Paris (Paris and Petite Couronne) and give birth or have a pregnancy termination in Parisian maternity units (approximately 38,000 births per year). The Registry follows the EUROCAT methodology and quality of data is routinely monitored both by the registry and the EUROCAT central registry. Procedures for data collection and storage, as well as quality of data of the Registry are examined on a regular basis by the National Committee of Registries in France. In addition, review of procedures regarding confidentiality of data is overseen both by the National Committee of Registries and the *Commission Nationale de l'Informatique et des Libertés (National Committee of Informatics and Freedom).* Data are collected from multiple sources of information, including maternity units, neonatology services, and cytogenetic and pathology services, in order to allow high case ascertainment for congenital malformations including chromosomal abnormalities.

Our study included two sets of analyses. The first set of analyses included cases of Down syndrome only. We examined the effects of maternal profession and geographic origin on the probability of: i) prenatal diagnosis, and ii) continuation of pregnancy after a prenatal diagnosis of Down syndrome. We estimated the probability and maternal age-adjusted odds of prenatal diagnosis in relation to maternal profession and geographic origin among all cases of Down syndrome in the Registry. We then assessed the probability and maternal age-adjusted odds of continuation of pregnancy among all cases of Down syndrome that had been diagnosed prenatally.

Hal author manuscript inserm-00119020, version 1

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

Cases were live births, pregnancy terminations and stillbirths with Down syndrome (for total odds) and live births with Down syndrome (for live birth odds). Controls were chosen among other malformations in the Registry, using the following a priori criteria: i) the prevalence of malformations selected as controls was not known to be associated with socioeconomic factors (e.g., neural tube defects were not included since their prevalence is known to be associated with socioeconomic factors[20]); ii) selected anomalies for controls were not subject to prenatal diagnosis on a routine basis (e.g., cases of congenital heart disease and gastro-intestinal abnormalities were not included) and iii) malformations selected as controls had a relatively high frequency of occurrence.

Our initial study population included 1,698 cases of Down syndrome (live births, pregnancy terminations and stillbirths) and 4,005 controls. The control group included the following set of isolated anomalies: congenital dislocation of the hip (N=1,562), cleft palate (N=166), syndactyly (N=172), clubfoot (N=966), angiomas (N=593), congenital abnormalities of the integument (N=450), and anorectal anomalies (N=96).

Available information on socioeconomic characteristics in the Registry includes data on maternal profession and geographic origin. Data on paternal profession are collected but include a considerable proportion of missing values. Data on other socioeconomic factors including

Hal author manuscript inserm-00119020, version 1

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 profession using the categories defined by the French National Institute of Statistics and Economic studies (INSEE). We used the following professional categories, which generally represent the order of highest to lowest professional categories in France: professional (N=1,246), intermediate (N=1,199), administrative/public service (N=1,199), "other"(N=363) and none (N=1,244). The group "other" included the following categories that comprised a relatively small number of women in each category: artisan/small business owner, shop keeper/shop assistant, service worker, skilled worker and unskilled worker. We classified the geographic origin of the mother in terms of four categories representing the major groups in France: French (N=3,560), North African (N=603), Other African (320), and Other (1,007).

Data on maternal profession were missing for 420 (7.4 %) women, and on geographic origin of the mother for 213 (3.7 %) women. We found no significant differences in the frequency of missing data for geographic origin of the mother for cases of Down syndrome vs. controls (3.7% vs. 3.8%). Missing data on maternal profession were more frequent (14.7%) for cases of Down syndrome as compared with controls (4.3%). In addition, women with missing maternal profession had prenatal diagnosis rates that were somewhat higher (79.0 %) as compared with the overall group of women with a known profession (70.6 %) . However, when women with missing maternal profession were excluded, prenatal diagnosis rate for the overall sample did not change appreciably (71.8 % vs. 70.6%).

Cases with missing data on maternal profession and geographic origin were excluded from the study population, which then comprised 1,433 cases of Down syndrome (461 live

Hal author manuscript inserm-00119020, version 1

births) and 3,731 controls (3,713 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 five cases (0.3 %) of Down syndrome, and information regarding continuation of pregnancy after a prenatal diagnosis of Down syndrome was missing for 24 cases (2.4 %) of Down syndrome that had been diagnosed prenatally. These cases were excluded from the analyses of the effects of maternal profession and geographic origin on prenatal diagnosis of Down syndrome (N = 1,428, Table 1) and continuation of pregnancy after prenatal diagnosis of Down syndrome (N = 984, Table 1).

Missing values on prenatal diagnosis did not differ significantly across categories of maternal profession or geographic origin. Missing data on continuation of pregnancy after a prenatal diagnosis of Down syndrome were more frequent for women who were in the professional categories intermediate (N = 5, 2.0%), administrative/public service (N=8, 4.4%), other (N = 4, 6.0%), and none (N = 4, 2.0%) as compared with women in the highest professional category (the "professional" group, N = 3, 1.0%). Missing data on continuation of pregnancy were also more frequent for women of North African (N = 3, 3.3%) and African origin (N = 5, 10.6%) as compared with women from France (N = 13, 1.9%).

Statistical analysis

Given the increased delayed childbearing for women of higher socioeconomic groups, and the strong effect of maternal age on the risk of Down syndrome in the fetus, adequate adjustment for maternal age is crucial in studies of the relation between socioeconomic factors and total or live birth prevalence of Down syndrome. We used two alternative strategies of adjustment for maternal age. In the first strategy, we used the cusum model for binary variables[21], a non-parametric technique to assess alternative strategies for adjustment of a continuous variable (e.g.,

Hal author manuscript inserm-00119020, version 1

maternal age) in logistic regression models. In the second strategy, we used fractional polynomials[22] to determine the optimal strategy for adjustment of maternal age. The two strategies of adjustment for maternal age gave similar results in terms of the estimates of the age-adjusted effects of maternal profession and geographic origin on total and live birth odds of Down syndrome. We present here the results of the age-adjusted analyses by fractional polynomials.

Hal author manuscript inserm-00119020, version 1

Results

Of the 1,428 cases of Down syndrome, 1,008 (70.6%, 95% CI, 68.1 – 72.9) had a prenatal diagnosis. There was a substantial socioeconomic gradient in the probability of prenatal diagnosis of Down syndrome for both maternal profession and geographic origin (Table 1). Women from higher professional categories had significantly higher probabilities of prenatal diagnosis for Down syndrome. Women of French origin also had a higher probability for prenatal diagnosis as compared with women of African origin. Differences in the odds of prenatal diagnosis across professional categories and for women of North African origin were independently significant and remained so after adjustment for maternal age (Table 2).

5.5 % (95% CI, 4.1 – 7.1) of women continued their pregnancy after prenatal diagnosis of Down syndrome (Table 1). Women from lower professional categories and those of African origin tended to have higher probabilities of continuing their pregnancy after prenatal diagnosis of Down syndrome. Differences in the probability of continuation of pregnancy across professional categories were no longer significant however, after adjustment for maternal age and geographic origin (Table 2). On the other hand, the maternal age and profession-adjusted odds of continuation of pregnancy after prenatal diagnosis of Down syndrome remained significantly higher for women of African origin.

Table 3 shows results of the logistic regression analyses of the case-control study for assessing socioeconomic differences in total and live birth odds of Down syndrome. The total odds of Down syndrome were lower for women in lower professional categories, suggesting a lower total prevalence of Down syndrome for women in these categories. This difference disappeared after adjustment for maternal age. We also found no significant difference in the odds of Down syndrome for women of different geographic origin, suggesting that total prevalence of Down syndrome is similar for women of different geographic origins.

Hal author manuscript inserm-00119020, version 1

In contrast, there were substantial socioeconomic differences in the odds of a live birth with Down syndrome. Women in lower professional categories had higher odds of a live birth with Down syndrome both before and after adjustment for maternal age and geographic origin. For example, women with intermediate professions had a 1.5-fold increase (maternal age and geographic origin-adjusted Odds Ratio (OR), 1.5, 95% CI, 1.1 – 2.1) and those with no profession a 2.4-fold increase (Adjusted OR, 2.4, 95% CI, 1.7 – 3.3) in the odds of a live birth with Down syndrome as compared with women in the highest professional category. In addition, after adjustment for maternal age and profession, women with North African origin had higher odds (Adjusted OR, 1.5, 95% CI, 1.1 – 2.0) of a live birth with Down syndrome as compared with women of French origin.

Hal author manuscript inserm-00119020, version 1

Discussion

Our results suggest considerable disparities in the prenatal diagnosis, and thereby in the odds of live birth with Down syndrome. This is particularly the case across maternal profession groups with increasingly higher odds of a Down syndrome live birth for lower professional groups. Women without a profession had more than a two-fold increase in the odds of a Down syndrome live birth as compared with women in the highest professional category. These disparities in prenatal diagnosis and live birth prevalence of Down syndrome persist in the context of a prenatal testing policy with egalitarian intentions and specific regulations and programs aimed at increasing reimbursed access to prenatal testing for Down syndrome[16,23]. In contrast, we did not find any evidence for socioeconomic differences in the total 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 (total prevalence) does not seem to vary by socioeconomic status after accounting for socioeconomic differences in the distribution of maternal age[24,25].

We also found differences in the probability of continuation of pregnancy after a prenatal diagnosis of Down syndrome for women of different geographic origins, which suggest that 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 study[18] by Kuppermann and colleagues of a socio-economically diverse sample of women in the United States, which included a comprehensive evaluation of women's preferences.

It should be noted however, that previous data[28,29] and the results from our study suggest that by far the majority of women across different socioeconomic groups do not continue their

Hal author manuscript inserm-00119020, version 1

pregnancy after a prenatal diagnosis of Down syndrome. Moreover, differences in use of prenatal testing appear to be for the most part due to 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 revealed preferences may be related in part to health provider factors, and in particular to miscommunications between providers and pregnant women from different cultural backgrounds[27].

The interpretation of our results is subject to several caveats and limitation. In our case-control study of differences in the total and live birth odds of Down syndrome, we made use of a selective set of malformed controls in our Registry. The limitations and advantages of the use of malformed controls in epidemiological studies of congenital malformations have been discussed in previous literature[30-33]. The main issue of concern has been the possibility for selection bias in use of malformed controls. We aimed to minimize such bias by setting a priori criteria for the selection of controls. These criteria included: i) lack of any known relation between anomalies included as controls and socioeconomic status, the main exposure of interest; and ii) absence of routine prenatal diagnosis for malformations selected as controls, as differences in prenatal diagnosis of Down syndrome were hypothesized to be the underlying mechanism of the effect of socioeconomic status on the main outcome of interest (odds of a live birth with Down syndrome).

Our results showing the absence of socioeconomic differences in the age-adjusted total odds of Down syndrome are consistent with previous literature[34]. In addition, the fact that we found no significant disparities in the maternal age-adjusted total odds of Down syndrome suggests that any bias related to socioeconomic differences in the malformations used as controls may have been negligible. Otherwise, such selection bias would need to exactly balance the differences we found regarding the live birth odds of Down syndrome in order to result in the absence of any socioeconomic effects on total odds of Down syndrome. This does not seem very

Hal author manuscript inserm-00119020, version 1

likely. Moreover, the socioeconomic differences we found in live birth odds of Down syndrome were consistent with our findings on disparities in prenatal diagnosis and continuation of pregnancy after a prenatal diagnosis of Down syndrome.

Missing data on maternal profession were more frequent for cases of Down syndrome as compared with controls. However, we found no significant differences in the prenatal diagnosis rate of cases of Down syndrome that had been initially included in the study as compared with those included in the final study population, which excluded those with missing maternal profession. We are also not aware of any a priori reason or empirical evidence to suggest that differential reporting of maternal profession occurs in relation to Down syndrome vis-à-vis the malformations included as controls.

Missing data on continuation of pregnancy after a prenatal diagnosis of Down syndrome were more frequent for certain professional groups and women of African origin. However, the number of cases with missing data on continuation of pregnancy was small and any differential misclassification due to missing data is unlikely to have had a substantial impact on our estimates.

We examined the effects of only two socioeconomic factors, maternal profession and geographic origin, as data on other socioeconomic variables were not available in our Registry. Clearly, socioeconomic status of women, and its possible effects on prenatal testing cannot be comprehensively represented by profession 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 profession and geographic origin.

Our analyses did not include examination of time trends in disparities, which merit their own separate analysis. A previous study[17] found substantial age-specific increases in the overall

Hal author manuscript inserm-00119020, version 1

proportion of Down syndrome cases diagnosed prenatally in the Parisian population. Trends in prenatal diagnosis showed substantial increases, particularly for younger women, until the early 90's with smaller increases thereafter. The study also found an overall trend of decrease in the live birth prevalence of Down syndrome in spite of an increase in its total prevalence due to delayed childbearing.

The estimates we provide in the present article may be taken as "average" effects over the study period. However, due to the much faster pace of the increases in prenatal diagnosis for Down syndrome in the 80's and early 90's as compared with the more recent period, our estimates reflect much more closely current rates of prenatal diagnosis, particularly for younger women, than the prenatal diagnosis rates in the 1980's. In addition, prenatal diagnosis rates of Down syndrome tend to be higher in Paris than in most other European registries[36]. Therefore, the available data suggest that the prenatal diagnosis rate reported in our article for the overall study period may be fairly representative of the current rates in several European countries.

Preferences and cultural values should clearly be considered in the evaluation 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, with increasing use of prenatal testing, a new set of disparities in the live birth prevalence of the more severe congenital anomalies are likely to emerge. Moreover, in the cases that prenatal diagnosis substantially improves the outcomes of newborns with congenital anomalies[40-42], disparities may also emerge in the mortality, morbidity and neuro-developmental outcomes of newborns with congenital anomalies.

Hal author manuscript inserm-00119020, version 1

Conclusion

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 by socioeconomic status. Hence, it appears that 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 do not exist initially. Such disparities come about as a result of 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, these disparities imply that the care of infants born with the more severe anomalies may be given disproportionately to families with fewer resources.

Hal author manuscript inserm-00119020, version 1

About the Authors

The authors are with the INSERM, UMR S149, IFR 69, Epidemiological Research Unit on Perinatal and Women's Health, Villejuif, F-94807 France; Université Pierre et Marie Curie-Paris6, Paris, F-75012 France.

Reprint Requests

Babak Khoshnood, Inserm U149, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, France
Tel: (33 1) 45 59 50 09
Fax: (33 1) 45 59 50 89
Email: khoshnood@vjf.inserm.fr

Contributors

B. Khoshnood, C. De Vigan and B. Blondel conceived the idea of the study. B. Khoshnood conducted the statistical analyses and wrote the first draft of the manuscript. B. Blondel and C. de Vigan participated in all discussions, contributed to the conceptualization of ideas and made suggestions about the required analyses. All authors contributed to the interpretation of findings and revisions of the manuscript.

Acknowledgements

We thank the staff of the Paris maternity units for their participation in the collection of data used for this analysis. The Paris Registry received financial support from the Institut National de la Santé et de la Recherche Médicale (INSERM), and the Institut de Veille Sanitaire (InVS).

Human Participation Protection

The Paris Registry of Congenital Malformations received an authorization from CNIL (*Commission Nationale de l'informatique et des libertés*) in 1989. This authorization was subsequently renewed in 1997 and remains valid at the present time.

Hal author manuscript inserm-00119020, version 1

References

(1) Wald NJ, Watt HC, Hackshaw AK. Integrated screening for Down's syndrome on the basis of tests performed during the first and second trimesters. N Engl J Med 1999; 341:461-467.

(2) Wapner R, Thom E, Simpson JL *et al.* First-trimester screening for trisomies 21 and 18. N Engl J Med 2003; 349:1405-1413.

(3) Roizen NJ, Patterson D. Down's syndrome. Lancet 2003; 361:1281-1289.

(4) Lee T, LeShane ES, Messerlian GM *et al.* Down syndrome and cell-free fetal DNA in archived maternal serum. Am J Obstet Gynecol 2002; 187:1217-1221.

(5) Hart JT. The inverse care law. Lancet 1971; 1:405-412.

(6) Fiscella K, Franks P, Gold MR, Clancy CM. Inequality in quality: addressing socioeconomic, racial, and ethnic disparities in health care. JAMA 2000; 283:2579-2584.

(7) Gortmaker SL, Wise PH. The first injustice: socioeconomic disparities, health services technology, and infant mortality. Annu Rev Sociol 1997; 23:147-170.

(8) Victora CG, Barros FC, Vaughan JP. The impact of health interventions on inequalities: infant and child health in Brazil. In: Leon D, Walt G, editors. Poverty, Inequality and Health: An international perspective. Oxford University Press, 2001: 125-136.

(9) Sokal DC, Byrd JR, Chen AT, Goldberg MF, Oakley GPJ. Prenatal chromosomal diagnosis. Racial and geographic variation for older women in Georgia. JAMA 1980; 244:1355-1357.

(10) Halliday J, Lumley J, Watson L. Comparison of women who do and do not have amniocentesis or chorionic villus sampling. Lancet 1995; 345:704-709.

(11) Kuppermann M, Gates E, Washington AE. Racial-ethnic differences in prenatal diagnostic test use and outcomes: preferences, socioeconomics, or patient knowledge? Obstet Gynecol 1996; 87:675-682.

(12) Khoshnood B, Pryde P, Wall S *et al.* Ethnic differences in the impact of advanced maternal age on birth prevalence of Down syndrome. Am J Public Health 2000; 90:1778-1781.

(13) Khoshnood B, Wall S, Pryde P, Lee KS. Maternal education modifies the age-related increase in the birth prevalence of Down syndrome. Prenat Diagn 2004; 24:79-82.

(14) Julian-Reynier C, Macquart-Moulin G, Moatti JP *et al.* Reasons for women's non-uptake of amniocentesis. Prenat Diagn 1994; 14:859-864.

Hal author manuscript inserm-00119020, version 1

(15) Khoshnood B, Blondel B, De Vigan C, Breart G. Socioeconomic barriers to informed decisionmaking regarding maternal serum screening for Down syndrome: results of the French National Perinatal Survey of 1998. Am J Public Health 2004; 94:484-491.

(16) Ayme S, Morichon N, Goujard J, Nisand I. Prenatal diagnosis in France. Eur J Hum Genet 1997; 5(suppl 1):26-31.

(17) Khoshnood B, De Vigan C, Vodovar V, Goujard J, Goffinet F. A population-based evaluation of the impact of antenatal screening for Down's syndrome in France, 1981-2000. BJOG 2004; 111:485-490.

(18) Kuppermann M, Nease Jr RF, Gates E *et al.* How do women of diverse backgrounds value prenatal testing outcomes? Prenat Diagn 2004; 24:424-429.

(19) Bishop J, Huether CA, Torfs C, Lorey F, Deddens J. Epidemiologic study of Down syndrome in a racially diverse California population, 1989-1991. Am J Epidemiol 1997; 145:134-147.

(20) Wasserman CR, Shaw GM, Selvin S, Gould JB, Syme SL. Socioeconomic status, neighborhood social conditions, and neural tube defects. Am J Public Health 1998; 88:1674-1680.

(21) Royston P. The use of cusums and other techniques in modelling continuous covariates in logistic regression. Stat Med 1992; 11:1115-1129.

(22) Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. Int J Epidemiol 1999; 28:964-974.

(23) De Vigan C, Vodovar V, Verite V, Dehe S, Goujard J. Current French practices for prenatal diagnosis of trisomy 21: a population-based study in Paris, 1992-97. Prenat Diagn 1999; 19:1113-1118.

(24) Casterline JB, Lee RD, Foote KA. Fertility in the United States: New patterns, new theories. New York: Population Council, 1996.

(25) Bréart G. Delayed childbearing. Eur J Obstet Gynecol Reprod Biol 1997; 75:71-73.

(26) Zlotogora J. Parental decisions to abort or continue a pregnancy with an abnormal finding after an invasive prenatal test. Prenat Diagn 2002; 22:1102-1106.

(27) Browner CH, Preloran HM, Casado MC, Bass HN, Walker AP. Genetic counseling gone awry: miscommunication between prenatal genetic service providers and Mexican-origin clients. Soc Sci Med 2003; 56:1933-1946.

(28) Pryde PG, Drugan A, Johnson MP, Isada NB, Evans MI. Prenatal diagnosis: choices women make about pursuing testing and acting on abnormal results. Clin Obstet Gynecol 1993; 36:469-509.

Hal author manuscript inserm-00119020, version 1

(29) Mansfield C, Hopfer S, Marteau TM. Termination rates after prenatal diagnosis of Down syndrome, spina bifida, anencephaly, and Turner and Klinefelter syndromes: a systematic literature review. European Concerted Action: DADA (Decision-making After the Diagnosis of a fetal Abnormality). Prenat Diagn 1999; 19:808-812.

(30) Wacholder S, Silverman DT, McLaughlin JK, Mandel JS. Selection of controls in case-control studies. II. Types of controls. Am J Epidemiol 1992; 135:1029-1041.

(31) Hook EB. Normal or affected controls in case-control studies of congenital malformations and other birth defects: reporting bias issues. Epidemiology 1993; 4:182-184.

(32) Lieff S, Olshan AF, Werler M, Savitz DA, Mitchell AA. Selection bias and the use of controls with malformations in case-control studies of birth defects. Epidemiology 1999; 10:238-241.

(33) Swan SH, Shaw GM, Schulman J. Reporting and selection bias in case-control studies of congenital malformations. Epidemiology 1992; 3:356-363.

(34) Vrijheid M, Dolk H, Stone D *et al.* Socioeconomic inequalities in risk of congenital anomaly. Arch Dis Child 2000; 82:349-352.

(35) Khoshnood B, Blondel B, De Vigan C, Bréart G. Effects of maternal age and education on the pattern of prenatal testing: implications for the use of antenatal screening as a solution to the growing number of amniocenteses. Am J Obstet Gynecol 2003; 189:1336-1342.

(36) EUROCAT Working Group. EUROCAT Report 8: Surveillance of Congenital Anomalies in Europe, 1980-1999. 2002. Newtownabbey, Northern Ireland, University of Ulster.

(37) Kuppermann M, Feeny D, Gates E *et al.* Preferences of women facing a prenatal diagnostic choice: long-term outcomes matter most. Prenat Diagn 1999; 19:711-716.

(38) Kuppermann M, Goldberg JD, Nease RF, Jr., Washington AE. Who should be offered prenatal diagnosis? The 35-year-old question. Am J Public Health 1999; 89:160-163.

(39) Asch A. Prenatal diagnosis and selective abortion: a challenge to practice and policy. Am J Public Health 1999; 89:1649-1657.

(40) Bonnet D, Coltri A, Butera G *et al.* Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999; 99:916-918.

(41) De Vigan C, Goujard J, Vodovar V, Uzan S. Management of the fetus with a correctable malformation in Paris maternity units: evolution 1985-1994. Fetal Diagn Ther 1997; 12:216-220.

(42) Khoshnood B, De Vigan C, Vodovar V *et al.* Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983-2000: a population-based evaluation. Pediatrics 2005; 115:95-10.