Twinning Rates in Developed Countries: Trends and Explanations

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THE TWINNING RATE has increased dramatically over the last four decades in nearly all countries for which we have information from vital statistics (Hoekstra et al. 2008; Pison and d'Addato 2006). The twinning rate is the proportion of twin deliveries in a given year out of the total number of deliveries, expressed per 1,000 deliveries. The rate increased in the United States from 9.5 twin deliveries per 1,000 deliveries in 1975 to 16.9 in 2011 (Martin et al. 2012). It roughly doubled in many other developed countries over the same period, increasing from 9.9 to 16.1 in England and Wales, 9.2 to 17.2 in Germany, 9.3 to 17.4 in France, 9.6 to 21.2 in Denmark, and 5.0 to 14.6 in South Korea (data based on national vital statistics).

This increase is an important public health issue, because twin babies are more fragile than singleton ones. They have lower birth weight, more complications at birth, and are more often born premature—all of which are associated with many long-term health problems (Delobel-Ayoub et al. 2009; Johnson and Schoeni 2011; Larroque et al. 2004). Stillbirth and infant mortality rates are also much higher among twins than among singletons (Fresson et al. 2015; Guo and Grummer-Strawn 1993; Monden and Smits 2014; Pison 1992). Twin births can have negative effects on parents as well. Twin pregnancies are associated with higher risk of gestational diabetes, pre-eclampsia, postpartum depression, and increased divorce risk (Bdolah et al. 2008; Choi, Bishai, and Minkovitz 2009; Jena, Goldman, and Joyce 2011; Rauh-Hain et al. 2009).

A major reason for the recent increase of twinning rates is the sharp rise of medically assisted reproduction (MAR)[1] since the 1970s. Techniques like ovarian stimulation and *in vitro* fertilization (IVF) are associated with a greatly increased risk of multiple births. However, in the same period, the mean age at childbearing has also increased considerably, and the incidence of multiple pregnancies is known to increase with the mother's age (Bulmer 1970).

Since the beginning of the twenty-first century, rising concerns about the high number of twins (and even triplets[2]), with the associated health risks for mother and child, have led to changes in MAR practices in some countries, including a reduction in the number of embryos transferred to the uterus (Hazekamp et al. 2000). At the same time, however, the number of treatments continues to increase, and the average age of women undergoing these treatments is rising (Kupka et al. 2014).

These developments raise a number of questions regarding the trends in twinning rates in developed countries. To what extent is the increase in twinning rates since the 1970s attributable to an increase in the maternal age at birth and to what extent to the rise of MAR? Will twinning rates continue to rise or will they reach a plateau or even start to decrease under the influence of changing MAR practices?

We attempt to answer these questions using a compilation of available statistical information on twin births in developed countries. In the next section, we describe how twinning rates have changed in these countries over the last century. We then estimate the share of the increase over the last 40 years caused by each of two main factors: the rise in the age at childbearing and the rising number of infertility treatments. We conclude by examining the recent reversal of the trend observed in some countries and discuss the reasons for this.

Trends in developed countries

Recent changes in the frequency of twin births in developed countries should be seen in their historical context. We collected data from the civil birth registration systems of the national statistical offices and from earlier studies where data from official registers had been collected and compiled.[3] Figure 1 presents data for five European countries for which long historical series of twinning rates are available. The series go back to around 1900 (with the exception of Greece, for which the series start in 1956). We added four non-European countries: the United States, for which the series start in 1915, and three East Asian countries or territories (Japan, Hong Kong, Singapore) for which they start in the 1970s.

Several insights can be drawn from Figure 1. First, twinning rates have changed considerably over the last 100 years in these countries, with two-fold variations in many of them, 2.5-fold in some cases (Denmark, Singapore), and even 3-fold in the most extreme cases (Greece, Hong Kong). Second, in all European countries and in the US, there has been a decrease since World War II, with a minimum in the 1970s followed by a marked increase. For most East Asian countries, no data are available to examine trends before the 1970s, but trends similar to those seen in the European countries and in the US are observed since the 1970s. Third, in some countries the twinning rate seems to have reached a plateau after 2000 and diminished thereafter. This is

FIGURE 1   Trends in the twinning rate in selected developed countries or territories, 1900–2013
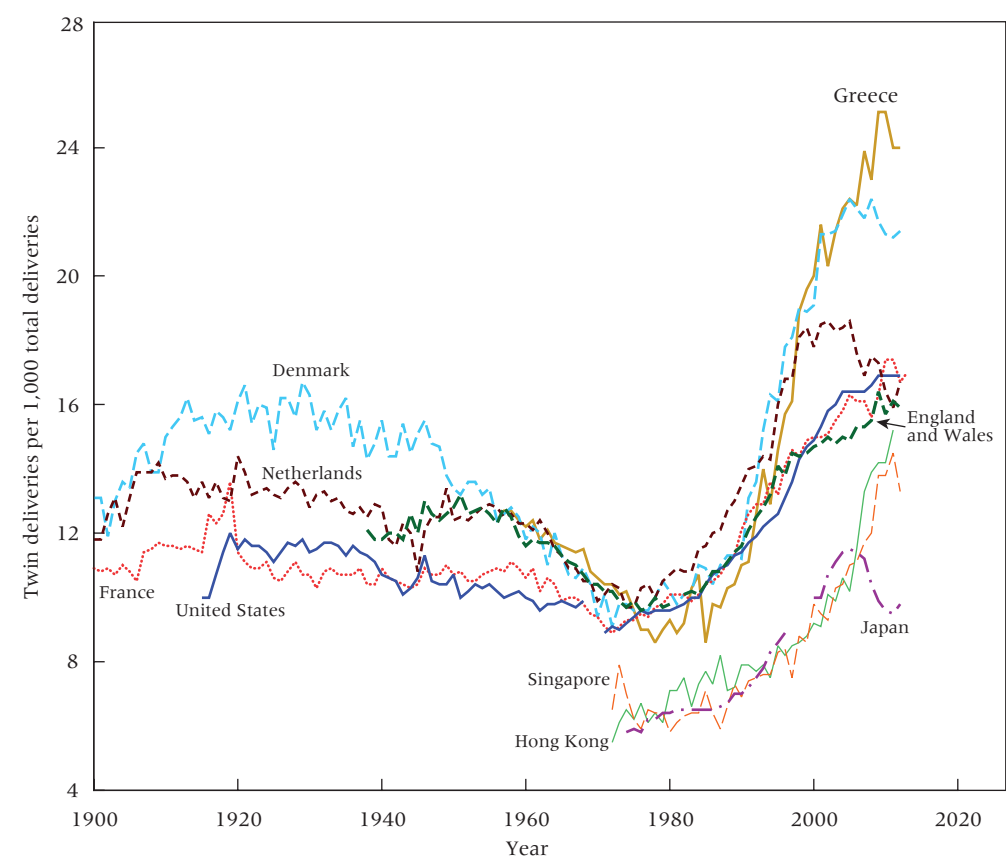
SOURCES: National statistical offices; authors' calculations.

the case for Denmark, the Netherlands, and Japan. In some other countries, the increase seems to have decelerated, but it is not clear whether a plateau has been reached. Fourth, this pattern of changes is observed regardless of the general level of twinning in the country. Although the twinning rate varies across regions and countries (Bulmer 1970; Smits and Monden 2011), these differences have little effect on the general pattern.

Effects of age at childbearing and medically assisted reproduction on twinning rates

Mean age at childbearing

The probability that a woman who conceives spontaneously or naturally, that is, without medical assistance, gives birth to twins is determined by various factors. The most important factors are maternal age, birth order, and region

or country (Bulmer 1970). Differences between regions and countries partly reflect genetic differences (Hoekstra et al. 2008).

Figure 2 shows twinning rates by age of the mother at birth in the 1960s in England and Wales, the US, France, and Japan.[4] We focus on the 1960s because this decade precedes the diffusion of MAR and thus shows us twinning rates under spontaneous conception. The frequency of twin births varies considerably with mother's age group. We observe similar patterns in England and Wales, the US, and France. From 6 per 1,000 before the age of 20, the frequency increases steadily until ages 35–39, where it reaches a maximum of around 15 per 1,000. After ages 35–39 it diminishes rapidly to around 7 per 1,000 for ages 45 and over. At all ages, the twinning rate is slightly higher in England and Wales than in France, the maximum at age 35–39 years being

FIGURE 2   Twinning rate by age group of mother at birth in the 1960s in England and Wales, United States, France, and Japan
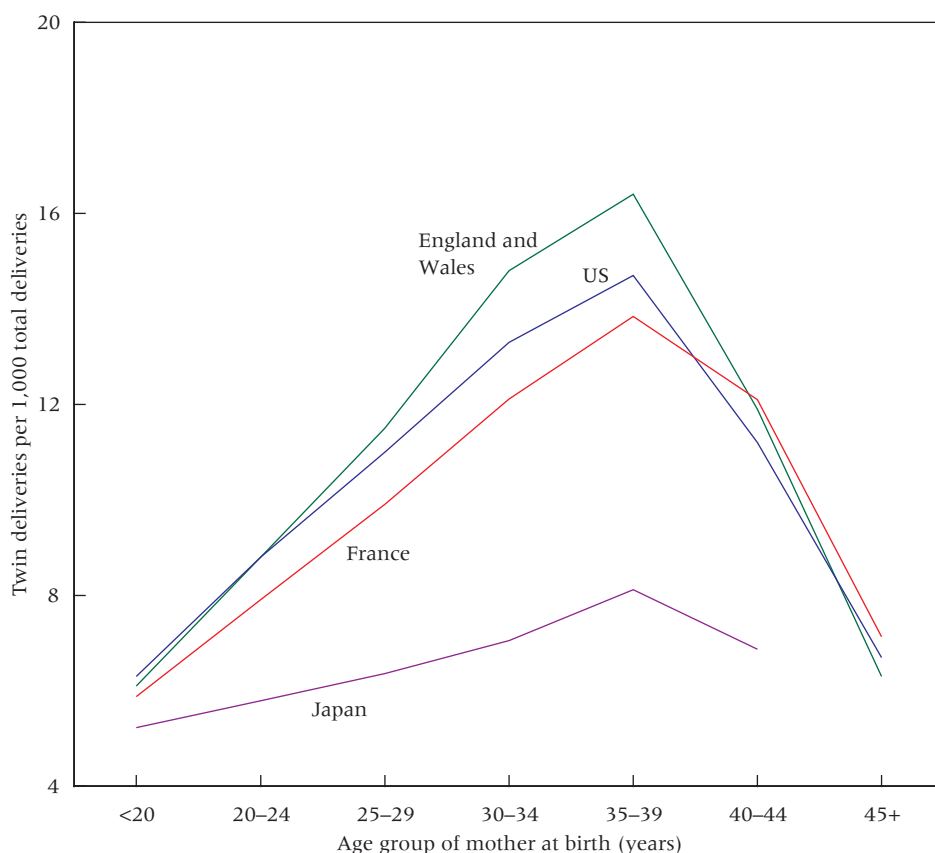
NOTES: Averages for 1965–69 (England and Wales, France), 1965–68 (US), 1960–67 (Japan). United States, France, and Japan: twin births only; England and Wales: all multiple births (including triplets, quadruplets, etc.). SOURCES: National statistical offices; authors' calculations.

respectively 16.4 and 13.8. Although twinning rates are much lower in Japan than in the three other countries, variations with mother's age follow a similar pattern with a maximum at ages 35–39. Twinning rates in Figure 2 combine rates for monozygotic (MZ) twins and dizygotic (DZ) twins. Variations in the frequency of each type of twins with mother's age follow two distinct patterns, and their combination explains the differences between the Japanese curve and the curves for the other three countries.[5]

Given the relationship between mother's age at birth and the twinning rate, we may expect changes in the overall twinning rate of a country when the distribution of the age at childbearing changes. We take the case of France as an example. At the beginning of the twentieth century, the mean age of French mothers was around 29.5 years. It declined over the first three quarters of the century to around 28 years in the middle of the century and reached a minimum of 26.5 years in 1977. A rapid increase then followed, and around 2010 the average age exceeded 30 years (Pison 2010).

Twinning rate changes are partly linked to modifications in childbirth schedules. The French twinning spike during World War I (see Figure 1) is partly due to the rise in the mean age of women at childbirth during wartime. Between 1910 and 1914, the average was close to 29; the outbreak of the war prompted a sudden increase, up to almost 30, between 1915 and 1919. After the war, the rate dropped back to prewar levels. Conversely, when the mean childbearing age fell, as in the 1960s and 1970s, the twinning rate declined as well. Similarly, when the mean age at childbirth increased at the end of the 1970s, the twinning rate rose again.

The trend toward later childbearing since the 1970s is observed in nearly all developed countries (Frejka et al. 2008). This trend is associated with the lengthening of time spent in education, the increase in female labor force participation, and the growing desire among women to postpone childbearing until they have a stable job and a lifetime partner (Frejka et al. 2008; Lesthaeghe and Van de Kaa 1986). The spread of modern contraception has contributed to this trend by reducing the frequency of unplanned pregnancies, notably at young ages.

Medically assisted reproduction

Medically assisted reproduction (MAR) consists of hormonal treatments and ART (see endnote 1). By the end of the 1960s, doctors began to prescribe hormonal treatments to stimulate ovulation in women who had difficulties in becoming pregnant. While these treatments allowed hypofertile women (whose probability of conceiving is below average) to conceive, they also significantly increased the risk of multiple pregnancies. When ovarian stimulation alone does not produce results, assisted reproductive technology (ART) is proposed. Its initial success dates back to 1978 with the birth of the first "test-tube baby" (Steptoe and Edwards 1978). To increase the chances of success, doctors who

practice ART often transfer several embryos, and this practice also increases the risk of multiple pregnancies (Vitthala et al. 2009).

Both types of treatment, non-ART ovarian stimulation and ART (including *in vitro* fertilization), have become more frequent in the developed world. This is reflected by yearly published statistics on ART based on clinic reports. Comparative tables for Europe are published yearly by the European Society of Human Reproduction and Embryology (ESHRE) (Kupka et al. 2014), and for the world by the International Committee for Monitoring Assisted Reproductive Technology (ICMART; last report (2005) (Zegers-Hochschild et al. 2014)). The average number of ART cycles per 1,000 women of reproductive age has increased by about 50 percent during the 2000s in European countries with (almost) complete statistics (Ferraretti et al. 2013; Kupka et al. 2014). There are large differences between countries, with high rates observed in the Nordic countries (around 12 ART cycles per 1,000 women of reproductive age in 2009–2010), around 6 cycles in France and the Netherlands, and around 4 cycles in the UK, Germany, and Italy. Denmark has the highest rate with around 18 cycles in 2010, and Belgium is second with 14.5 (Kupka et al. 2014).[6]

While the share of live-born children conceived through ART was around 2 percent in Europe in 2000, there were large differences between countries: 1 percent in the UK, 1.5 percent in France, and nearly 4 percent in Denmark (Ferraretti et al. 2013; Kupka et al. 2014; Mills et al. 2014). By 2009, the share had increased to 2 percent in the UK and France and 4.5 percent in Denmark. The share in the US increased from around 1 percent in 2005 (Mills et al. 2014) to 1.6 percent in 2011 (Sunderam et al. 2014). The share of children conceived through ovulation treatments alone (non-ART treatments) was 2.3 percent in France in 2010, which is similar to the ART contribution (Blondel et al. 2012). In the United States in 2005, the non-ART share has been estimated indirectly as 4 times greater than the ART contribution (Schieve et al. 2009).

The expansion of fertility treatments enlarged the twinning rate over the past 40 years, combining its effect with that of delayed childbearing. Because infertility increases with women's age (Leridon 2004), women over 30 are over-represented among those who seek such treatments. Women seeking treatment often have to wait several years before receiving it, and doctors tend to transfer more embryos in older women in order to increase the probability of a pregnancy (PCASRM and PCSART 2013). Moreover, given that many women prefer to have two children, some older women might ask for the transfer of more embryos to increase the chances of having twins (Van Wely et al. 2006). As a result, the increase in the twinning rate attributable to MAR has been more pronounced among older women than among younger ones.

This increase in twin births with age can be illustrated by examining trends in age-specific twinning rates in countries where they are available over a prolonged period. Figure 3 shows the trends in France (over the period

FIGURE 3 Trends in twinning rates by age group: France (1901–2011), England and Wales (1938–2011), United States (1949–2011)
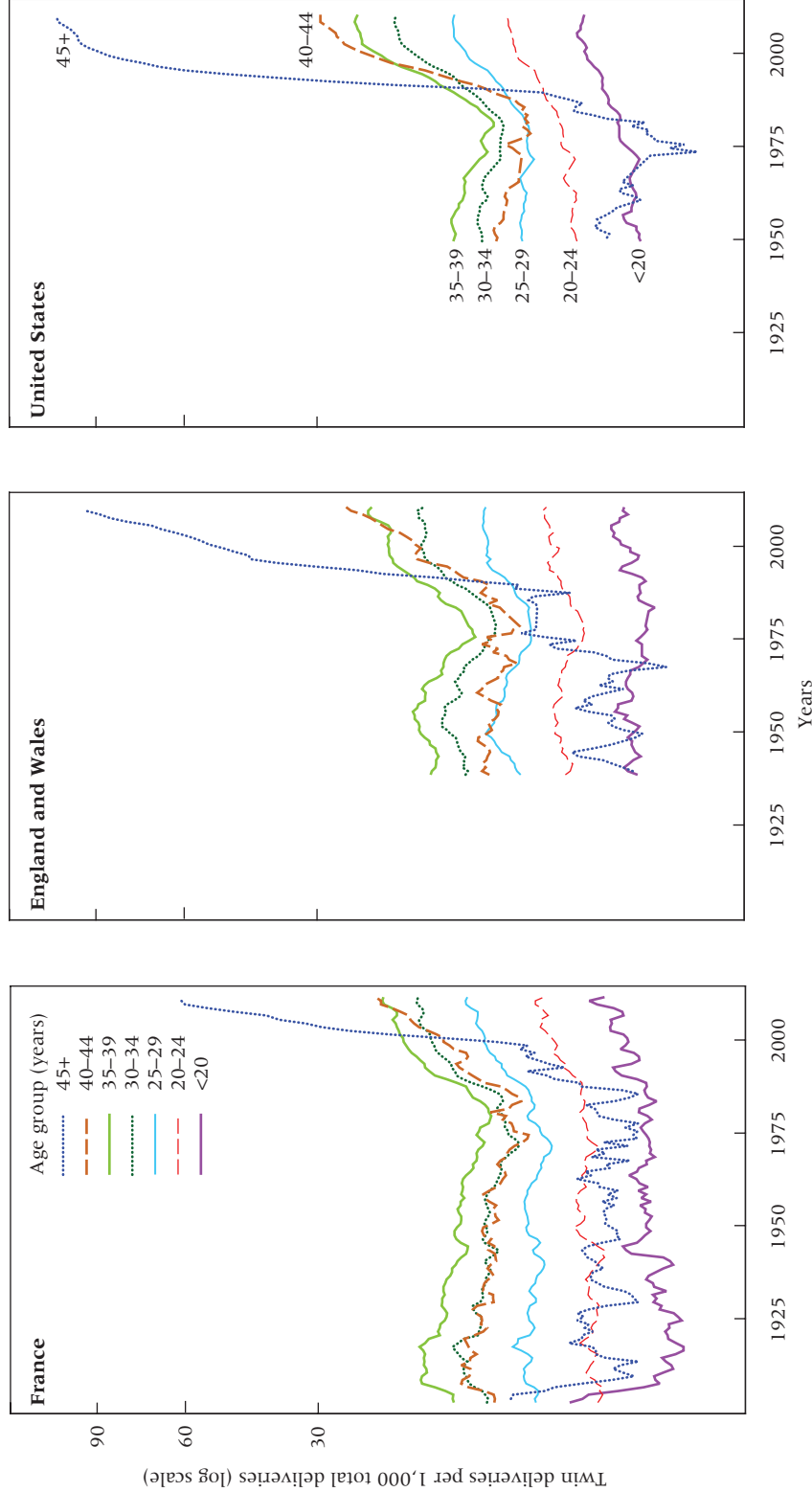
NOTES: France and United States: twin births only; England and Wales: all multiple births (including triplets, quadruplets, etc.). Age groups "less than 20 years" to "40–44," three-year moving averages; age group "45 years and above," five-year moving averages.
SOURCES: National statistical offices; authors' calculations.

1901–2011), England and Wales (1938–2011), and the US (1949–2011). In France, age-specific twinning rates declined during the first three quarters of the twentieth century at all ages over 25 years, reaching their lowest level in the 1970s. This secular trend was more pronounced at higher ages—that is, for age groups 30–34, 35–39, and 40–44. After the low point in the 1970s, the rates started rising at almost all ages, but the increase has been highest for the two oldest groups (40–44, 45+). The twinning rate more than doubled at ages 40–44 and increased tenfold at ages 45+.

In England and Wales, the secular trends follow a similar pattern for the period starting in 1938, the first year for which figures are available. The pattern is similar in the US, although the series starts only in 1949. The differences in twinning rates between age groups are somewhat more pronounced in England and Wales than in France and in the US during the downward trend before the 1970s. For the period since the 1970s, twinning rates in older age groups, particularly at ages 40–44 and 45+, started to increase in the US and in England and Wales about ten years earlier than in France, and reached even higher levels in recent years. In England and Wales the twinning rate at ages 40–44 increased 2.5-fold since the 1970s and 15-fold at ages 45+; the corresponding increases in the US are 3-fold and 20-fold.

Delayed childbearing versus medically assisted reproduction

Delayed childbearing and MAR are the major factors responsible for the sharp increase in twinning rates since the 1970s. While other factors may play a role too, their contribution is probably small. Birth order, genetic predisposition in families, and differences across regions and ethnic groups have been found to influence twinning rates (Bulmer 1970; Heuser and Statistics 1967; Hoekstra et al. 2008), but except for parity there is no reason to expect their influence to have changed much in recent decades. The parity effect (more twins at higher parity) may have played some role, as fertility levels have decreased and hence fewer higher-parity children are born. In the countries studied here, however, this decrease was almost completed at the end of the 1960s and changes since the 1970s, the period on which we focus, are small (Frejka et al. 2008).

The major remaining factors responsible for the increase in twinning rates since the 1970s are therefore the increase in mother's age at childbearing and the expansion of MAR. To identify the role of each of these factors, we separate their effects by estimating what the increase in the twinning rate would have been had the age distribution of mothers not changed. We compute a standardized twinning rate based on a constant age distribution of mothers equal to that of a particular year. To make this calculation, we use estimates of the twinning rate by age of the mother for each year. Such age-specific twinning rates are available for only a few developed countries, including the US, England and

Wales, and France. Figure 4 shows the observed trends in twinning rates for these countries as well as the trends in the standardized rates since 1970, based on the age distribution of 1970 (1971 for the US).

In France, the observed twinning rate increased from 9.4 per 1,000 in 1970 to 16.3 in 2005,[7] so it was multiplied by a factor of 1.73. If the age distribution of mothers had remained the same as in 1970, the increase would have been less, from 9.4 to 13.6, a multiplication by 1.45. If we consider that delayed childbearing and MAR are independent, we conclude that delayed childbearing alone would have multiplied the twinning rate by 1.20 (1.73/1.45).

The observed twinning rate in England and Wales increased from 10.4 per 1,000 in 1970 to 14.9 in 2005, so it was multiplied by a factor of 1.43. If the age distribution of mothers had remained the same as in 1970, the increase would have been from 10.4 to 12.5, a multiplication by 1.20, so delayed childbearing alone would have multiplied the twinning rate by 1.19 (1.43/1.20).

In the US, the observed twinning rate increased from 8.9 in 1971 to 16.4 in 2005, so it was multiplied by a factor of 1.84. If the age distribution

FIGURE 4   **Trends in the twinning rate in France, England and Wales, and the United States, 1970–2013: Comparison between observed and age-standardized rates**
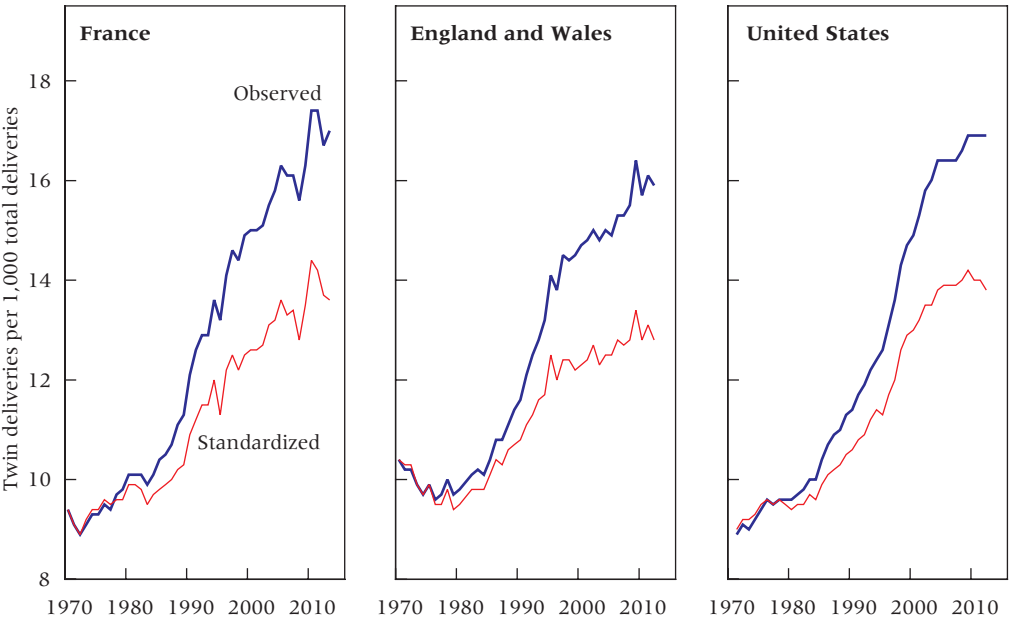
NOTE: Age-standardized rates: with constant age distribution of mothers (that of 1970 for France and England and Wales, 1971 for the United States).
SOURCES: National statistical offices; authors' calculations.

of mothers had remained the same as in 1971, the increase would have been from 8.9 to 13.9, a multiplication by 1.54, so delayed childbearing alone would have multiplied the twinning rate by 1.19 (1.84/1.54).

Unfortunately, the method used for France, England and Wales, and the US cannot be applied to all developed countries. Although the age distribution of births is available for nearly all countries, this is not the case for age-specific twinning rates. As an alternative, we use a simulation model to assess how much of the increase in twinning rates can be attributed to delayed childbearing and how much to MAR. First, we make the broadly accepted assumption that the MZ twinning rate is constant at an average of 4 per 1,000. Second, we suppose the DZ twinning rate, in the absence of MAR, increases monotonically from zero at age 15 to a maximum at age 37 and then decreases monotonically to zero at age 50. Thus, the only factor that differs among countries is the level of the maximum. Third, this level is estimated for each country as the best fit: when we derive the age-specific twinning rate function from this level and apply this function to the observed age distribution of births in 1970, our estimated twinning rate equals the observed rate for 1970. Fourth, we apply the age-specific twinning rate function to the observed distribution of births, by age of mother for each year in each country, to obtain the predicted overall twinning rate. Data on births by maternal age are taken from national statistics, the Human Fertility Database (Jasilioniene et al. 2012), and the United Nations *World Population Prospects* (United Nations 2015).

Figure 5 shows the observed and predicted twinning rates for selected countries. The difference between the predicted twinning rate in 1970 and the predicted rate for 2005 reflects the increase in twinning rates attributable exclusively to delayed childbearing. The difference between the observed twinning rate and the predicted twinning rate thus reflects the contribution of all other factors, primarily MAR.

We applied this method to all developed countries for which we have estimates of the total twinning rate (without distinguishing the age group of mother) since 1970. Table 1 shows the twinning rates in 1970 (or 1975) and 2005, the observed increase over the period 1970–2005 (expressed by the multiplication factor), the predicted multiplication factor if only delayed childbearing had been responsible for the increase, the estimated multiplication factor if only MAR had been responsible, the ratio between the increase due to delayed childbearing and the increase due to MAR, and the estimated percent of the overall increase due to MAR.

For countries for which age-specific twinning rates are available, the estimates obtained using the model can be compared to those obtained through computation of age-standardized twinning rates. In the case of France, where the twinning rate was multiplied by 1.73 from 1970 to 2005, age-standardized twinning rates indicate that it would have been multiplied by 1.45 if the distribution of mothers' ages had not changed. Using the model also results

FIGURE 5   Trends in the twinning rate in selected developed countries, 1970–2012: Comparison between observed rates and predicted rates if only age distribution of mothers had changed
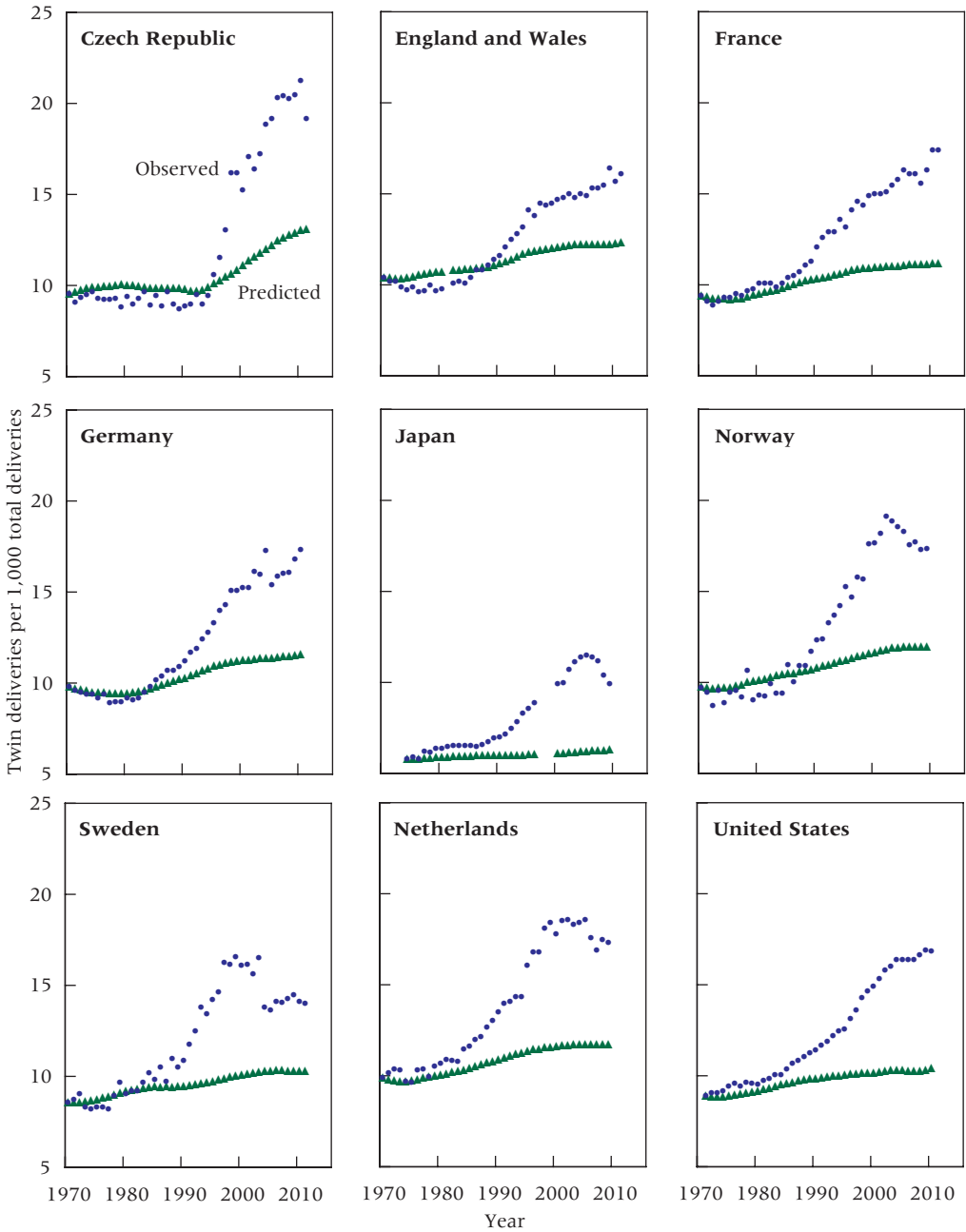
in a factor of 1.45. In England and Wales, where the twinning rate was multiplied by 1.43, age-standardized twinning rates indicate that it would have

TABLE 1 Increase in the twinning rate from 1970 to 2005 in selected developed countries and percent of the increase due to delay of childbearing and to medically assisted reproduction (MAR)

Country	Twinning rate (twin deliveries per 1,000 total deliveries) 1970 (or 1975) A	Twinning rate 2005 B	Increase in twinning rate during 1970–2005 (or 1975–2005) (multiplication factor) Observed C = A/B	Estimated if only delayed childbearing had been responsible D	Estimated if only MAR had been responsible E = C/D	Ratio between increase due to delayed childbearing and increase due to MAR (D–1)/(E–1)	Percent of increase due to MAR (E–1)/(C–1)
Australia[a]	9.5	16.2	1.70	1.19	1.43	0.43	62
Austria	9.0	14.9	1.65	1.19	1.39	0.47	60
Belgium	10.0	17.4	1.73	1.18	1.47	0.38	64
Bulgaria	6.9	9.8	1.42	1.11	1.28	0.39	67
Canada[a]	8.9	15.4	1.73	1.17	1.48	0.35	66
Chile[a]	7.7	8.8	1.15	1.05	1.09	0.57	62
Croatia	10.4	13.7	1.31	1.08	1.21	0.36	69
Cyprus[a]	9.6	22.7	2.35	1.13	2.08	0.12	80
Czech Republic	9.6	19.2	2.00	1.28	1.56	0.50	56
Denmark	9.4	22.4	2.37	1.22	1.95	0.23	69
England and Wales	10.4	14.9	1.43	1.14	1.26	0.53	60
Estonia	10.2	13.1	1.28	1.10	1.16	0.65	57
Finland[a]	11.3	15.0	1.33	1.15	1.16	0.96	47
France	9.4	16.3	1.73	1.20	1.45	0.43	61
Germany	9.8	15.4	1.57	1.20	1.32	0.62	55
Greece	10.6	22.4	2.12	1.17	1.82	0.21	73

Hong Kong[a]	6.2	10.2	1.64	1.12	1.46	0.27	72
Hungary	10.4	16.2	1.56	1.26	1.24	1.08	43
Ireland	13.1	15.5	1.18	1.12	1.05	2.41	28
Italy	10.1	13.0	1.29	1.18	1.09	1.95	32
Japan	5.9	11.5	1.96	1.07	1.83	0.08	87
Lithuania[a]	8.8	10.4	1.18	1.06	1.11	0.55	62
Netherlands	9.9	18.6	1.88	1.20	1.57	0.35	65
New Zealand[a]	10.6	15.5	1.47	1.21	1.22	0.95	46
Norway	9.8	18.3	1.88	1.19	1.58	0.33	66
Poland	9.9	11.5	1.17	1.12	1.04	3.33	22
Portugal	7.8	12.9	1.65	1.15	1.44	0.33	68
Singapore[a]	6.2	11.0	1.78	1.11	1.60	0.18	78
Spain	8.9	17.2	1.93	1.12	1.73	0.16	79
Sweden	8.6	13.7	1.60	1.19	1.34	0.56	57
Switzerland	8.8	16.4	1.85	1.16	1.60	0.27	70
United States[a]	9.4	16.4	1.74	1.14	1.53	0.26	72

[a]1975–2005.

been multiplied by 1.20 if the age distribution of mothers had not changed. Using the model results in 1.26, which is not much different. And in the US, where the twinning rate was multiplied by 1.74 between 1975 and 2005, age-standardized twinning rates indicate that it would have been multiplied by 1.46. Using the model, we find 1.53, which is also close. Thus, use of our model retains contrasts between countries.

If age at childbearing had not changed and only MAR had been in play, the twinning rate would have increased by 40 percent to 50 percent on average from 1970 to 2005 in the countries considered in Table 1, with large differences between countries, the lowest increase being in Poland (4 percent) and the highest in Cyprus (108 percent). If, on the contrary, only age at childbearing had changed, the increase in the twinning rate would have been 15 percent on average, the lowest increase being in Chile (5 percent) and the highest in the Czech Republic (28 percent). On average, therefore, the effect of MAR is about three times greater than the effect of delayed childbearing. However, there are large differences between countries: in Japan the effect of MAR is more than ten times greater than that of delayed childbearing; in Poland, the effect of MAR is only one third the effect of delayed childbearing; in Hungary and New Zealand, the effects of the two factors are similar.

Our estimates are based on the assumption that the effects of delayed childbearing and MAR are independent. Interaction effects may exist, however: older women who in the past would not have given birth can now do so through the use of MAR. As a result, mean age at childbearing has increased more than if MAR had not been available. On the other hand, delays in childbearing lead more couples or women to seek treatment, so use of MAR increased more than if there had been no rise in the age at childbearing. Although such interactions exist, their influence on our estimates is probably small. First, most older women who have a child today still become pregnant naturally. For example, an estimated 85 percent of women aged 40 and over who had a child in France in 2010 conceived naturally, as opposed to 94 percent of women below age 40 (Blondel, Kermarrec, and DREES 2011). Second, although the proportion of births to women aged 40 and over increased, it remains small: 5 percent in France in 2010, as compared to 3 percent in 1970 (Bellamy and Beaumel 2015).

Have we reached the peak in twinning rates?

An overview of peaks and reversals

In some countries the twinning rate has experienced a recent peak followed by a subsequent decline. Such peaks and reversals are observed in 12 out of 46 countries for which twinning rates could be estimated with enough certainty over recent decades. Table 2 indicates whether a peak was attained in each of these countries, and, if so, in which year or period it occurred (see also

TABLE 2 Countries experiencing a peak and reversal in twinning rates and countries in which no peak occurred

Peak and reversal (year/period of peak)	No peak
Europe	
Czech Republic (2010), Denmark (2005–2008), Finland (1998), Hungary (2006), Iceland (1997–2006), Netherlands (2001–2005), Norway (2002), Scotland (2008), Sweden (1999–2003)	Austria, Belarus, Belgium, Bulgaria, Croatia, Cyprus, England and Wales, Estonia, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Moldova, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Switzerland, Ukraine
Non-European OECD	
Australia (2002–2004), Japan (2005), New Zealand (2002)	Canada, Chile, Israel, United States, South Korea
Other	
	Cuba, Hong Kong, Singapore

Appendix figure).* The peaks mostly occur after 2000. Finland and Sweden are exceptions with a peak attained in 1998 and 1999 respectively. Iceland probably had an earlier peak, but the small size of the country's population makes it more difficult to date the reversal.

Among the 11 countries of Northern Europe, 6 had a reversal (the Scandinavian countries plus Scotland, considered here separately from England and Wales). By contrast, the reversal occurred in only one of 6 countries in Western Europe (the Netherlands), 2 of 10 countries in Eastern Europe (Czech Republic and Hungary), and in none of the 8 Southern European countries. Among the non-European OECD countries, a reversal occurred in Australia, Japan, and New Zealand, but not in Canada, Chile, Israel, the US, or South Korea.

In some countries where no reversal has occurred, the increase in the twinning rate decelerated recently, and in a few of them, a plateau appears to have been attained. In Europe this is the case in Belgium, Greece, and Slovenia; outside Europe, in Canada.

Reasons for a trend reversal

Pregnancies achieved through MAR result much more frequently in multiple births than do pregnancies achieved naturally. In the United States in 2005–2007, 9 percent of births resulting from non-ART treatment using clomifene were multiple ones, as were 14 percent with treatment using gonadotropin (Schieve et al. 2009). In 2000 over two thirds of women in the US undergo-

*Appendix is available at the supporting information tab at wileyonlinelibrary.com/journal/pdr.

ing ART had three or more embryos transferred. Around 35 percent of these ART pregnancies resulted in multiple births, and 53 percent of all ART infants were twins or triplets. In Europe, the most typical ART procedure at that time involved transferring of two embryos (44 percent of women), 26 percent of ART pregnancies resulted in multiple births, and 43 percent of twins or triplets were ART infants. In other words, the dizygotic (DZ) twinning rate following ART was about 20–30 times higher in Europe and the US than the natural DZ twinning rate (Mills et al. 2014).

ART multiple delivery rates started to decline gradually in most developed countries during the 2000s, reaching 30 percent in the US in 2009 and 20 percent in Europe in 2010 (Kupka et al. 2014; Mills et al. 2014), in part as a result of medical concerns. The high rates of multiple births after ART were labeled as problematic because of negative outcomes for infants' and mothers' health (Hansen et al. 2009; Pinborg 2005). As a consequence, medical professionals proposed new, stricter criteria for evaluating the success of ART, centered on successful singleton live birth delivery. They suggested as an indicator the BESST criterion (Birth Emphasizing a Successful Singleton at Term) (Min et al. 2004). Single embryo transfers became favored by health authorities and legislators, since studies indicated that the chances of birth after elective single embryo transfer[8] are as high as the chances of success after transfer of two fresh embryos (Min et al. 2004).

However, these shifts in clinical best practice did not result in a reversal of the overall twinning rate trend in these countries, because of the continuing increase in the prevalence of ART and non-ART ovarian stimulation (Kupka et al. 2014) and the continuing shift of childbearing to later ages. In countries where there has been a reversal, the decline in the twinning rate has been more modest than one would expect from ART statistics alone. This is illustrated by the example of Sweden. ART expanded early and was associated with a rapid increase in multiple births. The share of ART multiple deliveries was around 23 percent in the late 1990s (Mills et al. 2014). Following changes in ART regulations and practices, it fell to 12 percent in 2003 and 7 percent in 2004. The twinning rate among the total population declined more modestly, however, from 17 per 1,000 (the highest level observed in the country) in 1999 to 14 per 1,000 in 2004.

Conclusions

Our data indicate that the twinning rate in many developed countries has nearly doubled over the last four decades. The two factors mainly responsible are the increase in women's age at birth and the rise in medically assisted reproduction (MAR). Across developed countries the effect of MAR explained between 22 and 87 percent of the total change. Hence the role of MAR ranged from substantial to dominant. The increase in twinning rates due to MAR

raised concerns among public health authorities and medical authorities and around 2000 led to a change in MAR regulations and clinical practices in most developed countries. The number of embryos transferred has been reduced and new criteria for evaluating the success of ART have been developed, centered on successful singleton live birth delivery. We believe that these changes are responsible for our finding that, in about a quarter of the countries studied here, twinning rates reached a plateau in the early 2000s and decreased afterward.

In the other three-quarters of the countries, the increase has, however, continued in the last decade. Hence the association between regulatory changes, new clinical practices, and trends in twinning rates is not straightforward. Major reasons for this may be the continuing increase in recourse to MAR procedures; the influence of non-ART ovarian stimulation, the frequencies and trends of which are unknown; and the development of cross-border reproductive care.

Several recommendations related to data follow from our findings. First, given the lack of reliable statistics on MAR to monitor policies and practices and evaluate their effects, twinning rates are a useful proxy indicator. This measure is produced by many national statistical offices routinely, rapidly, and at no extra cost; it should be used more frequently. Second, only a handful of national statistical offices publish data on twinning rates broken down by year and mother's age. We recommend that all national statistical offices publish statistics on births by plurality of birth, age of mother, and year. Finally, national statistics on ART are likely biased because cross-border treatments are not systematically recorded, despite evidence that the number of cross-border fertility treatments is not insignificant and varies substantially across countries (Shenfield et al. 2010). We recommend that ART reports submitted by clinics and compiled by national and international groups provide statistics by women's country of residence.

Notes

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1 The term medically assisted reproduction (MAR) is broader than the often-used term assisted reproductive technology (ART). ART consists of treatments in which both sperm and oocytes are handled outside (i.e., *in vitro*) of the woman's body and embryos are transferred for the purpose of establishing a pregnancy. This includes, but is not limited to, *in vitro* fertilization (IVF) and its variant, intracytoplasmic sperm injection (ICSI). MAR includes ART and simpler techniques, like ovarian stimulation alone, that also increase the likelihood of twin births. MAR also includes artificial insemination during which women often receive an ovarian stimulation treatment.

2 The share of triplet births has undergone even faster changes than twinning rates, following a rapid increase and then usually reaching a peak and reversing. However, trip-

lets are rare. In France, there were around 10 triplet deliveries per 100,000 deliveries up to the end of the 1960s. The rate then increased rapidly to a maximum of 43 per 100,000 in 1989, and then decreased to 23 in 2014 (INSEE 2015). In the United States, it was also around 10 per 100,000 up to the end of the 1960s and then increased to a maximum of 64 per 100,000 in 2004, after which it decreased to 42 in 2012 (CDC 2015).

3 Statistics published by statistical offices do not always use the same definition of a twin delivery. For example, in some countries, in the case of multiple births, only births in which at least one child was born alive are included. In other countries, all births are reported, including those in which all children were born dead (stillborn). However, such variations in the definition have only a minor effect on the estimates.

4 National statistical offices in the US, France, Japan, and England and Wales all publish statistics on multiple births by age group. While the first three countries provide statistics broken down by type of multiple births—i.e., twins, triplets, quadruplets, etc.—England and Wales provides statistics only for all multiple births combined. The inclusion of deliveries with more than two births, however, scarcely changes the estimate since these deliveries represented a maximum of 1 percent of all multiple deliveries during the period 1965–69. This proportion increased during the "triplet boom" in the 1980s and 1990s to a maximum of 4 percent of all multiple deliveries, after which it decreased again to 2 percent or less.

5 There are two types of twins, monozygotic (MZ) (also called identical twins) and dizygotic (DZ) (fraternal twins). MZ twins are the result of a single fertilized ovum splitting in two during the early stages of development. In the case of DZ twins, the ovaries release two ova during a single cycle and both ova are fertilized. While the outcome in both cases is a multiple birth, the two phenomena are independent and are the result of separate biological events. The proportion of MZ twin births remains rather constant regardless of the mother's age, birth order, or geographic origin. For decades before 1970, MZ twin rates

varied between 3.5 and 4.5 per 1,000 deliveries (Bortolus et al. 1999; Bulmer 1970). Over the past 40 years, however, the frequency of MZ twin births has increased in developed countries, rising for example by about 50 percent in France (Couvert 2011). In contrast to MZ twin rates, the frequency of DZ twin deliveries is highly variable according to maternal age, birth order, and region or country. The natural rate is low in East Asia and Latin America (about 2–4 per 1,000), high in sub-Saharan Africa (about 15 per 1,000), and at an intermediate level in Europe and the US (about 7 per 1,000) (Hoekstra et al. 2008; Smits and Monden 2011). The twin pregnancies resulting from transferring several embryos are DZ twins, so ART influences mostly the DZ twinning rate.

6 An unknown, but probably substantial, number of individuals or couples travel to another country to obtain fertility treatments (Shenfield et al. 2010). Primary reasons for this "reproductive tourism" are difficulty of access because of restrictive legislation or long waiting lists and expected quality of care (Gomez and de La Rochebrochard 2013). Cross-border reproductive care has become an important activity in countries like Denmark, Belgium, Switzerland, Spain, the Czech Republic, Greece, and Israel, where foreign patients represent a significant share of all patients. After becoming pregnant, these women return to their country of residence and deliver there. The ART statistics are therefore biased, which makes it difficult to properly assess the impact of ART on births in individual countries. This problem might be particularly significant in countries with a relatively small population and a sizable ART sector serving foreigners, such as Belgium and Denmark. One solution to partly overcome these difficulties is for national and international reports to specify ART statistics by women's country of residence.

7 We focus on the period until 2005 because we wanted to terminate the analysis at a period before the trend in twinning rates reversed and started falling in some countries.

8 In a single embryo transfer, one fresh embryo is transferred and a second one is frozen for a second single embryo transfer if necessary.

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