Factors Associated with Recent Increase of Multiple Births in Spain

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The increased incidence of multiple deliveries in Spain, in addition to changes in age at maternity and parity, is attributed to assisted reproductive treatments, but the relative contribution of the latter to this rise remains uncertain, due to the scarce information provided by clinics practicing those treatments. Population based data (1984–2004), including information on mother's age, nationality, marital status, date of delivery, and the characteristics of each (parity, single or multiple), and sex of newborns were provided by the Spanish Institute of Statistics. Twinning and triplet deliveries relate to maternal age, parity, and nationality. For younger ages (≤ 19, 20–24, 25–29) rates remained constant over time, but for older women (30–34, 35–39, ≥ 40) rates increased after 1994. From 1984 to 2004 the percentage of twins of opposite sex increased from 24.31 to 36.58 per cent. Since 1997, Spanish and non-Spanish mothers differentiate with respect to multiple maternity at ages over 30. In addition to unmarried Spanish women, immigrants constitute a reliable reference group that determines the convenience of segregating information on multiple deliveries respecting origin. The proportion of twins and triplets of opposite sex, maternal age, and parity patterns observed are concordant with a differential access to reproductive treatments depending on the woman's age. The present norm regulating the maximum number of fertilizations per cycle and the demand for these treatments explain the high incidence of multiple deliveries in Spain. A modified logistic curve predicts a stabilization of multiple deliveries, which will probably continue to be high in Spain.

Differences among populations regarding multiple deliveries have been attributed more to dizygotic (DZ) than to monozygotic (MZ) twins (Bulmer, 1970). The rates of these two types of twins, based on official birth registers, are usually estimated from the proportions of same/opposite sex twins, according to Weinberg's differential rule, the reliability of which has been recently verified by Fellman and Eriksson (2006).

Although twinning is mainly related to the mother's age through variations in the FSH hormone and prenatal mortality (Bulmer, 1970; Pison & Couvert, 2004), other factors such as birth order, season (Garza-Chapa et al., 1984), socioeconomic factors (Murphy & Botting, 1989), ethnic group (Madrigal, 1994; Madrigal et al., 2001), and rural–urban differences perhaps related to industrialization (Eriksson & Fellman, 1973), have also been the object of study.

In the early 1950s, a decrease in multiple births was reported in many populations (James, 1982; Hajn, 1997). Astolfi et al. (2003) found that in many European countries, minimum multiple birth rates occurred between 1975 (Sweden) and 1980 (Austria and Italy). Some authors (Bortolus et al., 1999; Bulmer, 1970; Eriksson & Fellman, 1973; Parazzini et al., 1991) attributed this reduction to a lowering of age at maternity, as well as to a reduction of parities. However, according to Fellman & Eriksson (1990) those factors are insufficient to explain the regional and temporal changes reported. Since the 1980s, multiple deliveries have become more common in many developed countries (Astolfi et al., 2003; Elwood, 1983; Eriksson & Fellman, 2004; Imaizumi, 2003; Jewell & Yip, 1995).

In Spain, the standardized rate reported by Bulmer (1960) for the period 1951–1953 was 9.10 per 1000 deliveries, which does not differ significantly from the value of 9.49 for 1951–1967 (Valls, 1972). A slightly lower rate (8.87) was reported by Bertranpetit & Marín (1986) for the years 1975–1979. Information concerning twins is not available at the Spanish Institute of Statistics for the years 1968–1974, so the date of the lowest level of multiple births for Spain remains undetermined.

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The increase in the twinning rate has been attributed to the change in age structure of mothers (Pison & D'addato, 2006), as well as to the extensive practice of assisted reproduction techniques (ART), including the use of ovulation promoters, which began in 1978 (Steptoe & Edwards, 1978). In order to achieve a greater chance of a successful implantation using ART, a large number of embryos are transferred, so the effect of these techniques is expected to be more evident for triplets than for twin deliveries (Astolfi et al., 2003; Eriksson & Fellman, 1973; Eriksson & Fellman, 2004; Luke, 1994).

In 1980, the twinning rate for Spain reported by Fuster et al. (2006) was as low as 7.4 per 1000 deliveries. Thereafter, a continuous increase in the number of multiple deliveries occurred, increasing to 12.4 in 1996, although rates for 1981–1982 remain doubtful. In contrast to other European countries, Spain is underrepresented, not only in terms of studies on multiple deliveries in the general population, but also regarding ART, for which information is limited to less than one quarter of the clinics providing IVF/ICSI techniques (Andersen et al., 2004; Marqueta et al., 2005). At present 203 clinics, 81.2% of which are private, are authorized in Spain to provide reproduction treatments. Most patients go directly to private centers because treatments in public hospitals are not available in all regions, women over 40 are excluded, and the delay in beginning treatment for women under 40 is usually 3 years (www.adeces.org). Information regarding multiple maternities in Spain is of interest, considering the socioeconomic transformation experienced in the country in recent decades, and the present study intends to compensate for the previous lack of such information available.

The delay in age at first maternity (24.72 years in 1984; 29.25 in 2004) that has occurred in Spain since the eighties, in addition to other social changes, such as a progressively greater proportion of extramarital reproduction, as well as the contribution of immigrant deliveries, need to be considered in order to accurately analyze how maternal origin, maternal age, and parity relate to the temporal variation of multiple deliveries, and to their balance regarding sex in Spain. The possible influence of subfertility treatments is also considered.

Materials and Methods

The Spanish Institute of Statistics (INE) provided information regarding births and deliveries (N = 8,440,991) occurring during the period 1984–2004. Date, mother's age, nationality (Spanish, immigrant), marital status, maternal place of residence, the characteristics of each delivery (single or multiple), and sex of newborns were collected. Only mothers with declared residence in Spain were included in the analysis.

Prior to 1997, data was organized by births, rather than by deliveries. Therefore, in order to calculate the twinning rates, a new variable that identified newborns in the same delivery was generated in the present study for each birth

The yearly number of twins and triplets occurring between 1984 and 2004 is expressed as rates per 1000 and 10,000 deliveries, respectively, 1984 being the year of the first birth resulting from in vitro fertilization (Matey, 1997. In order to relate maternal age and parity with twinning, six categories were established for age: ≤ 19, 20–24, 25–29, 30–34, 35–39, and ≥ 40 years, and two for birth order: first parity, ≥ second parity.

The sex of the newborns (same/opposite) was considered only in cases where there was information about all members of the multiple delivery and there was separate information for twins and triplets. Dizygotic twins may be of the same or opposite sex, but MZ twins are necessarily of identical sex. The decision to analyze the frequencies of same/opposite sex twins instead of DZ rates is based on the fact that the latter are estimated from the same frequencies. In this way the comparison with other recent studies is possible.

Statistical analysis was performed using SPSS and Statgraphics Plus statistical packages. The parameters of the logistic curve fitted have been computed by the module of Non-Linear regression of the Statgraphics Plus (Marquardt algorithm in the Advanced Regression command). From this logistic curve, the inflexion point was computed by means of a numerical procedure (Newton-Raphson algorithm) coded in FORTRAN SALFORD FT95.

Results

Figure 1 shows the rates of twins (N = 97,236) and triplets (N = 3,082) occurring in Spain from 1984 to 2004. Throughout this period the yearly twinning rate increased continuously.

The twinning rate fits a variation of the logistic curve according to:

Twinning rate = $A/[1+BEXP(CX^3)]$

where X = years–1984.

For the coefficients A = 17.4385, B = 1.14036, and C = –0.000526, the model produces a significant fit to

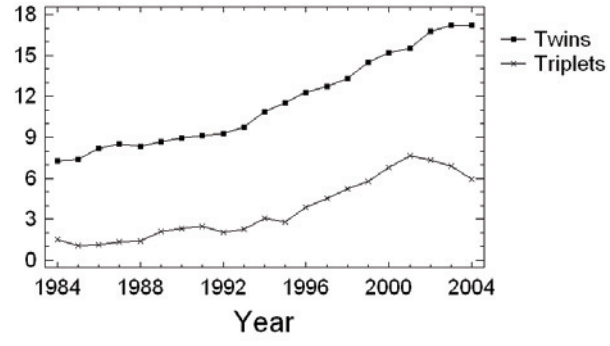

Figure 1

Yearly twinning rate per 1000 deliveries and triplet rate per 10,000 deliveries.

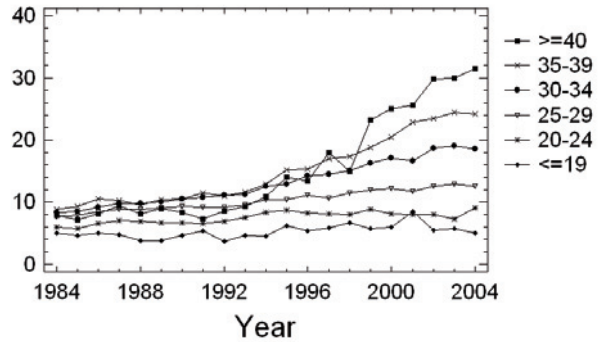

Figure 2

Yearly twinning rate per maternal age.

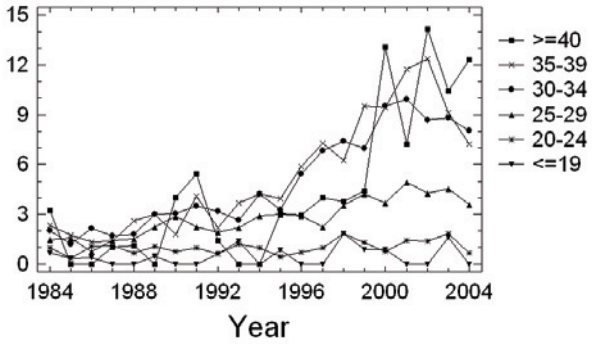

Figure 3

Triplets: yearly rate per 10000 deliveries according to maternal age.

data (r^2 = 0.986), and makes it possible to determine the inflexion point of the function that occurred in 1997. Since this year, the increase in the twinning rate has slowed in comparison to preceding years.

The temporal change in the twinning rate regarding age at maternity is represented in Figure 2. For the three younger age groups (≤ 19, 20–24, 25–29) rates remained constant over time, but for categories over 30 years, while rates remained initially stable, they increased after 1994.

A similar rising tendency applied to triplets from 1984 to 2002, but rates have since lowered (Figure 3). Stochastic fluctuations are explained by the fewer yearly number of triplets (range: 49–306) in comparison to twins (range: 3336–7712). The age effect is clear for categories over 30; the group 25–29 occupying an intermediate position.

During the period 1997–2004, for which nationality was consigned, while the contribution of immigrant mothers to total deliveries increased from 3.80% in 1997 to 13.88% in 2004, the corresponding percentages for multiple deliveries were 3.63% and 9.16%, respectively, indicating that in 2004, immigrants contributed to total multiple motherhood comparatively less than did native born Spaniards.

The Spanish group was separated by marital status, but immigrant women were not (Figure 4). The twinning rates have lowered since 2000 among immigrant mothers, while among Spanish mothers they have increased, a fact in part reflecting a differential average age at motherhood variation from 1997 to 2004: Spanish 29.78 to 31.03 years; immigrants 28.81 to 28.04 years. These averages reflect unequal temporal change in the age distribution at motherhood: the first categories (≤ 19, 20–24, and 25–29) for Spanish mothers decreased from 3.0 to 2.3%; 10.7 to 7.7%, and 32.0 to 24.7%, respectively. For immigrant mothers on the contrary, the values for the corresponding ages increased from 4.3 to 5.7, 19.7 to 24.0, and 30.7 to 31.3, respectively

Both groups also differentiate regarding age at multiple maternity, but only for maternities over 30. From initial coincident twinning rates for married Spanish and non-Spanish mothers, rates have diverged since 1999. Rates were progressively higher among married Spanish mothers, with final values of 20 per 1000. Unmarried Spanish and immigrant mothers maintained rates around 12 per 1000.

As the effect of age at delivery on twinning is appreciable for ages over 30, the forthcoming analysis is focused on late maternities. The simultaneous consideration of maternal age and birth order (Figure 5) results in a distinct temporal variation of first

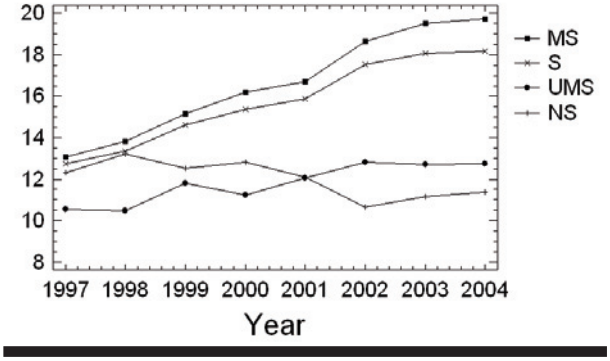

Figure 4

Twinning rates for married Spanish mothers (MS), Spanish unmarried (UMS), Spanish mothers (S) and non Spanish (NS).

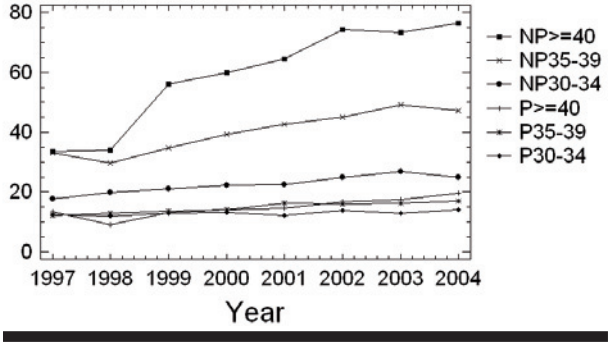

Figure 5

Twinning rate per maternal age (30-34, 35-39, ≥ 40 years) and parity (P: with previous children; NP: no previous children). Married Spanish mothers.

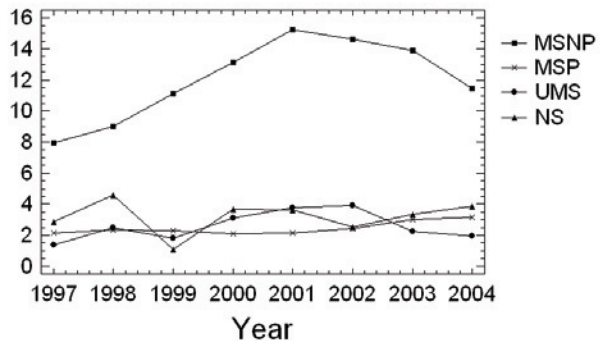

Figure 6

Triplets per 10000 deliveries: yearly rate (1997-2004) for married Spanish mothers without previous children (MSNP), for married Spanish with previous children (MSP), unmarried Spanish (UMS) and for non-Spanish (NS).

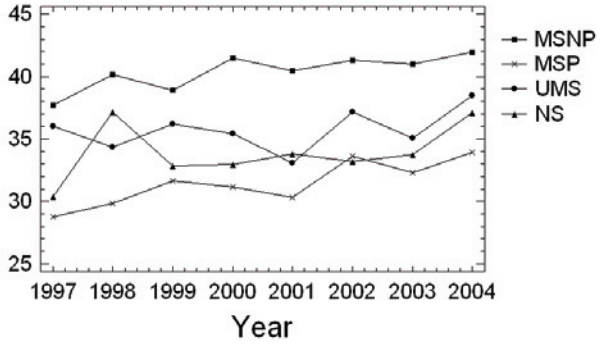

Figure 7

Twins of opposite sex: yearly percentage for maternal age ≥ 30 years in non Spanish (NS), married Spanish with previous children (MSP), married Spanish without previous children (MSNP) and unmarried Spanish (UMS).

maternities of married women older than 30, while those who have had previous children remain stable. This temporal variation is also shown by using Kendall's Tau-B correlation coefficients. These values increased from .5 for ages 30 to 40 (parity greater than 1) to .929 for mothers older than 40 without previous children.

The triplet rates began to decrease in 2002 in Spain, a reduction attributable only to Spanish women without previous children (Figure 6); the remaining groups did not show any clear increasing or decreasing pattern. In particular, among immigrant mothers rates remain practically constant irrespective of time, with a Tau-B coefficient of Kendall of .071.

To determine whether the number of twins of opposite sex could be an indicator of twinning associated with techniques of reproduction, children born from multiple deliveries were classified according to sex. From 1984 to 2004 the percentage of twins of opposite sex increased in Spain from 24.31 to 36.58. Opposite sex in triplet deliveries had even greater variation, increasing from 39.13 in 1984 to 66.79 in 2004. For the period 1997 to 2004 and for mothers older than 30, Figure 7 shows for married Spanish mothers the percentages of twins of opposite sex, according to parity (parity1; parity ≥ 2) and marital status. For comparison, values are also shown for corresponding immigrant mothers without distinguishing by parity, since no variation was found for this factor. Higher percentages of twins of unlike sex appear in married Spanish mothers delivering a first child than in married Spanish mothers of parity ≥ 2, unmarried Spanish mothers, and immigrant mothers.

With the exception of 2004, parity has the same influence for triplets as for twins: married Spanish women delivering for the first time had triplets of opposite sex (70.53%) more frequently than married Spanish mothers with previous children (62.50 %). Corresponding percentages for unmarried Spanish and immigrant mothers were 64.13 and 63.93, respectively. In the latter two groups, the number of cases was insufficient to consider parity.

Discussion

The initial rates of twins and triplets (Figure 1) are low compared to other European countries (Imaizumi, 2003), although they are close to those of Italy and Austria (Astolfi et al., 2003), and after 1995 approaching only those of Switzerland, Germany, England and Wales. The twinning rate fits a variation of the logistic curve instead of following a linear function or a quadratic model as applied by Astolfi et al. (2003), which determines an inflexion point in 1997. The rate in this year could be explained by an age effect due to immigrant mothers delivering for the first time at a younger age than Spanish mothers.

The variation in the twinning rate with regard to maternal age (Figure 2) only affected women older than 30 after 1994. Eriksson and Fellman (2007), in a study on twinning in England and Wales, have also identified changes in the age-specific rates that show an increase in twinning levels in older mothers. In Spain, the decrease of triplet rates since 2002 in mothers older than 30, is equivalent to that seen in Figure 1, regardless of age, perhaps as a consequence of the reduction in the number of embryos transferred (García Velasco, 2005; Marqueta et al., 2004).

The observed age patterns for twins and triplets (Figures 2 and 3), which show that initial stable rates increased after 1994 only for mothers older than 30, are consistent with a greater proportion of older women requiring reproductive treatments such as reported by Pison & D'addato (2006). For Spain in the year 2000 the corresponding percentages per group of ages of these women were: 14% (≤ 29 years), 37% (30–34), 37% (35–39), and 11% (≥ 40; Andersen et al., 2004).

Extramarital births have been considered good indicators of natural twinning (Parazzini et al., 1994), and Murphy et al. (2000) reported that the

corresponding twinning rates did not increase after 1980. At present, extramarital births do not reflect any influence attributable to sub-fertility treatments, and illegitimacy is not considered a significant factor in reproduction. Moreover, in Spain immigration has recently increased, which should be taken into account when considering the contribution of reproductive treatments to multiple deliveries. For this reason, the 1997–2004 mean rates for immigrants in each group of ages were considered for comparison, in addition to unmarried native Spaniards.

When considering nationality from 1997 to 2004, immigrants contributed to total multiple motherhoods comparatively less than did Spanish women. For the latter, twinning rates were higher among married (20 per 1000) than for either unmarried or immigrant mothers (about 12 per 1000). The increase in double deliveries from 12 to 20 per thousand, expressed in percentages, is equal to the figure of 40% attributed to multiple deliveries after reproductive treatments (Ombelet et al., 2005).

Immigrants are expected to produce multiple deliveries influenced by age and parity, but to a lesser degree by assisted reproduction, since unfavourable socioeconomic circumstances may limit their access to expensive reproductive treatments, which, in most cases, are not provided by the National Public Health System, but by private clinics. Differences in multiple delivery, noticeable only for women older than 30, indicate that, for the youngest categories, the relationship between maternal age and twinning is the same in both groups. The predominance of older Spanish mothers is probably the result of a larger proportion of these women receiving reproductive treatments.

Twinning rates for married women older than 30 differentiate temporally only for parity 1, a situation also reported by Astolfi et al. (2003) in Italy. The demand for reproductive treatments is dependent on age, and Pison and Couvert (2004) estimated that in France, delayed maternity explains about one third of the twinning increase, and treatments against sterility two thirds.

The reduction in triplets since 2002 (Figure 6) is seen in Spanish women without previous children, but not unmarried or immigrant mothers, possibly due to changes in the number of embryos transferred.

Although the number of embryos implanted between 1998 and 2000 in Spain was lowered (García Velasco, 2005), due to a reduction in the transfer of four embryos in favour of two (Marqueta et al., 2004), the figure remained high in comparison to other European countries, mainly Sweden where in 2001 80% of transfers involved two embryos in comparison to 25% in Spain (Simón & Pellicer, 2005). Using 2001 data, Bruna Catalán et al. (2005) reported that Spain showed one of the highest incidences of multiple births following assisted reproduction, the rate for triplets being nearly three times higher than the European rate (4.1 vs. 1.5). Since November 2003, the maximum number of embryos to be implanted was limited by law to three in Spain (Bruna Catalán et al., 2005), but no regulation exists regarding induction of ovulation.

Fertilization using in vitro techniques is expected to produce an increased proportion of twins derived from distinct eggs; in such a scenario the proportion of twins or triplets consisting of siblings of unlike sex would be greater than in natural reproduction (Kapidaki et al., 1995). In a French regional population based study, Khoshnood & Blondel (2006) reported that in relative terms, the increase in different sex twins was substantially greater than that of same sex twin births. The results obtained in the present analysis are concordant with the above: the percentage of twins and triplets of opposite sex increased from 1984 to 2004 (24.31 to 36.58 and 39.13 to 66.79, respectively). Taking into consideration age at delivery, since 1997 Spanish married women older than 30 and with parity 1 had an elevated frequency of twins of unlike sex. Except for the year 2004, this was also true for triplets.

The necessity of segregating information on multiple deliveries with regard to maternal origin is made clear from the present study. Immigrant mothers constitute as reliable a reference group as unmarried Spanish mothers. Not taking them into consideration would bias the data. The results obtained are consistent with the demand for reproductive treatment according to maternal age and parity. The progressively extensive use of reproductive treatments against sterility in Spain depends on the age of the women requesting them, and the slight variations observed at the end of the period studied could be related to changes in the number of embryos implanted using these techniques. The most efficient way to reduce the medical cost associated with infertility treatments is the prevention of multiple pregnancies, not only triplets and quadruplets, but, even more important, the reduction in twin pregnancies (Ombelet et al., 2005). The norm of May 2006 on assisted reproduction in Spain differs slightly from the 1988 rule, which was partially modified in 2003. With the present change, the limitation established in 2003 of a maximum of three fecundations per cycle has been abolished, leaving Spain as one of the most permissive in this regard in Europe (Abellán, 2006). Data adjusted to the modified logistic curve indicate a stabilizing of multiple deliveries at the end of the period studied, which predicts that twinning rates will remain high in Spain. This is possible, considering the sustained demand for ART at ages over 30, a consequence of delaying the decision to have children for socioeconomic reasons. However, higher rates of multiple births, with the increased probability of low weight or premature newborns associated with multiple deliveries, may occur if the Spanish Public

Health System eventually provides universal free access to ART and the age limit for receiving treatment is eliminated.

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References

Abellán, F. (2006). Algunas reflexiones sobre el nuevo marco legal regulatorio de la reproducción asistida en España [Some reflections on the new legal regulation for assisted reproduction in Spain]. *Revista Iberoamericana de Fertilidad*, *23*, 209–212.

Andersen, N., Gianaroli, L., & Nygren, K. G. (2004). Assisted reproductive technology in Europe, 2000. Results generated from European registers by ESHRE. *Human Reproduction, 19*, 490–503.

Astolfi, P., Ulizzi, L., & Zonta, L. A. (2003). Changes in twinning rate: Italy 1950–1996. *Human Reproduction, 18,* 207–211.

Bertranpetit, J., & Marín, A. (1986). Nacimientos múltiples en España (1975–1979) [Multiple births in Spain (1975–1979)]. *Trabajos de Antropología*, *20*, 75–80.

Bortolus, R., Parazzini, F., Chatenoud, L., Benzi, G., Bianchi, M. M., & Marini, A. (1999). The epidemiology of multiple births. *Human Reproduction Update*, *5*, 179–187.

Bruna Catalan, I., Pérez Milán, F., Tur Padró, R., Ricciarelli, E., de la Fuente Hernández, A., Monzó Miralles, A., Martínez-Salazar, J., Fernández-Shaw, S., Ardoy Vilches, M., Torelló Ibáñez, M. J., & Vila Alvarez, J. (2005). Embarazo múltiple derivado de FIV-ICSI en España: incidencia y criterios sobre la transferencia embrionaria [Multiple pregnancy after FIV-ICSI in Spain: incidence and criteria on the transference of embryos]. *Revista Iberoamericana de Fertilidad, 22*, 99–110.

Bulmer, M. G. (1960). The twinning rate in Europe and Africa. *Annals of Human Genetics London,* 24, 121–125.

Bulmer, M. G. (1970). *The biology of twinning in man.* Oxford: Clarendon Press.

Elwood, J. M. (1983). The end of the drop in twinning rates? *The Lancet, 26*, 470.

Eriksson, A. W., & Fellman, J. (1973). Differences between Finns and Swedes in the twinning trends. *American Journal of Human Genetics*, *25*, 141–151.

Eriksson, A. W., & Fellman, J. (2004). Demographic analysis of the variation in the rates of multiple maternities in Sweden since 1751. *Human Biology*, *76*, 343–359.

Eriksson, A. W., & Fellman, J. (2007). Temporal trends in the rates of multiple maternities in England and Wales. *Twin Research and Human Genetics, 10*, 626–32.

Fellman, J. O., & Eriksson, A. W. (1990). Standardization of the twinning rate. *Human Biology*, *62*, 803–816.

Fellman, J. & Eriksson, A. W. (2006). Weinberg's differential rule reconsidered. *Human Biology*, *78*, 253–275.

Fuster, V., De Blas, C., Colantonio, S., & Alonso, V. (2006). Evolución y variabilidad de las tasas de gemelaridad en la población española [Evolution and variability of twinning rates in the Spanish population]. *Revista Española de Antropología Física*, *26*, 19–24.

García Velasco, J. A. (2005). Prevención de la gestación múltiple desde la perspectiva de las estimulaciones ováricas en España [Prevention of multiple pregnancy regarding ovarian stimulation in Spain]. *Revista Iberoamericana de Fertilidad*, *22*, 323–326.

Garza-Chapa, R., Escobar, M. S., Cerda, R., & Leal-Garza, C. H. (1984). Factors related to the frequency of twinning in the state of New Leon, Mexico during 1977 and 1978. *Human Biology*, *56*, 277–290.

Hajn, V. (1997). Long-term trends in frequency of multiple births in 1643–1900 in the Deanery Sumperk (Schönberg). *Acta Universitatis Palackinae Olomucensis Facultas Rerum naturalium. Biologica*, *335,* 41–45.

Imaizumi, Y. (2003). A comparative study of zygotic twinning and triplet rates in eight countries, 1972–1999. *Journal of Biosocial Science, 35*, 287–302.

James, W. H. (1982). Second survey of secular trends in twinning rates. *Journal of Biosocial Science, 14*, 481–497.

Jewell, S. E., & Yip, R. (1995). Increasing trends in plural births in the United States. *Obstetrics & Gynecology*, *85*, 229–232.

Kapidaki, M., Roupa, Z., Sparos, L., Tzonou, A., Olsen, J., & Trichopoulus, D. (1995). Coffee intake and other factors in relation to multiple deliveries: a study in Greece. *Epidemiology*, *6,* 294–298.

Khoshnood, B., & Blondel, B. (2006). Regional variations in trends for multiple births: A population-based evaluation in France, 1972–2003. *Twin Research and Human Genetics*, *10*, 406–415.

Luke, B. (1994). The changing pattern of multiple births in the United States: maternal and infant characteristics, 1973–1990. *Obstetric Gynecology*, *84*, 101–106.

Madrigal, L. (1994). Twinning rates in admixture Costa Rican population. *American Journal of Human Biology*, *6*, 215–218.

Madrigal, L., Saenz, G., Chaves, M., & Dykes, D. (2001). Frequency of twinning in two Costa Rican ethnic groups. *American Journal of Human Biology*, *13*, 220–226.

Marqueta, J., Hernández, J., Matorras, R., Coroleu, B., Simón, C., Pérez Milán, F., Báez, D., López Villaverde,

V., Cabello, Y. & Romeu, A. (2004). Registro FIV-ICSI de la Sociedad Española de Fertilidad. Año 2000 [Spanish Society for fertility FIV-ICSI register. Year 2000]. *Revista Iberoamericana de Fertilidad*, *21*, 133–143.

Marqueta, J., Hernández, J., Coroleu, B., Simón, C., Pérez-Milán, F., Arnott, I., Blanes, R., Monzó, A., Cabello, Y. & Matorral, R. (2005). Registro FIV-ICSI de la Sociedad Española de Fertilidad. Año 2001 [Spanish Society for fertility FIV-ICSI register. Year 2001]. *Revista Iberoamericana de Fertilidad*, *22*, 237–248.

Matey, P. (1997, December 4). En busca de hijos sanos [Looking for healthy children]. El Mundo, Salud. Retrieved November 30, 2007, from http://www.elmundo.es/salud/1997/272/01713.html

Murphy, M., & Botting, B. (1989). Twinning rates and social class in Great Britain. *Archives of Disease in Childhood*, *64*, 272–274.

Murphy, M. F. G., Hey, K., Whiteman, D., O´Donnell, M., Willis, B., & Barlow, D. (2000). Is the natural twinning rate now stable? *Journal of Biosocial Science*, *32*, 279–281.

Ombelet, W., de Sutter, P., Van der Elst, J., & Martens, G. (2005). Multiple gestation and infertility treatment: registration, reflection and reaction – the Belgian project. *Human Reproduction Update*, *11*, 3–14.

Parazzini, F., Tozzi, L., Mezzanotte, G., Bocciolone, L., La Vecchia, C., Fedele, L., & Benzi, G. (1991). Trends in multiple births in Italy: 1955–1983. *British Journal of Obstetrics and Gynecology*, *98*, 535–539.

Parazzini, F., Restelli, S., Moroni, S., & Crosignani, P. G. (1994). Trend in legitimate and illegitimate multiple births. *Human Reproduction*, *9*, 1784–1785.

Pison, G., & Couvert, N. (2004). La fréquence des accouchements gémellaires en France. La triple influence de la biologie, de la médicine et des comportements familiaux. [The frequency of twin births in France. The triple influence of family biology, medicine and behavior]. *Population*, *59*, 877–908.

Pison, G., & D'addato, A. V. (2006). Frequency of twin births in developed countries. *Twin Research and Human Genetics*, *9*, 250–259.

Simón, C., & Pellicer, A. (2005). Encuentro de expertos sobre gestaciones múltiples. Introducción [Meeting of experts on multiple pregnancy. Introduction]. *Revista Iberoamericana de Fertilidad*, *22*, 309–310.

Steptoe, R. C., & Edwards, R .G. (1978). Birth after the reimplantation of a human embryo. *Lancet*, *2*, 336.

Valls, A. (1972). Sobre la repartición de la gemelaridad en España [On the distribution of twinning in Spain]. *Revista Española de Antropología Americana*, *7*, 235–244.