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Assisted Reproductive Technology Surveillance — United States, 2005

Malaria Surveillance — United States, 2006

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CONTENTS

Assisted Reproductive Technology Surveillance — United States, 2005

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Abstract

Problem/Condition: Assisted reproductive technology (ART) includes fertility treatments in which both eggs and sperm are handled in the laboratory (i.e., in vitro fertilization and related procedures). Patients who undergo ART procedures are more likely to deliver multiple-birth infants than women who conceive naturally. Multiple births are associated with increased risk for mothers and infants (e.g., pregnancy complications, premature delivery, low-birthweight infants, and long-term disability among infants). This report presents the most recent national data and state-specific results.

Reporting Period Covered: 2005.

Description of System: In 1996, CDC initiated data collection regarding ART procedures performed in the United States, as mandated by the Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA) (Public Law 102-493 [October 24, 1992]). Beginning with 2004, CDC has contracted with a statistical survey research organization, Westat, Inc., to obtain data from ART medical centers in the United States. Westat, Inc., maintains CDC's web-based data collection system called the National ART Surveillance System (NASS).

Results: In 2005, a total of 134,260 ART procedures were reported to CDC. These procedures resulted in 38,910 live-birth deliveries and 52,041 infants. Nationwide, 73% of ART procedures used freshly fertilized embryos from the patient's eggs, 15% used thawed embryos from the patient's eggs, 8% used freshly fertilized embryos from donor eggs, and 4% used thawed embryos from donor eggs. Overall, 42% of ART transfer procedures resulted in a pregnancy, and 35% resulted in a live-birth delivery (delivery of one or more live-born infants). The highest live-birth rates were observed among ART procedures that used freshly fertilized embryos from donor eggs (52%). The highest numbers of ART procedures were performed among residents of California (18,655), New York (12,032), Illinois (9,449), New Jersey (9,325), and Massachusetts (8,571). These five states also reported the highest number of live-birth deliveries. Of 52,041 infants born through ART, 49% were born in multiple-birth deliveries. The multiple-birth risk was highest for women who underwent ART transfer procedures that used freshly fertilized embryos from either donor eggs (41%) or their own eggs (32%). Approximately 1% of U.S. infants born in 2005 were conceived through ART. Those infants accounted for 17% of multiple births nationwide. Approximately 9% of ART singletons, 57% of ART twins, and 95% of ART triplets or higher-order multiples were low birthweight. Similarly, 15% of ART singletons, 66% of ART twins, and 97% of ART triplets or higher-order multiples were born preterm.

Interpretation: Whether an ART procedure resulted in a pregnancy and live-birth delivery varied according to different patient and treatment factors. ART poses a major risk for multiple births that are associated with adverse maternal and infant outcomes (e.g., preterm delivery, low birthweight, and infant mortality). This risk varied according to the patient's age, the type of ART procedure performed, the number of embryos available for transfer to the uterus, the number actually transferred, and the day of transfer (day 3 or day 5).

Public Health Actions: ART-related multiple births represent a sizable proportion of all multiple births nationwide and in selected states. To minimize the adverse maternal and child health effects that are associated with multiple pregnancies, ongoing efforts to limit the number of embryos transferred in each ART procedure should be continued and strengthened. Adverse maternal and infant outcomes (e.g., low birthweight and preterm delivery) associated with ART treatment choices should be explained fully when counseling patients who are considering ART.

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Introduction

Since 1978, assisted reproductive technology (ART) procedures have been used to overcome infertility. ART procedures include those infertility treatments in which both eggs and sperm are handled in the laboratory for the purpose of establishing a pregnancy (i.e., in vitro fertilization [IVF] and related procedures). Since the birth of the first U.S. infant conceived with ART in 1981, use of these treatments has increased dramatically. Both the number of medical centers providing ART services and the number of procedures performed annually in the United States have steadily increased (*1*).

In 1992, Congress passed the Fertility Clinic Success Rate and Certification Act (FCSRCA),* which requires each medical center in the United States that performs ART procedures to report data to CDC annually on every ART procedure initiated. CDC uses the data to report medical center–specific pregnancy success rates. In 1997, CDC published the first surveillance report under this mandate (*2*). That report was based on ART procedures performed in 1995. Since then, CDC has continued to publish a surveillance report annually that details each medical center's success rates. CDC also has used this surveillance data file to perform more in-depth analyses of infant outcomes (e.g., multiple births) (*3–10*). Multiple-infant births are associated with greater health problems for both mothers and infants, including higher rates of caesarean deliveries, prematurity, low birthweight, and infant death and disability (*11,12*). In the United States, ART has been associated with a substantial risk for multiple gestation pregnancy and multiple birth (*3–10*). In addition to the multiple-birth risks, studies suggest an increased risk for low birthweight among singleton infants conceived through ART (*13,14*). This report is based on ART surveillance data provided to CDC's National Center for Chronic Disease Prevention and Health Promotion, Division of Reproductive Health, regarding procedures performed in 2005. A report of these data, according to the medical center in which the procedure was performed, was published separately (*1*). In this report, emphasis is on presenting state-specific data and more detailed data regarding risks associated with ART (e.g., multiple birth, low birthweight, and preterm delivery).

Methods

CDC contracted with Westat, Inc., to collect data on ART procedures performed in 2005 from medical centers in the United States and its territories. Data collected include patient demographics, medical history and infertility diagnoses, clinical information pertaining to the ART procedure, and information regarding resultant pregnancies and births. The data file is organized with one record per ART procedure performed. Multiple procedures from a single patient are not linked. Ninety percent of ART medical centers reported their 2005 data (*1*). The names of nonreporting programs were published as prescribed by the FCSRCA.

ART data and outcomes from ART procedures are presented by patient's state of residence at time of treatment. If the patient's state of residency was missing, the state of residency was assigned as the state in which the ART procedure was performed. In addition, data regarding the number of ART procedures in relation to the total population for each state are indicated.† Data regarding number of procedures also are presented by treatment type and stage of treatment. ART procedures are classified into four groups according to whether the ART cycle involved the retrieval and fertilization of eggs (fresh cycle) or the thawing of previously frozen embryos (frozen cycle), and whether the eggs or embryos were those of the intended mother or were from a donor. Because both live-birth rates and multiple-birth risk vary substantially among these four treatment groups, data are presented separately for each type.

In addition to treatment types, within a given treatment procedure, different stages of treatment exist. A typical ART procedure begins when a woman starts taking drugs to stimulate egg production or her ovaries are monitored with the intent of transferring embryos to her uterus. If eggs are produced, the procedure progresses to the egg retrieval stage. After the eggs are retrieved, they are combined with sperm in the laboratory (IVF), and if IVF is successful, the resulting embryos are selected for transfer. If the embryo implants in the uterus, a clinical pregnancy is diagnosed by the presence of a gestational sac detectable by ultrasound. Depending on the age of the mother, between 13% and 55% of clinical pregnancies are lost at a later point, mostly during the 12 weeks (*16*). Beyond 12 weeks of gestation, the pregnancy usually progresses to a live-birth delivery, which is defined as the delivery of one or more live-born infants. Only ART procedures involving freshly

* Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA), Public Law 102-493 (October 24, 1992).

† Data regarding population size are based on July 1, 2005, estimates from the U.S. Census Bureau (*15*).

fertilized embryos include an egg-retrieval stage. ART procedures using thawed embryos do not include egg retrieval because eggs were fertilized during a previous procedure, and the resulting embryos were frozen until the current procedure. An ART procedure can be discontinued at any step for medical reasons or by the patient's choice.

Although a typical ART procedure includes IVF of gametes, culture for ≥2 days, and embryo transfer into the uterus (i.e., transcervical embryo transfer), in certain cases, unfertilized gametes (eggs and sperm) or zygotes (early embryos [i.e., a cell that results from fertilization of the egg by a sperm]) are transferred into the fallopian tubes within 1–2 days of retrieval. These are known as gamete and zygote intrafallopian transfer (GIFT and ZIFT). Another variation is intracytoplasmic sperm injection (ICSI), in which IVF is accomplished by selection of a single sperm that is injected directly into the egg. This technique was developed originally for couples with male factor infertility but now is commonly used for an array of diagnostic groups.

This report presents data for each of the four treatment types: freshly fertilized embryos from the patient's eggs, freshly fertilized embryos from donor eggs, thawed embryos from the patient's eggs, and thawed embryos from donor eggs. In addition, it provides detailed data for the most common treatment type, those using freshly fertilized embryos from the patient's eggs. These procedures account for >70% of the total number of ART procedures performed each year. For procedures that progressed to the embryo-transfer stage, the report presents the percentage distribution of selected patient and treatment factors and the success rates (defined as live-birth deliveries per ART-transfer procedure), according to the same patient and treatment characteristics.

Patient factors included the age of the woman undergoing ART, whether she had previously given birth, the number of previous ART attempts, and the infertility diagnosis of both the female and male partners. The patient's age at the time of the ART procedure was grouped into five age groups: age <35 years, 35–37 years, 38–40 years, 41–42 years, and >42 years. Infertility diagnoses ranged from one factor in one partner to multiple factors in one or both partners, as follows:

- tubal factor — the woman's fallopian tubes are blocked or damaged, causing difficulty for the egg to be fertilized or for an embryo to travel to the uterus;
- ovulatory dysfunction — the ovaries are not producing eggs normally; such dysfunctions include polycystic ovarian syndrome and multiple ovarian cysts;
- diminished ovarian reserve — the ability of the ovary to produce eggs is reduced; reasons include congenital, medical, or surgical causes or advanced age;
- endometriosis — involves the presence of tissue similar to the uterine lining in abnormal locations; this condition can affect both fertilization of the egg and embryo implantation;
- uterine factor — a structural or functional disorder of the uterus that results in reduced fertility;
- male factor — a low sperm count or problems with sperm function that cause difficulty for a sperm to fertilize an egg under normal conditions;
- other causes of infertility — immunologic problems or chromosomal abnormalities, cancer chemotherapy, or serious illnesses;
- unexplained cause — no cause of infertility was detected in either partner;
- multiple factors, female — diagnosis of one or more female cause; or
- multiple factors, male and female — diagnosis of one or more female cause and male factor infertility.

Treatment factors included the following:

- the number of days the embryo was cultured;
- the number of embryos that were transferred;
- whether the procedure was IVF-transfer only, IVF with ICSI, GIFT, ZIFT, or a combination of IVF with or without ICSI and either GIFT or ZIFT;
- whether extra embryos were available and cryopreserved; and
- whether a gestational carrier (i.e., surrogate) received the transferred embryos with the expectation of gestating the pregnancy.

The number of embryos transferred in an ART procedure was categorized as 1, 2, 3, 4, or ≥5. The number of days of embryo culture was calculated using dates of egg retrieval and embryo transfer and was categorized as 1, 2, 3, 4, 5, or 6. Because of limited sample sizes, live-birth rates are presented only for the two most common days, day 3 and day 5. For the same reason, live-birth rates are presented for IVF with and without ICSI and not for GIFT and ZIFT. ICSI was subdivided as to whether it was used among couples receiving a diagnosis involving male factor (the original indication for ICSI treatment) or not.

Chi-square tests evaluated the significance of differences in live-birth rates by select patient and treatment factors within each age group. Multivariable logistic regression models evaluated the independent effects of patient factors (diagnosis, number of previous ART procedures, and number of previous births) on the chance to have a live birth as

a result of an ART treatment. Because patient age is a strong predictor for live birth, separate models were constructed for each age group; these models provide an indication of the variability in live-birth rates based on patient factors separately for each age category. For these analyses, the referent groups included patients with a tubal factor diagnosis, no previous ART procedures, and no previous births. Multivariable models did not include treatment factors because of multicollinearity between certain treatment factors and multiple potential effect modifications. Rather, detailed stratified analyses were performed to elucidate additional details related to associations among different treatment factors and the live-birth rate.

In addition to the overall live-birth rate, the report presents a second measure of success based on the delivery of a live singleton. Singleton live births are a key measure of ART success because they carry a much lower risk than multiple-infant births for adverse health outcomes, including prematurity, low birthweight, disability, and death.

The report addresses multiple birth as a separate outcome measure. First, each multiple-birth delivery is evaluated as a single event, defined as the delivery of two or more infants, at least one of which was live-born. The multiple-birth risk thus was calculated as the proportion of multiple-birth deliveries among total live-birth deliveries. In additional analyses, each infant in a multiple birth was considered separately to compute the proportion of all infants born from multiple deliveries and the proportion of all live-born infants who were multiples.[§] Each of these measures represents a different focus. The multiple-birth risk, which is based on the number of deliveries or infant sets, provides an estimate of the risk of multiple birth posed by ART to the woman. The proportion of infants born in a multiple-birth delivery provides a measure of the impact of ART procedures on children in the population. The report presents both measures by type of ART procedure and by maternal age for births conceived with the patient's eggs, and provides details on the multiple-birth risk by patient's age, number of embryos transferred, and whether additional embryos were available and cryopreserved for future use. Embryo availability (an indicator of embryo quality) is an independent predictor of the number of embryos transferred (*3,6*). The report also presents the multiple-birth risk for embryos cultured through day 3 and day 5 by patient's age, number of embryos transferred, and whether additional embryos were available and cryopreserved for future use. The proportion of infants born in a multiple-birth delivery is presented separately by patient's state of residency at the time of ART treatment.

Additional analyses evaluated the impact of ART procedures on total births in the United States in 2005. Because the goal of the analysis was to assess the effect of ART on the 2005 U.S. birth cohort and the ART surveillance system is organized according to the date of the ART procedure rather than the infant's date of birth, these analyses employed data drawn from two different ART reporting years and covered 1) infants conceived from ART procedures performed in 2004 and born in 2005 (approximately two thirds of the live-birth deliveries reported to the ART surveillance system for 2004); and 2) infants conceived from ART procedures performed in 2005 and born in 2005 (approximately one third of the live-birth deliveries reported to the ART surveillance system for 2005). The U.S. natality files from CDC's National Center for Heath Statistics provided data on the total number of live births and multiple births registered in the United States in 2005 (*17*). The report presents the results of these analyses by plurality of birth.

Additional analyses addressed adverse infant health outcomes, including low birthweight, very low birthweight, and preterm delivery. Because ART providers do not provide continued prenatal care after a pregnancy is established, birthweight and date of birth were collected via active follow-up with ART patients (85%) or their obstetric providers (15%). Although ART clinic staff collects limited information on infant outcomes, maternal health outcomes are not investigated systematically. Low birthweight and very low birthweight were defined as <2,500 grams and <1,500 grams, respectively. The exact gestational age was calculated as date of birth minus date of egg retrieval (and fertilization). If the date of retrieval was missing, and for procedures that used frozen embryos, gestational age was calculated as date of birth minus date of embryo transfer. For comparability with the general population, which is based on the date of the last menstrual period (LMP), the exact gestational age was adjusted by adding 14 days to the gestational age estimate. Preterm delivery was defined as gestational age <37 weeks. Preterm low birthweight was defined as gestational age <37 weeks and birthweight <2,500 grams. Term low birthweight was defined as gestational age ≥37 weeks and birthweight <2,500 grams. The rates for low birthweight, very low birthweight, preterm low birthweight, and term low birthweight among ART

[§] Includes only the number of infants live-born in a multiple-birth delivery. For example, if three infants were born in a live-birth delivery and one of the three infants was stillborn, the total number of live-born infants would be two. However, these two infants still would be counted as triplets.

infants born in 2005 are presented by plurality of birth. In addition, data for each of the five outcomes are presented for ART singletons born in 2005 by type of procedure. For the most common procedure type, those using freshly fertilized embryos from the patient's eggs, the rates for each outcome also are presented according to maternal age and number of previous live births. Chi-square tests evaluated the significance of differences in these five outcomes by type of ART procedure, maternal age, and number of previous births. All analyses were performed using the SAS® software system (*18*).

Results

Of 475 medical centers in the United States and surrounding territories that performed ART procedures in 2005, a total of 422 (90%) provided data to CDC (Figure 1). The majority of medical centers that performed ART procedures were in the eastern United States, in or near major cities. The number of medical centers performing ART procedures varied by state. The states with the largest number of ART medical centers reporting data for 2005 were California (59), New York (33), Florida (29), Illinois (29), and Texas (29). Four states (Alaska, Maine, Montana, and Wyoming) and three U.S. territories (Guam, the Federated States of Micronesia, and the U.S. Virgin Islands) had no ART medical centers.

Number and Type of ART Procedures

A total of 134,260 ART procedures performed in 2005 were reported to CDC (Table 1). This number excludes 358 ART procedures (<1%) performed in 2005 that involved the evaluation of a new treatment procedure. The largest number of ART procedures occurred among patients who used their own freshly fertilized embryos (97,442 [73%]). Of the 134,260 procedures started, 112,255 (84%) progressed to embryo transfer. Overall, 42% of ART procedures that progressed to the transfer stage resulted in a pregnancy; 35% resulted in a live-birth delivery; and 24% resulted in a singleton live birth. Pregnancy rates, live-birth rates, and singleton live-birth rates varied according to type of ART. ART procedures that used donor eggs and freshly fertilized embryos had the highest success rates (61% pregnancy rate, 52% live-birth rate, and 31% singleton live-birth rate), and procedures using the patient's eggs and thawed embryos had the lowest (36% pregnancy rate, 28% live-birth rate, and 22% singleton live-birth rate).

The 38,910 live-birth deliveries from ART procedures performed in 2005 resulted in 52,041 infants (Table 1); the number of infants born was higher than the number of live-birth deliveries because of multiple-infant births. A total of 26,572 singleton infants were born as a result of ART. The largest proportion of infants born (36,300 or 70%) was from ART procedures in which patients used freshly fertilized embryos from their own eggs.

The two states that had the most ART medical centers (California and New York) also had the highest numbers of ART procedures performed (Table 2). The largest numbers of ART procedures performed in 2005 were among residents of California (18,655), New York (12,032), Illinois (9,449), New Jersey (9,325), and Massachusetts (8,571). The five states with the largest number of ART procedures performed also ranked highest for numbers of live-birth deliveries. ART procedures were performed for residents of certain states and territories without an ART medical center (Alaska, Maine, Montana, Guam, Federated States of Micronesia, U.S. Virgin Islands, and Wyoming); however, each accounted for a limited percentage (<1%) of total ART usage in the United States. Non-U.S. residents accounted for <1% of ART procedures, live-birth deliveries, and infants born. The ratio of number of ART procedures per 1 million population ranged from 108 in Puerto Rico to 1,340 in Massachusetts, with an overall average of 453 ART procedures started per 1 million persons.

Characteristics of Patients and ART Treatments Among Women Who Used Freshly Fertilized Embryos from Their Own Eggs

Forty-five percent of ART transfer procedures that used freshly fertilized embryos from the patient's eggs were performed on women aged <35 years, 24% on women aged 35–37 years, 19% on women aged 38–40 years, 8% on women aged 41–42 years, and 4% on women aged >42 years. Patient and treatment characteristics of these women varied by age (Table 3). Tubal factor and male factor infertility were more common among ART procedures in women aged ≤40 years than among procedures in older women. In contrast, diminished ovarian reserve, reported for only 2% of women aged <35 years, was reported for 20% of procedures in women aged 41–42 years and 28% of procedures in women aged >42 years. Unexplained infertility was reported in 9%–15% of ART transfer procedures, multiple female factors in 9%–16%, and both male and female factors in 18%–21%.

Approximately 65% of ART procedures among women aged <35 years were reported as the first ART procedure

for that patient. The percentage of ART procedures among women who had undergone at least one previous procedure increased with age: only 43% of procedures among women aged >42 years were reported as the first procedure for that patient. The percentage of procedures performed in a woman who had had a previous birth also increased with age, from 21% in women aged <35 years to 37% of women in the oldest age group.[¶]

The majority of ART procedures used IVF, and <1% used GIFT or ZIFT. Use of ICSI was common among couples with or without a diagnosis of male factor infertility, and varied by patient age. Despite variation among all age groups, the total proportion of procedures using ICSI was greater than the proportion of IVF without ICSI.

The majority of procedures included embryo culture for 3 days; the next most common procedure involved embryo culture to day 5. Culture to day 5 often coincides with development of the embryo to the blastocyst stage; this technique was used more frequently among younger women, possibly because ART procedures performed in younger women yielded more embryos that can survive in culture through day 5.

The majority of ART procedures involved transfer of more than one embryo. Among women aged <35 years, 93% of procedures involved the transfer of two or more embryos, and 34% involved transfer of three or more embryos. For women aged >42 years, 81% involved transfer of two or more embryos, and 61% involved transfer of three or more embryos. The availability of extra embryos (an indicator of overall embryo quality) decreased with age. Extra embryos were available and cryopreserved for 45% of procedures among women aged <35 years, whereas only 5% of procedures among women aged >42 years yielded extra embryos that were cryopreserved. Data were not available regarding extra embryos that were not cryopreserved for future use. Overall, 1% of ART transfer procedures used a gestational carrier or surrogate.

Live-Birth Rates Among Women Who Used Freshly Fertilized Embryos from Their Own Eggs

Live-birth rates for women who underwent ART procedures that used freshly fertilized embryos from their own eggs also varied by patient age and selected patient and treatment factors (Table 4). Although the average live-birth rate for ART-transfer procedures performed among women who used their own freshly fertilized eggs was 34%, it sharply declined with age, from 43% among women aged <35 years to 6% among women aged >42 years. Success rates did not vary significantly across diagnostic categories. Live-birth rates were higher than the age-specific average rate for procedures among women aged <35 years whose infertility diagnosis was classified as ovulatory dysfunction, endometriosis, or male factor infertility, and for procedures among women aged >42 years with an infertility diagnosis of ovulatory dysfunction or male factor. Live-birth rates were lower than average for procedures among women aged >42 years with an infertility diagnosis of endometriosis or uterine factor. Live-birth rates were lower for procedures in women aged ≤42 years who had undergone a previous ART procedure than for first procedures. The system does collect information on whether previous ART procedures were successful. Live-birth rates were higher for procedures in women who had one or more previous births and had higher live-birth rates than for procedures in women with no previous births. However, this difference was not statistically significant for procedures in women aged >40 years. Multivariable adjustment for patient factors within each age strata demonstrated similar patterns (data not presented).

Live-birth rates were higher for procedures in women who had ART procedures that used IVF-ET without ICSI, in comparison with procedures that used ICSI, regardless of whether male factor infertility was reported (Table 4). In all age groups except women aged 41–42 years, live-birth rates were lowest for procedures in couples who used ICSI in the absence of male factor infertility; however, in all age groups, live-birth rates were higher than average for procedures among women who had extended embryo culture to day 5, transferred two or more embryos, and had extra embryos available and cryopreserved for future use. Variations in live-birth rates were statistically significant for these treatment factors within all age groups. Live-birth rates increased in all age groups except for women aged >42 years when a gestational carrier was used; however, these results did not achieve statistical significance in any age group. All of the results for treatment factors need to be considered cautiously because treatment was not randomized but rather based on medical center assessment and patient choice. Thus, comparisons in success rates are prone to confounding by indication.

Although variability in live-birth rates among patients who used different treatment options cannot be completely adjusted for determinants of treatment assignment (i.e., confounding by indication might remain after adjustment), stratified analyses were used to examine associations

[¶] Data were not available to distinguish whether previous births were conceived naturally, with ART, or with other infertility treatments.

between treatment factors and live-birth rates among more homogenous groups of patients. To address concerns that, in the absence of male factor infertility, ICSI might be used preferentially for women considered difficult to treat, multiple groups of patients with poor prognostic profiles were evaluated separately (data not presented). These groups included women who underwent previous ART cycles but had no previous pregnancies or births, women diagnosed with diminished ovarian reserve, and women with fewer than five eggs retrieved. Within each of these groups, age-specific–live-birth rates for IVF-ET with and without ICSI were examined. In all analyses, except for women aged >42 years with less than five eggs retrieved, women who used IVF with ICSI had lower success rates than women who used IVF without ICSI; the pattern of these results (data not presented) is consistent with the findings presented in this report (Table 4). Data regarding women deemed to have a higher probability of success (i.e., women with more than 10 eggs retrieved, women with diagnoses other than diminished ovarian reserve, and women with extra embryos cryopreserved for future use) were evaluated separately (data not presented) to adjust for the possibility that day 5 embryo transfers might have been used preferentially for women with better prognoses. Within each of these subgroups, age-specific–live-birth rates were lower for embryo transfers on days 1–4 compared with day 5 transfers. Finally, additional analyses were stratified by patient age, number of embryos transferred, day of embryo transfer (day 3 or day 5), and number of embryos available simultaneously. These results are included with the discussion regarding multiple-birth risk.

Total live-birth rates were compared with singleton live-birth rates for procedures employing freshly fertilized embryos from the patient's eggs (Figure 2). Both live-birth rates and singleton live-birth rates decreased with patient age. Across all age groups, singleton live-birth rates were lower than live-birth rates. However, the magnitude of the difference between these two measures declined with patient age.

Multiple-Birth Risks Associated with ART

Of 12,338 multiple-birth deliveries, 8,662 (70%) were from pregnancies conceived with freshly fertilized embryos from the patient's eggs, 1,199 (10%) were from thawed embryos from the patient's eggs, 2,059 (17%) were from freshly fertilized embryos from a donor's eggs, and 418 (3%) were from thawed embryos from a donor's eggs (Table 5). In comparison with ART procedures that used the patient's eggs and freshly fertilized embryos, the risks for multiple-birth delivery were increased when eggs from a donor were used and decreased when thawed embryos were used. Among ART procedures in which freshly fertilized embryos from the patient's own eggs were used, a strong inverse relation existed between multiple-birth risk and patient age. The average multiple-birth risk for ART procedures in which freshly fertilized embryos from the patient's eggs were used was 32%. The multiple-birth risk varied from 36% among women aged <35 years to 13% among women aged >42 years.

Of 52,041 infants born through ART, 49% (25,469) were born in multiple-birth deliveries (Table 5). The proportion of infants born in a multiple-birth delivery also varied by type of ART procedure and patient age. Among ART transfer procedures in which the patient used freshly fertilized embryos from their own eggs, the proportion of infants born in a multiple-birth delivery ranged from 53% in women aged <35 years to 23% in women aged >42 years. Among ART transfer procedures in which thawed embryos from the patient's eggs were used, the proportion of infants born in a multiple-birth delivery ranged from 40% in women aged <35 years to 21% in women aged >42 years. When thawed embryos from donor eggs were used, the proportion of infants born in a multiple-birth delivery was 43%. The proportion of infants born in a multiple-birth delivery was highest (59%) in women who used freshly fertilized embryos from donor eggs.

A more detailed examination of multiple-birth risk for ART procedures employing freshly fertilized embryos from the patient's own eggs revealed that the number of embryos transferred was a key risk factor for multiple-birth delivery, but that the magnitude of the association varied by patient age (Table 6). Among all age groups, transfer of two or more embryos was associated with increased live-birth delivery rates. However, the multiple-birth risk also was increased substantially. Among women aged ≤37 years, the percentage of triplet or higher-order deliveries increased steadily with increasing number of embryos transferred from two to five or more. For women aged 38–40 years, the percentage of twin deliveries increased steadily with the number of embryos transferred. This trend was not apparent for procedures in women aged >40 years, possibly because women in these age groups have embryos with reduced implantation potential and therefore are less likely to have multiple births.

Additional analyses addressed multiple-birth risk among patients who used freshly fertilized embryos from their own eggs and set aside extra embryos for future use (Table 6). These patients can be thought of as those with elective

embryo transfer because they chose to transfer fewer embryos than the total number that were available. For procedures in women with elective embryo transfer who were aged <35 years, live-birth rates were 43% when only one embryo was transferred and 53% when two embryos were transferred. The higher live-birth rate after transfer of two embryos was associated with a large increase in the multiple-birth risk (38.5% compared with 1.9% after single embryo transfer).

For procedures in women aged 35–37 years, live-birth rates were 39% with elective embryo transfer of a single embryo and 47% when two embryos were transferred. As in the younger age category, the higher live-birth rate after transfer of two embryos was associated with a large increase in the multiple-birth risk (32.7% compared with 2.1% after single embryo transfer).**

Among patients who used freshly fertilized embryos from their own eggs, the live-birth rates and multiple-birth risks typically were higher for embryo transfers on day 5 than on day 3 (Table 7). Overall, across all age groups, fewer embryos were transferred on day 5 than on day 3. For example, among women aged <35 years, two or fewer embryos were transferred in 86% of day 5 transfers and in 57% of day 3 transfers. Similarly, in women aged <35 years, 92% of day 5 elective transfers and 67% of day 3 elective transfers involved the transfer of two or fewer embryos. As noted previously, both live-birth rates and multiple-birth risks were higher for patients who had elective embryo transfers. For women with elective embryo transfer on day 5 who were aged <35 years, the percentage of transfers resulting in live births was 48% when one embryo was transferred and 58% when two embryos were transferred. By contrast, the multiple-birth risks in these two groups were 3% and 44%, respectively. Thus, the 10% increase in the live-birth rate was accompanied by a 41% increase in the risk for a multiple delivery. If success is measured in terms of singleton live-birth, the highest success rates for this group were with one embryo transferred. This also was true for women aged 35–37 years with elective single embryo transfers on day 5 (Table 7).

The states with the highest number of ART-associated live-birth deliveries also had the highest number of infants born in multiple-birth deliveries (Table 8). These include California (3,635), New York (1,768), New Jersey (1,692), Texas (1,666), Illinois (1,501), and Massachusetts (1,293). Nationwide, the percentage of ART-born infants who were born in multiple-birth deliveries was 49%; the percentage of twins was 44% and that of triplets or higher-order multiples was 5%. The percentage of ART-born infants in multiple-birth deliveries was ≥50% in the majority of states. The states with the highest proportion of ART-born infants in multiple-birth deliveries were New Mexico (56%), Utah (56%), Oregon (56%), Montana (56%), Idaho (54%), Texas (54%), Alabama (54%), and Kansas (54%); however, these findings should be interpreted with caution because of an overall low number of live births resulting from ART in certain states.

Of 4,138,349 infants born in the United States in 2005, a total of 49,308 (1%) were conceived with ART (Table 9). Infants conceived with ART accounted for 0.6% of singleton births and 17% of multiple births nationwide; 16% of all twins and 38% of infants born in triplets or higher-order multiples were conceived with ART.

Perinatal Risks Associated with ART

The percentage of infants with low birthweight varied from 9% among singletons to 95% among triplets or higher-order multiples. The percentages of very low birthweight, preterm, and preterm low birthweight followed similar patterns (Table 10).

The percentages of ART singletons that were low birthweight and preterm varied by procedure type and selected maternal factors (Table 11). In comparison with singletons born after procedures that used freshly fertilized embryos derived from the patient's eggs, singletons born after procedures that used freshly fertilized embryos derived from donor eggs were at increased risk for three perinatal outcomes: low birthweight, preterm delivery, and preterm low birthweight. Singletons born after procedures that used thawed embryos were at decreased risks for low birthweight and term low birthweight; however, they were at increased risk for preterm delivery overall. The variation in risk across procedure types was not statistically significant for very low birthweight and preterm low birthweight.

More detailed analysis of maternal factors among singletons born after procedures that used freshly fertilized embryos derived from the patient's eggs indicated higher risks of low birthweight, very low birthweight, preterm delivery, and preterm low birthweight for women aged 41–42 years. Higher risks for low birthweight and term low birthweight were observed among mothers with no previous births; the variation in risks was statistically significant ($p<0.01$) for both of these outcomes.

** Results are based on total multiple-birth risk and therefore do not provide an indication of pregnancies that began as twins, triplets, or a higher order but reduced (either spontaneously or through medical intervention) to singletons or twins (Tables 6 and 7).

Discussion

According to the most recent estimates of infertility in the United States, 10% of women of reproductive age (15–44 years) reported a previous infertility-associated health-care visit, and 2% reported a visit during the previous year (*19*). Among married couples in which the woman was of reproductive age, 7% reported they had not conceived after 12 months of unprotected intercourse. With advances in ART, couples are increasingly turning to this form of treatment to overcome their infertility.

Since the birth of the first infant through ART in the United States in 1981, use of ART has grown substantially. The use of ART has consistently increased in the United States since 1996, when CDC began ART surveillance. The increased use of ART, coupled with higher ART success rates, has resulted in dramatic increases in the number of children conceived through ART each year. The number of ART procedures reported to CDC has more than doubled, from 64,681 in 1996 to 134,260 in 2005 (*1*). During the same period, the number of infants conceived through ART procedures more than doubled, from 20,840 to 52,041.

This report documents that in 2005, ART use varied according to the patient's state of residency. Residents of California, New York, Illinois, New Jersey, Massachusetts, and Texas reported the highest number of ART procedures. These states also reported the highest number of infants conceived through ART. In 2005, ART use by state of residency was not completely in line with expectations based on the total population within states (*15*). Whereas Massachusetts had the fifth highest number of ART procedures performed, it ranked fourteenth in total population size.[††] Similarly, residents of District of Columbia, Rhode Island, and Hawaii underwent more ART procedures than would have been expected based on their population sizes. As a result, state-specific ratios of ART procedures by population varied according to state of residency. The highest ratios of the number of ART procedures among state residents per 1 million population were observed in Massachusetts (1,340), District of Columbia (1,166), New Jersey (1,070), Maryland (837), Connecticut (783), and Rhode Island (774). This divergence is not unexpected because, in 2005, Connecticut, Massachusetts, New Jersey, and Rhode Island had statewide mandates for insurance coverage for ART procedures. Variation within states also might be related to availability of ART services within each state. However, the relation between demand for services and availability cannot be disentangled (e.g., increased availability in certain states might reflect the increased demand for ART among state residents).

Among women who used fresh fertilized embryos from their own eggs, patient factors (e.g., infertility diagnoses, history of previous ART procedures, and previous births) varied considerably by age. The proportion of procedures in which the couple received a diagnosis of ovulatory dysfunction, endometriosis, or male factor infertility decreased with the woman's age, whereas the proportion of procedures in which the couple received a diagnosis of diminished ovarian reserve increased with the woman's age. History of previous ART and previous births were more common among older women. In addition, treatment factors varied considerably by the age of the woman. The proportion of procedures in which embryo transfer occurred on day 5 (i.e., the blastocyst stage) declined with the age of the woman, whereas the proportion of procedures in which three or more embryos were transferred increased steadily with age.

Because ART success rates are affected by multiple patient and treatment factors, using a single measure of success is not sufficient to evaluate ART efficacy. At a minimum, ART procedures should be subdivided on the basis of the source of the egg (patient or donor) and the status of the embryos (freshly fertilized or thawed) because success rates vary substantially across these types. Within the type of ART procedure, further variation exists in success rates by patient and treatment factors, most notably patient age. Other factors to consider when assessing success rates are infertility diagnosis, number of previous ART procedures, number of previous births, method of embryo fertilization and transfer, number of days of embryo culture, number of embryos transferred, availability of extra embryos, and use of a gestational carrier (i.e., surrogate). Variation exists in success rates according to each of these factors.

CDC's primary focus in collecting ART data has been on live-birth deliveries as an indicator of success because ART surveillance activities were developed in response to a federal mandate to report ART success rate data. This mandate requires that CDC collect data from all ART medical centers and report success rates, defined as all live births per ovarian stimulation procedures or ART procedures, for each ART medical center. Therefore, a key role for CDC has been to publish standardized data related to ART success rates, including information regarding factors that affect these rates. With these data, persons and couples can make informed decisions regarding whether to undergo this

[††] Data regarding population size are based on July 1, 2005, estimates from the U.S. Census Bureau (*15*).

time-consuming and expensive treatment (*20*).[§§] However, success-rate data also should be balanced with consideration of effects on maternal and infant health. CDC receives data on pregnancy outcomes of public health significance, which enables CDC to monitor multiple-birth rates, preterm delivery, and low birthweight associated with ART.

In the United States, multiple births have increased substantially since the 1980s (*17,21*). The increase in multiple births has been attributed to an increased use of ART and delayed childbearing (*5,22,23*). Although infants conceived with ART accounted for 1% of the total births in the United States in 2005, the proportion of twins and triplets or higher-order multiples attributed to ART were 16% and 38%, respectively. In 1999, the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine issued voluntary guidelines (*24*) on the number of embryos transferred; these guidelines were revised in 2004 (*25*) and 2006 (*26*).

In certain states, ART procedures are not covered by insurance carriers, and patients might feel pressured to maximize the opportunity for live-birth delivery. In addition, if success is defined solely as total live-birth delivery, anecdotal evidence suggests that certain ART providers might feel pressure to transfer multiple embryos to maximize their publicly reported success rates (*27*). In the United States, multiple embryo transfer was still a common practice in 2005; approximately 47% of ART procedures that used fresh, nondonor eggs or embryos and progressed to the embryo-transfer stage involved the transfer of three or more embryos. Approximately 18% of procedures involved the transfer of four or more, and 6% of procedures involved the transfer of five or more embryos (*1*). Among women aged <35 years, the proportion of ART procedures that involved four or more embryos transferred was approximately 8% because women in this age category typically experience higher success rates with fewer embryos transferred. Multiple scientific reports have advocated that singleton live-birth rates be presented as a distinct indicator of ART success (*28–34*). This report includes this measure (Figure 2) and presents it with total live-birth rates. Success rates based on singleton live-birth deliveries will provide patients with a measure that more directly highlights infant outcomes with the optimal short- and long-term prognosis. Twins, albeit to a lesser extent than triplets or higher-order multiples, have substantially increased risks for infant morbidity and mortality. The risks for low birthweight and preterm birth both exceed 57% for twins, and the risk for very low birthweight is 9% (*17*). In addition, because twins are at substantially increased risk for perinatal and infant mortality (*11,21*), singleton live-birth rates are a valid measure of success.

Data in this report indicate that 49% of infants born through ART in 2005 were born in multiple–birth deliveries, compared with 3% in the general U.S. population (*17*). The twin rate was 44%, compared with 3% in the general U.S. population, and the rate of triplets and higher-order multiples was 5%, approximately 25 times higher than the general U.S. population rate (0.2%). Regarding the specific type of ART procedure, the percentage of infants born in multiple-birth deliveries were among the highest for women who underwent ART procedures that used freshly fertilized embryos from their own eggs (49%) or from donor eggs (59%).

In 26 states, District of Columbia, and Puerto Rico, ≥50% of infants conceived through ART were born in multiple-birth deliveries. Multiple births resulting from ART are an increasing public health concern, nationwide and for the majority of states.

For women who underwent ART procedures using freshly fertilized embryos from their own eggs, the multiple-birth risk increased when multiple embryos were transferred. Embryo availability, an indicator of embryo quality, also was a strong predictor of multiple-birth risk independent from the number of embryos transferred. In analyses stratified by patient age, number of embryos transferred, day of embryo culture (day 3 or 5), and embryo availability, high live-birth rates and singleton live-birth rates were achieved, particularly among younger women as transfer of a single embryo was efficacious. In the majority of groups, limiting the number of embryos transferred can minimize the multiple-birth risk without severely compromising the success rates.

In addition to the known multiple-birth risks associated with ART, singleton infants conceived from ART procedures are at increased risk for low birthweight and preterm delivery. In 2005, of all singleton infants conceived with ART, 9% were low birthweight, compared with 6% in the general U.S. population (*16*). Approximately 2% of singleton infants conceived from ART were very low birthweight, compared with approximately 1% of singletons conceived in the general U.S. population. The percentage of ART singletons born preterm was higher than the general U.S. population (15% and 11%, respectively). Thus, adverse infant health outcomes among singletons (e.g., low

[§§] Estimated cost for one procedure of IVF averages $12,400 (*20*).

birthweight and preterm delivery) also should be considered when assessing the efficacy and safety of ART.

A comparison of perinatal outcomes among ART twins and triplets or higher-order multiples with their counterparts in the general population is not useful for at least two reasons. First, both ART and non-ART infertility treatments are estimated to account for a substantial proportion of multiple births in the United States, and distinguishing naturally conceived from iatrogenic multiple births is not possible. ART accounts for only 1% of the total U.S. births; however, it accounts for 16% of twins and 38% of triplets or higher-order multiples. Second, the majority of multiple births conceived after ART treatment are likely dizygotic from multiple embryo transfer. Among natural conceptions, approximately one third to one half of twins might be monozygotic, depending on maternal age (*35*). Monozygotic twins are at increased risk for adverse outcomes in comparison with dizygotic twins (*36*).

Multiple births are associated with an increased health risk for both mothers and infants (*11,12,20,22*). Women with multiple-gestation pregnancies are at increased risk for maternal complications (e.g., hemorrhage and hypertension). Infants born in a multiple-birth delivery are at increased risk for prematurity, low birthweight, infant mortality, and long-term disability.

The contribution of ART to preterm births in the United States also is a key concern. This report documents that approximately 42% of ART infants born in 2005 were preterm (Table 10), compared with approximately 13% of preterm births in the general U.S. population (*17*). Preterm infants have increased risk of death and have more health and developmental problems than full-term infants (*37–40*). The health risks associated with preterm births have contributed to increasing health-care costs. The economic burden associated with preterm births in the United States in 2005 has been estimated to be $26 billion ($51,600 per infant born preterm) (*40*). ART infants born preterm accounted for approximately 4% of all preterm births in the United States in 2005, a total economic burden estimated at $1 billion. ASRM and SART guidelines on the number of embryos transferred in an ART cycle might help in further reducing the incidence of preterm deliveries, the majority of which are multiples.

The findings in this report are subject to several limitations. First, ART surveillance data were reported for each ART procedure performed rather than for each patient who used ART. Linking procedures among patients who underwent more than one ART procedure in a given year is not possible. Because patients who underwent more than one procedure in a given year were most likely to include those in which a pregnancy was not achieved, the success rates reported might underestimate the true per-patient success rate. In addition, ratios of ART procedures per population might be higher than the unknown ratio of the number of persons undergoing ART per population. Second, these data represent couples who sought ART services in 2005; therefore, success rates do not represent all couples with infertility who were potential ART users in 2005. Third, because treatment was not randomized but rather based on medical center assessment and patient choice, results for treatment factors must be considered with caution. Finally, approximately 11% of medical centers that performed ART in 2005 did not report their data to CDC as required.

ART data are reported to CDC by the ART medical center in which the procedure was performed rather than by the state in which the patient resided. In this report, ART data are presented by the female patient's state of residence. Residency data were missing for approximately 8% of all live-birth deliveries resulting from ART procedures started in 2005. In cases of missing residency data, residency was assigned as the state in which the ART procedure was performed. Thus, the number of procedures performed among state residents, number of infants, and number of multiple-birth infants might have been overestimated for certain states. Concurrently, the numbers might be underestimated in states that border states with missing residency data, particularly states in the Northeast region of the United States. Nonetheless, the effects of missing residency data were not substantial. Statistics were evaluated separately according to the location of the ART medical center rather than the patient's state of residence. The rankings of the ART medical center location by total number of infants and multiple-birth infants were similar to the rankings based on patient's state of residence (data not presented).

The patient's state of residence was reported at the time of ART treatment. The possibility of migration during the interval between ART treatment and birth exists. U.S. Census Bureau data indicate that approximately 3% of the U.S. population moves between states annually; this rate is even higher for persons aged 20–34 years (*41*).

Members of the U.S. armed forces have a high potential for migration. Therefore, ART procedures performed among patients who attended military medical centers were evaluated separately. In 2005, 0.7% ART procedures were performed in four military medical centers (California, District of Columbia, Hawaii, and Texas). In certain facilities, a substantial number of distinct states were listed for patient's state of residence. States and territories for which ≥1% of

ART procedures among residents were performed in a military medical center were Alaska, Delaware, District of Columbia, Guam, Hawaii, Kansas, Maryland, New Mexico, North Carolina, Oklahoma, South Carolina, Texas, Virginia, and Wyoming. States for which >5% of ART procedures among state residents were performed in a military medical center were District of Columbia, Guam, and Hawaii. Despite these limitations, findings from national surveillance of ART procedures performed in the United States provide useful information for patients contemplating ART, ART providers, and health-care policy makers. ART surveillance data can be used to monitor trends in ART use and outcomes from ART procedures. Data from ART surveillance can be used to assess patient and treatment factors that contribute to higher success rates. Ongoing surveillance data can be used to assess the risk for multiple births and adverse perinatal outcomes among singleton births. Surveillance data provide information to assess changes in clinical practice related to ART treatment.

Increased use of ART procedures and the practice of transferring multiple embryos during ART treatments have led to high multiple-birth rates in the United States (*5,10*). Balancing the chance of success of ART against the risk for multiple births is challenging. Implementation of approaches to limit the number of embryos transferred for patients undergoing ART should reduce the occurrence of multiple births resulting from ART. Such efforts ultimately might lead ART patients and providers to view treatment success in terms of singleton pregnancies and births. In addition, continued research is needed to understand the adverse effects of ART on maternal and child health. CDC will continue to provide updates of ART use in the United States as data become available.

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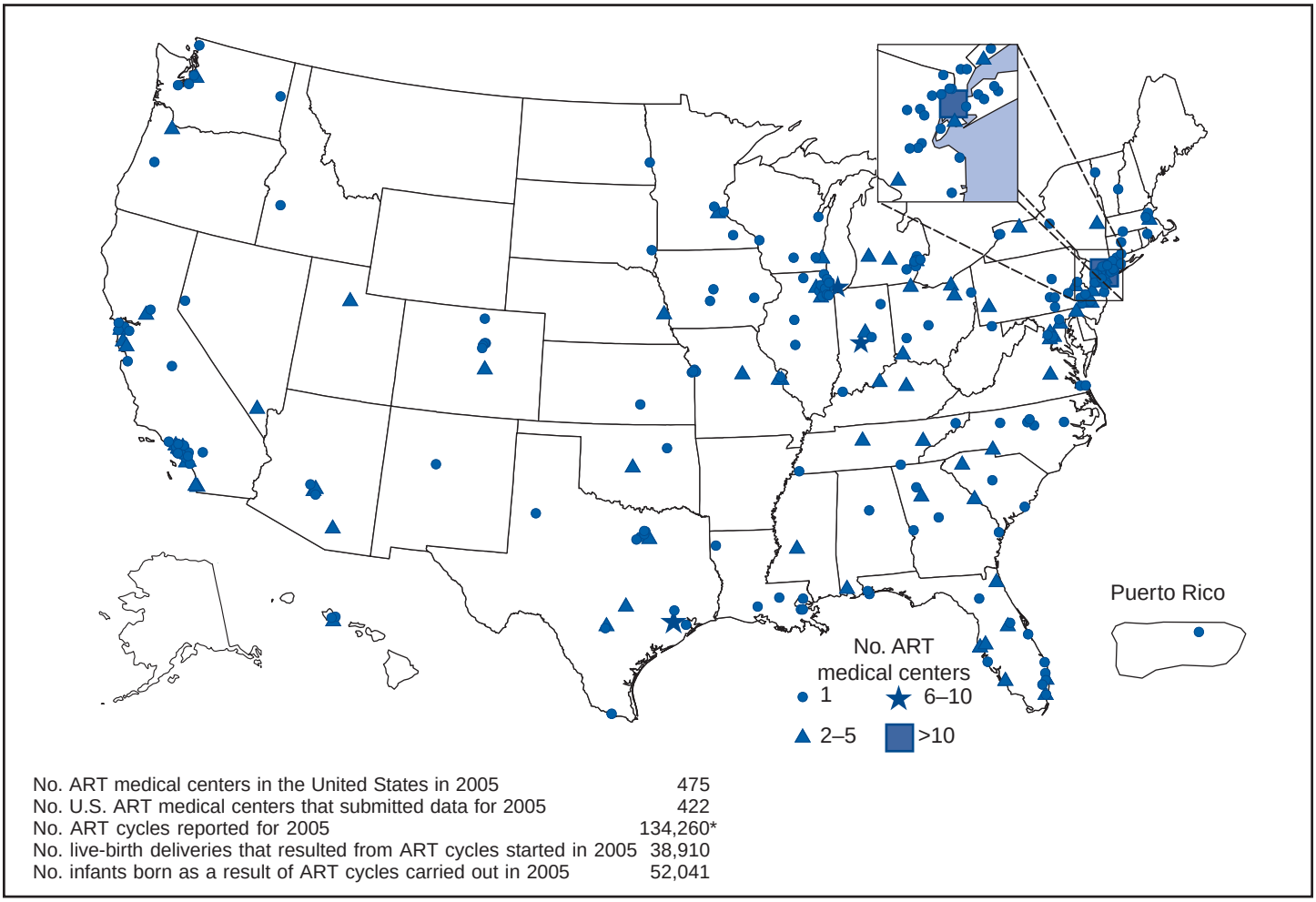
FIGURE 1. Location of assisted reproductive technology (ART) medical centers — United States and Puerto Rico, 2005



No. ART medical centers in the United States in 2005	475
No. U.S. ART medical centers that submitted data for 2005	422
No. ART cycles reported for 2005	134,260*
No. live-birth deliveries that resulted from ART cycles started in 2005	38,910
No. infants born as a result of ART cycles carried out in 2005	52,041

*This number does not include 358 cycles in which a new treatment procedure was being evaluated.

FIGURE 2. Percentage of transfers resulting in live births and singleton live births for assisted reproductive technology procedures performed among women who used freshly fertilized embryos from their own eggs, by patient's age group — United States, 2005

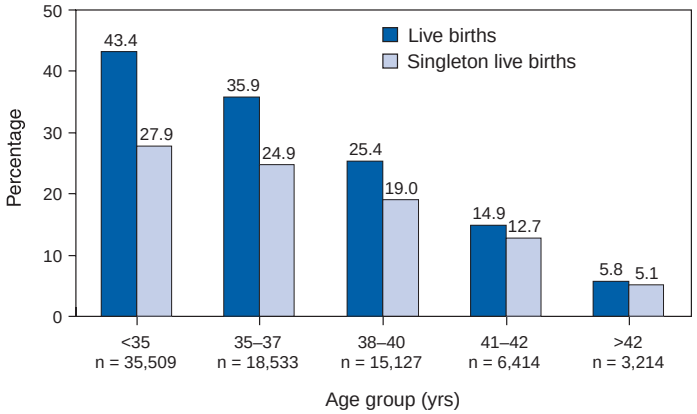


TABLE 1. Number and outcomes of assisted reproductive technology (ART), by procedure type — United States, 2005

ART procedure type	No. ART procedures started	No. procedures progressing to retrievals	No. procedures progressing to transfers	No. pregnancies	Transfers resulting in pregnancies (%)	No. live-birth deliveries	Transfers resulting in live births (%)	No. singleton live births	Transfers resulting in singleton live births (%)	Total no. live-born infants
Patient's eggs used										
Freshly fertilized embryos	97,442	85,713	78,797	33,101	42.0	27,047	34.3	18,385	23.3	36,300
Thawed embryos	20,657	NA*	18,812	6,721	35.7	5,275	28.0	4,076	21.7	6,563
Donor eggs used										
Freshly fertilized embryos	10,620	9,989	9,649	5,877	60.9	5,043	52.3	2,984	30.9	7,190
Thawed embryos	5,541	NA	4,997	1,952	39.1	1,545	30.9	1,127	22.6	1,988
Total	**134,260†**	**NA**	**112,255**	**47,651**	**42.4**	**38,910**	**34.7**	**26,572**	**23.7**	**52,041**

* Not applicable.
† This number does not include 358 ART procedures in which a new treatment procedure was being evaluated.

TABLE 2. Number of reported assisted reproductive technology (ART) procedures performed, number of pregnancies, number of live-birth deliveries, and number of infants born, by patient's state/territory of residence* at time of treatment — United States, 2005

Patient's state/territory of residence	Procedures started		Transfers		Pregnancies		Live-birth deliveries		Infants born		Ratio of no. ART procedures started/ population (millions)†
	No.	No. with missing residency	No.	No. with missing residency	No.	No. with missing residency	No.	No. with missing residency	No.	No. with missing residency	
Alabama	736	0	600	0	291	0	244	0	338	0	161.5
Alaska	150	0	132	0	62	0	47	0	63	0	226.0
Arizona	2,117	83	1,788	73	728	28	585	21	767	26	356.4
Arkansas	483	0	426	0	179	0	160	0	215	0	173.8
California	18,655	1,856	16,151	1,584	6,495	587	5,278	485	7,159	637	516.3
Colorado	1,810	52	1,568	50	860	32	731	31	999	46	388.0
Connecticut	2,749	54	2,224	46	980	24	782	19	1,025	23	783.1
Delaware	346	0	281	0	140	0	113	0	148	0	410.2
District of Columbia§	642	59	500	44	190	19	151	16	202	21	1,166.2
Federated States of Micronesia	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶
Florida	6,364	149	5,191	124	2,213	53	1,822	45	2,418	60	357.7
Georgia	2,938	1,344	2,521	1,148	1,119	506	940	427	1,286	574	323.8
Guam	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶
Hawaii	849	3	702	3	244	1	193	1	264	2	665.8
Idaho	399	0	361	0	187	0	172	0	241	0	279.2
Illinois	9,449	41	7,673	33	3,030	14	2,438	12	3,211	16	740.3
Indiana	1,854	4	1,540	4	580	3	488	2	669	2	295.6
Iowa	839	0	681	0	370	0	312	0	414	0	282.8
Kansas	625	1	507	1	245	0	196	0	271	0	227.7
Kentucky	929	1	800	1	363	1	291	1	403	2	222.6
Louisiana	751	1	585	1	253	0	222	0	301	0	166.0
Maine	217	0	174	0	80	0	71	0	95	0	164.2
Maryland	4,685	57	3,829	48	1,599	23	1,261	20	1,656	24	836.5
Massachusetts	8,571	3,035	7,185	2,536	2,853	905	2,303	737	2,964	964	1,339.5
Michigan	3,183	16	2,610	12	1,121	5	945	5	1,285	7	314.5
Minnesota	1,864	6	1,665	6	833	3	717	3	971	3	363.2
Mississippi	439	0	367	0	165	0	141	0	187	0	150.3
Missouri	1,703	492	1,403	423	689	197	575	167	740	217	293.6
Montana	165	0	138	0	66	0	56	0	79	0	176.3
Nebraska	656	3	514	1	224	0	192	0	255	0	373.0
Nevada	1,184	38	1,052	38	477	22	392	19	526	24	490.3
New Hampshire	774	0	656	0	275	0	221	0	292	0	590.9
New Jersey	9,325	465	7,466	383	3,205	159	2,586	124	3,459	169	1,069.6
New Mexico	311	1	255	1	151	0	121	0	169	0	161.3
New York	12,032	390	9,901	348	3,707	154	2,896	113	3,807	148	624.9
New York City	4,681	1,706	3,737	1,387	1,555	596	1,234	468	1,604	610	569.9
North Carolina	2,587	3	2,185	3	923	3	771	2	1,029	2	297.9
North Dakota	204	0	188	0	74	0	66	0	84	0	320.4
Ohio	3,361	41	2,870	36	1,185	10	1,002	9	1,365	11	293.2
Oklahoma	569	2	495	2	264	2	219	1	288	2	160.4
Oregon	1,010	5	879	5	460	5	382	4	533	8	277.4
Pennsylvania	5,071	472	4,155	361	1,650	127	1,346	107	1,808	134	408.0
Puerto Rico	422	23	358	20	148	5	109	0	148	0	107.9
Rhode Island	833	2	699	1	290	0	244	0	331	0	774.0
South Carolina	974	0	888	0	461	0	376	0	513	0	228.9
South Dakota	176	0	154	0	64	0	56	0	74	0	226.8
Tennessee	1,031	2	880	2	441	1	377	1	511	2	172.9
Texas	6,582	109	5,611	99	2,764	47	2,245	37	3,103	51	287.9
Utah	662	3	582	3	291	1	264	1	371	1	268.1
Vermont	174	0	143	0	53	0	39	0	47	0	279.3
Virgin Islands, U.S.	25	0	23	0	12	0	11	0	11	0	230.0
Virginia	4,232	63	3,579	55	1,471	15	1,204	14	1,572	19	559.2
Washington	1,668	28	1,459	24	726	10	612	8	811	9	265.3
West Virginia	209	0	181	0	79	0	67	0	92	0	115.0
Wisconsin	1,570	22	1,360	7	604	2	510	1	685	1	283.6
Wyoming	71	0	64	0	33	0	29	0	39	0	139.4
Non-U.S. resident	345	0	310	0	126	0	103	0	141	0	—**
Total	**134,260**	**10,632**	**112,255**	**8,913**	**47,651**	**3,560**	**38,910**	**2,901**	**52,041**	**3,815**	**453.0**

* In cases of missing residency data, the patient's state of residency was assigned as the state in which the ART procedure was performed.
† Source of population size: July 1, 2005, state population estimates. Population Division, U.S. Census Bureau.
§ Of all ART procedures, 0.7% were reported from military medical centers located in California, District of Columbia, Hawaii, and Texas. States and territories for which ≥1% of ART procedures among state residents were performed in a military medical center were Alaska, Delaware, District of Columbia, Guam, Hawaii, Kansas, Maryland, New Mexico, North Carolina, Oklahoma, South Carolina, Texas, Virginia, and Wyoming. In District of Columbia, Guam, and Hawaii, >5% of ART procedures among residents were performed in a military medical center.
¶ Data not provided to preserve confidentiality but included in totals.
** Non-U.S. residents excluded because the appropriate denominators were unknown.

TABLE 3. Percentage distribution of selected patient and treatment factors for assisted reproductive technology (ART) transfer procedures among patients who used freshly fertilized embryos from their own eggs, by patient's age group — United States, 2005

	Patient age group (yrs)				
Patient/Treatment factors	<35 (n = 35,509) (%)	35–37 (n = 18,533) (%)	38–40 (n = 15,127) (%)	41–42 (n = 6,414) (%)	>42 (n = 3,214) (%)
Patient factors					
Diagnosis					
Tubal factor	11.2	12.2	11.0	7.8	6.3
Ovulatory dysfunction	9.2	5.4	3.2	2.5	1.7
Diminished ovarian reserve	2.2	4.5	10.6	19.5	27.7
Endometriosis	7.2	6.4	4.2	2.4	1.8
Uterine factor	1.1	1.4	2.0	2.0	1.3
Male factor	24.7	19.6	14.3	9.3	6.8
Other causes	5.6	7.1	8.3	9.5	9.8
Unexplained cause	12.0	14.6	13.3	11.3	8.9
Multiple factors, female only	9.0	10.9	13.4	15.0	16.3
Multiple factors, female and male	17.7	17.8	19.6	20.6	19.3
No. previous ART procedures					
0	64.6	55.1	50.1	45.9	43.0
≥1	35.4	44.9	49.9	54.1	57.0
No. previous births					
0	78.7	68.6	66.2	63.7	63.5
≥1	21.3	31.4	33.8	36.3	36.5
Treatment factors					
Method of embryo fertilization and transfer*					
IVF-ET without ICSI	29.7	32.1	33.4	33.5	33.0
IVF-ET with ICSI	70.0	67.7	66.2	66.0	66.2
IVF-ET with ICSI among couples diagnosed with male factor infertility	39.4	34.4	30.6	26.4	22.8
IVF-ET with ICSI among couples not diagnosed with male factor infertility	30.6	33.3	35.6	39.6	43.4
GIFT	0.0	0.0	0.1	0.1	0.3
ZIFT	0.2	0.2	0.2	0.3	0.3
Combination	0.0	0.0	0.1	0.1	0.2
No. of days of embryo culture†					
1	0.1	0.1	0.1	0.0	0.1
2	0.2	0.2	0.3	0.4	0.4
3	3.4	3.8	3.9	4.8	5.9
4	62.6	67.3	72.3	74.3	77.4
5	2.9	3.5	4.3	5.1	5.4
6	28.3	22.9	17.4	13.9	9.8
≥7	2.3	2.0	1.6	1.3	0.9
No. embryos transferred					
1	7.0	9.0	10.9	14.2	18.9
2	58.8	41.0	25.2	19.9	20.0
3	26.7	35.0	33.5	23.6	20.3
4	5.8	11.7	21.6	21.8	17.3
≥5	1.8	3.3	8.7	20.5	23.5
Extra embryo(s) available and cryopreserved					
Yes	55.0	67.0	80.5	89.8	95.5
No	45.0	33.0	19.5	10.2	4.5
Use of gestational carrier					
Yes	1.0	1.1	1.2	1.3	1.3
No	99.0	98.9	98.8	98.7	98.7

* IVF-ET = in vitro fertilization with transcervical embryo transfer; ICSI = intracytoplasmic sperm injection; GIFT = gamete intrafallopian transfer; ZIFT = zygote intrafallopian transfer; and Combination = a combination of IVF with or without ICSI and either GIFT or ZIFT.
† In cases of GIFT, gametes were not cultured but were transferred on day 1.

TABLE 4. Percentages of transfers resulting in live births for assisted reproductive technology (ART) procedures performed among patients who used freshly fertilized embryos from their own eggs, by patient's age group and selected patient and treatment factors — United States, 2005

	Transfers resulting in live births				
Patient/Treatment factors	**<35 yrs (%)**	**35–37 yrs (%)**	**38–40 yrs (%)**	**41–42 yrs (%)**	**>42 yrs (%)**
Patient factors					
Diagnosis					
Tubal factor	43.1*	34.0	26.2*	16.0	4.9
Ovulatory dysfunction	45.8	37.6	30.6	16.0	7.1
Diminished ovarian reserve	40.3	30.4	23.2	13.1	5.5
Endometriosis	44.2	36.9	27.1	18.5	1.8
Uterine factor	35.9	38.5	22.1	16.5	2.4
Male factor	44.3	38.0	28.1	16.1	8.6
Other causes	43.2	35.6	23.1	13.1	6.0
Unexplained cause	44.5	37.9	27.9	15.3	6.3
Multiple factors, female only	41.1	34.3	23.6	17.2	6.7
Multiple factors, female and male	41.9	35.1	24.1	13.8	5.0
No. previous ART procedures					
0	45.6*	37.8*	27.2*	15.1	5.0
≥1	39.4	33.7	23.7	14.7	6.4
No. previous births					
0	42.4*	35.0*	24.3*	13.9	5.0
≥1	46.8	38.0	27.6	16.6	7.2
Treatment factors					
Method of embryo fertilization and transfer†					
IVF-ET without ICSI	46.1*	38.1*	28.2*	15.6	6.6
IVF-ET with ICSI among couples diagnosed with male factor infertility	43.3	36.6	25.5	14.5	5.6
IVF-ET with ICSI among couples not diagnosed with male factor infertility	40.9	33.2	22.8	14.7	5.4
No. days of embryo culture§					
3	40.9*	34.6*	24.1*	14.2*	5.2*
5	50.5	41.8	33.5	21.0	11.1
No. embryos transferred					
1	28.0*	17.8*	10.2*	5.9*	1.6*
2	47.2	39.0	26.1	11.8	4.7
3	40.8	37.5	27.2	16.4	6.3
4	38.0	36.5	29.0	18.0	8.3
≥5	33.2	30.3	26.9	19.0	7.9
Extra embryos available and cryopreserved					
Yes	37.1*	31.2*	22.5*	13.6*	5.3*
No	51.1	45.7	37.4	26.7	16.0
Use of gestational carrier					
Yes	43.3	35.9	25.4	14.9	5.9
No	47.9	39.2	30.7	15.1	2.4
Total transfers resulting in live births	**43.4**	**36.0**	**25.4**	**14.9**	**5.8**

* p<0.05, chi-square to test for variations in live-birth rates across patient and treatment factor categories within each age group.

† IVF-ET = in vitro fertilization with transcervical embryo transfer, and ICSI = intracytoplasmic sperm injection. ART procedures including gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), and a combination of IVF with or without ICSI and either GIFT or ZIFT were not included because each of these accounted for a small proportion of procedures.

§ Limited to 3 and 5 days to embryo culture. ART procedures including 1, 2, 4, 6 and ≥7 days to embryo culture were not included because each of these accounted for a limited proportion of procedures.

TABLE 5. Multiple-birth risk, by type of assisted reproductive technology (ART) transfer procedure performed — United States, 2005

Procedure type	Patient age group (yrs)	No. live-birth deliveries	Multiple-birth deliveries		No. infants born	Infants born in multiple-birth deliveries	
			No.	(%)*		No.	(%)
Patient's eggs used							
Freshly fertilized embryos	All ages	27,047	8,662	32.0	36,300	17,915	49.4
	<35	15,396	5,478	35.5	21,261	11,343	53.4
	35–37	6,662	2,056	30.8	8,854	4,248	47.9
	38–40	3,847	966	25.1	4,875	1,994	40.9
	41–42	955	138	14.4	1,099	282	25.7
	>42	187	24	12.8	211	48	22.7
Thawed embryos	All ages	5,275	1,199	22.7	6,563	2,487	37.9
	<35	3,035	740	24.4	3,835	1,540	40.2
	35–37	1,329	275	20.7	1,617	563	34.8
	38–40	676	143	21.1	832	299	36.0
	41–42	155	32	20.6	189	66	35.0
	>42	80	9	11.3	90	19	21.1
Donor's eggs used†							
Freshly fertilized embryos	All ages	5,043	2,059	40.8	7,190	4,206	58.5
Thawed embryos	All ages	1,545	418	27.1	1,988	861	43.3
Total	**All ages**	**38,910**	**12,338**	**31.7**	**52,041**	**25,469**	**48.9**

* Multiple-birth risk.
† Age-specific statistics are not presented for procedures that used donor eggs because only limited variation by age exists among these procedures.

TABLE 6. Percentages of transfers resulting in live births and percentages of singletons, twins, and triplets or higher-order multiples for assisted reproductive technology (ART) procedures that used freshly fertilized embryos from the patient's own eggs, by patient's age group, number of embryos transferred, and embryo availability — United States, 2005

	All ART transfer procedures					ART transfer procedures for women known to have more embryos available than transferred				
Patient age group (yrs)/No. embryos transferred	No.	Transfers resulting in live births (%)	Singletons (%)	Twins (%)	Triplets or higher-order multiples (%)	No.	Transfers resulting in live births (%)	Singletons (%)	Twins (%)	Triplets or higher-order multiples (%)
<35										
1	2,477	28.0	98.6	1.4	0.0	712	43.3	98.1	1.9	0.0
2	20,863	47.2	63.8	35.2	1.0	11,496	52.8	60.2	38.5	1.2
3	9,485	40.8	60.9	32.8	6.3	3,166	47.5	55.5	36.0	8.5
4	2,043	38.0	61.0	30.9	8.1	485	45.8	54.1	32.4	13.5
≥5	629	33.2	60.3	32.1	7.7	98	41.8	48.8	39.0	12.2
35–37										
1	1,662	17.8	97.6	2.4	0.0	242	38.8	97.9	2.1	0.0
2	7,592	39.0	71.1	28.4	0.4	3,366	47.4	66.7	32.7	0.6
3	6,492	37.5	65.9	30.6	3.6	1,998	43.6	59.1	35.7	5.2
4	2,175	36.5	63.1	31.8	5.2	427	47.1	59.2	34.3	6.5
≥5	603	30.3	60.7	31.1	8.2	86	38.4	57.6	30.3	12.1
38–40										
1	1,652	10.2	97.0	3.0	0.0	67	35.8	95.8	4.2	0.0
2	3,818	26.1	79.2	20.5	0.3	942	41.8	71.8	27.7	0.5
3	5,065	27.2	75.1	23.0	1.9	1,203	33.6	69.8	27.5	2.7
4	3,267	29.0	68.8	27.7	3.5	587	39.5	62.9	33.2	3.9
≥5	1,321	26.9	67.7	30.3	2.0	155	32.3	64.0	34.0	2.0
41–42										
1	913	5.9	94.4	5.6	0.0	9	*	*	*	*
2	1,278	11.8	88.7	10.6	0.7	106	31.1	87.9	12.1	0.0
3	1,511	16.4	85.9	14.1	0.0	188	30.9	79.3	20.7	0.0
4	1,397	18.0	87.3	11.1	1.6	199	22.6	82.2	13.3	4.4
≥5	1,313	19.0	79.6	18.8	1.6	150	24.0	63.9	27.8	8.3
>42										
1	608	1.6	100.0	0.0	0.0	7	*	*	*	*
2	644	4.7	93.3	6.7	0.0	13	30.8	50.0	50.0	0.0
3	651	6.3	85.4	14.6	0.0	34	17.6	66.7	33.3	0.0
4	555	8.3	91.3	6.5	2.2	42	14.3	83.3	16.7	0.0
≥5	755	7.9	80.0	20.0	0.0	48	12.5	83.3	16.7	0.0

* Statistics not provided for cases in which the denominator is <10.

TABLE 7. Percentage of transfers resulting in live births and multiple-birth risk for assisted reproductive technology (ART) procedures using freshly fertilized embryos from the patient's own eggs, by patient's age group, number of embryos transferred, day of embryo transfer, and embryo availability — United States, 2005

	Day 3						Day 5					
	All ART transfer procedures			ART transfer procedures for women known to have more embryos available than transferred			All ART transfer procedures			ART transfer procedures for women known to have more embryos available than transferred		
Patient age group (yrs)	No.	Transfers resulting in live births (%)	Multiple-birth deliveries (%)	No.	Transfers resulting in live births (%)	Multiple-birth deliveries (%)	No.	Transfers resulting in live births (%)	Multiple-birth deliveries (%)	No.	Transfers resulting in live births (%)	Multiple-birth deliveries (%)
<35												
1	1,324	22.2	0.3	221	34.8	0.0	812	39.4	2.8	446	48.2	2.8
2	11,291	43.5	32.0	5,807	49.2	36.0	7,814	53.6	41.5	4,881	57.5	43.7
3	7,463	41.2	39.1	2,511	48.3	44.2	1,178	39.9	40.4	377	43.5	48.8
4	1,653	38.7	39.7	390	46.7	44.5	179	37.4	37.3	50	44.0	54.5
≥5	495	33.5	41.0	73	45.2	51.5	56	42.9	33.3	5	*	*
35–37												
1	999	13.8	2.9	76	27.6	4.8	385	30.6	0.8	141	48.2	1.5
2	4,024	35.2	24.2	1,515	44.4	29.1	2,872	45.5	33.5	1,649	50.3	36.5
3	5,098	37.4	32.9	1,573	42.8	39.2	820	38.2	45.0	247	44.9	55.0
4	1,851	37.1	36.5	363	48.5	39.8	135	25.2	38.2	26	34.6	22.2
≥5	496	32.7	39.5	73	41.1	43.3	39	15.4	50.0	7	*	*
38–40												
1	1,061	7.8	3.6	20	20.0	0.0	308	17.9	3.6	37	48.6	5.6
2	2,098	19.3	14.3	289	34.3	23.2	1,242	38.2	27.2	579	45.9	31.2
3	3,859	26.3	24.2	897	32.0	30.0	790	34.3	28.8	226	40.7	31.5
4	2,781	29.2	31.5	514	39.3	37.6	223	30.0	28.4	43	46.5	35.0
≥5	1,138	28.2	33.3	134	34.3	39.1	69	21.7	33.3	7	*	*
41–42												
1	572	3.7	0.0	0	*	*	178	12.4	9.1	9	*	*
2	794	9.1	8.3	18	33.3	0.0	279	20.1	8.9	76	34.2	11.5
3	1,081	14.6	12.0	119	31.9	13.2	261	25.3	21.2	52	32.7	35.3
4	1,169	18.1	11.3	175	22.3	17.9	116	20.7	25.0	16	31.3	20.0
≥5	1,146	18.4	18.5	133	22.6	30.0	57	33.3	31.6	7	*	*
>42												
1	412	1.0	0.0	3	*	*	90	3.3	0.0	2	*	*
2	469	2.8	7.7	6	*	*	75	16.0	8.3	5	*	*
3	502	5.4	11.1	23	13.0	33.3	61	13.1	25.0	9	*	*
4	445	8.8	7.7	33	18.2	16.7	56	12.5	14.3	6	*	*
≥5	660	7.0	15.2	42	9.5	0.0	32	15.6	60.0	3	*	*

*Statistics are not provided in cases in which the denominator is <10.

TABLE 8. Number and percentage of infants born in multiple-birth deliveries, by patient's state/territory of residence* at time of assisted reproductive technology (ART) procedure — United States, 2005

Patient's state of residency	No. infants born		No. infants born in multiple-birth deliveries		Infant born in multiple-birth deliveries† (%)	Infants born in twin deliveries (%)	Infants born in triplet or higher-order deliveries (%)
	No.	No. with missing residency	No.	No. with missing residency			
Alabama	338	0	181	0	53.6	44.2	2.6
Alaska	63	0	32	0	50.8	39.0	12.7
Arizona	767	26	347	10	45.2	51.2	4.9
Arkansas	215	0	109	0	50.7	42.3	4.1
California	7,159	637	3,635	294	50.8	45.8	5.0
Colorado	999	46	525	30	52.6	48.5	1.5
Connecticut	1,025	23	480	8	46.8	44.2	5.3
Delaware	148	0	69	0	46.6	49.8	2.7
District of Columbia§	202	21	101	10	50.0	42.8	4.8
Federated States of Micronesia	¶	¶	¶	¶	¶	¶	¶
Florida	2,418	60	1,160	29	48.0	41.9	4.5
Georgia	1,286	574	663	282	51.6	43.6	8.0
Guam	¶	¶	¶	¶	¶	¶	¶
Hawaii	264	2	136	2	51.5	42.1	4.6
Idaho	241	0	131	0	54.4	44.5	6.3
Illinois	3,211	16	1,501	8	46.7	45.9	6.1
Indiana	669	2	347	0	51.9	0.0	0.0
Iowa	414	0	197	0	47.6	32.1	8.3
Kansas	271	0	145	0	53.5	44.6	2.0
Kentucky	403	2	208	2	51.6	45.6	8.7
Louisiana	301	0	153	0	50.8	46.3	3.2
Maine	95	0	47	0	49.5	46.4	3.4
Maryland	1,656	24	769	8	46.4	43.3	7.6
Massachusetts	2,964	964	1,293	440	43.6	27.7	6.4
Michigan	1,285	7	650	4	50.6	40.6	3.0
Minnesota	971	3	500	0	51.5	43.6	8.2
Mississippi	187	0	89	0	47.6	41.5	8.9
Missouri	740	217	318	100	43.0	0.0	0.0
Montana	79	0	44	0	55.7	46.5	4.2
Nebraska	255	0	121	0	47.5	53.3	2.6
Nevada	526	24	262	10	49.8	46.8	8.9
New Hampshire	292	0	139	0	47.6	46.9	1.0
New Jersey	3,459	169	1,692	89	48.9	44.5	3.1
New Mexico	169	0	95	0	56.2	48.5	5.0
New York	3,807	148	1,768	68	46.4	50.0	0.0
New York City	1,604	610	729	276	45.4	46.0	5.1
North Carolina	1,029	2	498	0	48.4	54.4	1.8
North Dakota	84	0	34	0	40.5	40.7	4.6
Ohio	1,365	11	688	4	50.4	43.5	7.1
Oklahoma	288	2	138	2	47.9	42.8	2.6
Oregon	533	8	298	8	55.9	38.5	6.8
Pennsylvania	1,808	134	896	54	49.6	41.6	5.9
Puerto Rico	148	0	77	0	52.0	44.6	7.0
Rhode Island	331	0	174	0	52.6	0.0	0.0
South Carolina	513	0	261	0	50.9	48.0	5.5
South Dakota	74	0	37	0	50.0	37.3	5.7
Tennessee	511	2	261	2	51.1	42.5	5.1
Texas	3,103	51	1,666	27	53.7	49.2	3.3
Utah	371	1	208	0	56.1	50.8	0.0
Vermont	47	0	16	0	34.0	43.5	4.2
Virgin Islands, U.S.	11	0	0	0	0.0	41.0	7.7
Virginia	1,572	19	713	10	45.4	48.3	5.4
Washington	811	9	387	2	47.7	43.3	5.1
West Virginia	92	0	48	0	52.2	43.2	4.8
Wisconsin	685	1	344	0	50.2	48.4	3.1
Wyoming	39	0	19	0	48.7	43.9	5.1
Non-U.S. resident	141	0	70	0	49.6	36.9	12.8
Total	**52,041**	**3,815**	**25,469**	**1,779**	**48.9**	**43.9**	**5.1**

* In cases of missing residency data, the patient's place of residency was assigned as that in which the ART procedure was performed.
† Statistics might not sum to total because of rounding.
§ Of all ART procedures, 0.7% were reported from military medical centers located in California, District of Columbia, Hawaii, and Texas. States and territories for which >1% of ART procedures among state residents were performed in a military medical center were Alaska, Delaware, District of Columbia, Guam, Hawaii, Kansas, Maryland, New Mexico, North Carolina, Oklahoma, South Carolina, Texas, Virginia, and Wyoming. In District of Columbia, Guam, and Hawaii, >5% of ART procedures among residents were performed in a military medical center.
¶ Data not provided to preserve confidentiality but included in total.

TABLE 9. Contribution of assisted reproductive technology (ART) to the total number of live-born infants in the United States, by plurality — United States, 2005

Plurality	ART infants*†		U.S.-born infants§		Contribution of ART to total no. U.S.-born infants (%)
	No.	% of total	No.	% of total	
Infants born in singleton deliveries	2,5143	(51.0)	3,998,533	(96.60	0.6
Infants born in multiple-birth deliveries	2,4165	(49.0)	139,816	(3.40	17.3
Twins	2,1598	(43.8)	133,122	(3.20	16.2
Triplets or higher order	2,567	(5.2)	6,694	(0.20	38.3
Total no. infants	**49,308**		**4,138,349**		**1.2**

* **Source:** Assisted Reproductive Technology Surveillance System.
† Includes infants conceived from ART procedures performed in 2004 and born in 2005 and infants conceived from ART procedures performed in 2005 and born in 2005.
§ **Source:** U.S. natality file, CDC, National Center for Health Statistics.

TABLE 10. Percentage of adverse perinatal outcomes* among assisted reproductive technology (ART) infants† born in 2005, by plurality — United States, 2005

Plurality	LBW (%)	VLBW (%)	Preterm (%)	Preterm LBW (%)	Term LBW (%)
ART singletons (n = 25,143)	9.4	1.8	14.9	7.1	2.3
ART twins (n = 21,598)	57.1	8.7	66.3	48.2	8.8
ART triplets or higher-order multiples (n = 2,567)	94.6	31.2	97.1	92.8	1.9

* LBW = low birthweight (<2,500 g); VLBW = very low birthweight (<1,500 g); preterm = gestational age <37 weeks; preterm LBW = gestational age <37 weeks and low birthweight (<2,500 g); and term LBW = gestational age ≥37 weeks and low birthweight (<2,500 g).
† Includes infants conceived from ART procedures performed in 2004 and born in 2005 and infants conceived from ART procedures performed in 2005 and born in 2005. Samples for calculations of percentages of outcomes were reduced from totals because of missing values for birthweight and gestational age.

TABLE 11. Adverse perinatal outcomes* among assisted reproductive technology (ART) singleton infants born in 2005, by procedure type and selected maternal factors — United States†

Procedure/Maternal factor	LBW (%)	VLBW (%)	Preterm (%)	Preterm LBW (%)	Term LBW (%)
Freshly fertilized embryos, patient eggs (n = 17,642)	**9.5§**	**1.7**	**13.4§**	**6.9**	**2.7§**
Maternal age group (yrs)					
<35	9.2	1.7	13.0	6.5	2.7
35–37	9.9	1.8	14.0	7.5	2.4
38–40	9.4	1.9	13.1	6.5	2.8
41–42	11.6	2.3	15.8	8.7	3.0
>42	7.5	0.7	11.8	4.1	3.4
No. previous births					
0	10.2¶	1.9	13.5	7.2	3.1¶
1	7.3	1.3	12.7	5.9	2.0
≥2	8.9	1.7	14.6	7.0	1.5
Freshly fertilized embryos, donor's eggs (n = 2,864)	**11.0**	**2.0**	**16.9**	**9.0**	**2.1**
Thawed embryos (n = 4,637)**	**7.9**	**1.7**	**19.5**	**6.8**	**1.1**

* LBW = low birthweight (<2,500 g); VLBW = very low birthweight (<1,500 g); preterm = gestational age <37 weeks; preterm LBW = gestational age <37 weeks and low birthweight (<2,500 g); and term LBW = gestational age ≥37 weeks and low birthweight (<2,500 g).
† Includes infants conceived from ART procedures performed in 2004 and born in 2005 and infants conceived from ART procedures performed in 2005 and born in 2005. Analysis excludes 542 singletons (416 for missing birth weight, 113 for missing gestational age, and 13 for missing both).
§ p<0.01; chi-square to test for variations in adverse perinatal outcomes across procedure types.
¶ p<0.01; chi-square to test for variations in adverse perinatal outcomes across maternal factor categories.
** Includes cycles in which thawed embryos were used from patient eggs and donor eggs.

Malaria Surveillance — United States, 2006

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Abstract

Problem/Condition: Malaria in humans is caused by intraerythrocytic protozoa of the genus *Plasmodium* (i.e., *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*). These parasites are transmitted by the bite of an infective female *Anopheles* species mosquito. The majority of malaria infections in the United States occur among persons who have traveled to areas with ongoing malaria transmission. In the United States, cases can occur through exposure to infected blood products, congenital transmission, or local mosquitoborne transmission. Malaria surveillance is conducted to identify episodes of local transmission and to guide prevention recommendations for travelers.

Period Covered: This report summarizes cases in persons with onset of illness in 2006 and summarizes trends during previous years.

Description of System: Malaria cases confirmed by blood film or polymerase chain reaction (PCR) are mandated to be reported to local and state health departments by health-care providers or laboratory staff members. Case investigations are conducted by local and state health departments, and reports are transmitted to CDC through the National Malaria Surveillance System (NMSS), National Notifiable Diseases Surveillance System (NNDSS), and direct CDC consultations. Data from these reporting systems serve as the basis for this report.

Results: CDC received reports of 1,564 cases of malaria among persons in the United States with onset of symptoms in 2006, six of which were fatal. This is an increase of 2.4% from the 1,528 cases reported for 2005. *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale* were identified in 39.2%, 17.6%, 2.9%, and 3.0% of cases, respectively. Ten patients (0.6%) were infected by two or more species. The infecting species was unreported or undetermined in 36.6% of cases. Compared with 2005, the largest increases in cases were from Asia (16.0%). Based on estimated volume of travel, the highest estimated relative case rates of malaria among travelers occurred among those returning from West Africa. Of 602 U.S. civilians who acquired malaria abroad and for whom chemoprophylaxis information was known, 405 (67.3%) reported that they had not followed a chemoprophylactic drug regimen recommended by CDC for the area to which they had traveled. Seventeen cases were reported in pregnant women, among whom only one reported taking chemoprophylaxis precautions. Six deaths were reported; five of the persons were infected with *P. falciparum* and one with *P. malariae*.

Interpretation: Despite the 2.4% increase in cases from 2005 to 2006, the numbers of malaria cases remained relatively stable during 2001–2006. No change was detected in the proportion of cases by species responsible for infection. U.S. civilians traveling to West Africa had the highest estimated relative case rates. In the majority of reported cases, U.S. civilians who acquired infection abroad had not adhered to a chemoprophylaxis regimen that was appropriate for the country in which they acquired malaria.

Public Health Actions: Additional investigations were conducted of the six fatal cases that occurred in the United States. Persons traveling to a malarious area should take one of the recommended chemoprophylaxis regimens appropriate for the region of travel and use personal protection measures to prevent mosquito bites. Any person who has been to a malarious area and who subsequently has a fever or influenza-like symptoms should seek medical care immediately and report their travel history to the clinician; investigation should always include blood-film tests for malaria, with results made available immediately. Malaria infections can be fatal if not diagnosed and treated promptly. CDC recommendations concerning malaria prevention are available at http://wwwn.

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cdc.gov/travel/contentdiseases.aspx#malaria or by calling the CDC Malaria Branch on weekdays (telephone: 770-488-7788; Monday–Friday, 8:00 A.M.–4:30 P.M. EST); during evenings, weekends, and holidays, call the CDC Director's Emergency Operations Center (telephone: 770-488-7100), and ask to page the person on call for the Malaria Branch. Recommendations concerning malaria treatment are available at http://www.cdc.gov/malaria/diagnosis_treatment/treatment.htm or by calling the CDC Malaria Hotline.

Introduction

Malaria in humans is caused by infection with one or more species of *Plasmodium* (i.e., *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*) that can infect humans. The infection is transmitted by the bite of an infective female *Anopheles* species mosquito. Malaria remains a devastating global problem, with an estimated 350–500 million cases and 1 million deaths occurring annually, 80% of them in sub-Saharan Africa (*1*). Forty-nine percent of the world's population lives in areas where malaria is transmitted (e.g., 109 countries in parts of Africa, Asia, the Middle East, Eastern Europe, Central America and South America, the Caribbean, and Oceania) (*1*). Before the 1950s, malaria was endemic throughout the southeastern United States; an estimated 600,000 cases occurred in 1914 (*2*). During the late 1940s, a combination of improved housing and socioeconomic conditions, water management, vector-control efforts, and case management interrupted malaria transmission in the United States. Since then, malaria case surveillance has been maintained to detect locally acquired cases that could indicate the reintroduction of transmission and to monitor patterns of resistance to antimalarial drugs. Anopheline mosquitoes remain seasonally present in all states and territories except Hawaii.

The majority of reported cases of malaria diagnosed each year in the United States are imported from regions where malaria transmission is known to occur, although congenital infections and infections resulting from exposure to blood or blood products are also reported in the United States. In addition, occasionally a limited number of cases are reported that might have been acquired through local mosquitoborne transmission (*3*).

State and local health departments and CDC investigate malaria cases acquired in the United States, and CDC analyzes data from imported cases to detect trends in acquisition. This information is used to guide malaria prevention recommendations for international travelers.

The signs and symptoms of malaria illness vary, but the majority of patients have fever. Other common symptoms include headache, back pain, chills, increased sweating, myalgia, nausea, vomiting, diarrhea, and cough. The diagnosis of malaria should always be considered for persons with these symptoms who have traveled to an area with known malaria transmission. Malaria also should be considered in the differential diagnosis of persons who have fever of unknown origin, regardless of their travel history. Untreated *P. falciparum* infections can rapidly progress to coma, renal failure, pulmonary edema, and death. This report summarizes malaria cases reported to CDC among persons with onset of symptoms in 2006.

Methods

Data Sources

Malaria case data are reported to the National Malaria Surveillance System (NMSS) and the National Notifiable Diseases Surveillance System (NNDSS) (*4*). Although both systems rely on passive reporting, the numbers of reported cases might differ because of differences in collection and transmission of data. A substantial difference between the data collected in these two systems is that NMSS receives more detailed clinical and epidemiologic data regarding each case (e.g., information concerning the area to which the infected person has traveled). Malaria cases can be reported to CDC through NMSS, NNDSS, or direct consultation with CDC; therefore, cases identified through these various paths are compared and compiled, duplicates are eliminated, and cases are analyzed. This report presents data on the aggregate of cases reported to CDC through all reporting systems.

Malaria cases confirmed by blood film or polymerase chain reaction (PCR) among civilians and military personnel are identified by health-care providers or laboratories. Each confirmed malaria case is reported to local or state health departments and to CDC on a uniform case-report form that contains clinical, laboratory, and epidemiologic information.* CDC reviews all report forms received and requests additional information from the provider or the state, if necessary (e.g., when no recent travel to a malarious country is reported). Other cases are reported by telephone to CDC directly by health-care providers, usually when they are seeking assistance with diagnosis or treatment. Information regarding cases reported directly to CDC is shared with the relevant state health department. All cases

* Malaria case-report surveillance form available at http://www.cdc.gov/malaria/clinicians.htm#case.

that have been reported as acquired in the United States are investigated further, including all induced and congenital cases and possible introduced or cryptic cases. Information derived from uniform case-report forms is entered into a database and analyzed annually.

A case rate for each country was estimated using estimates of travel volume for U.S. travelers to each country where cases of malaria were acquired and the number of cases among U.S. travelers attributable to each country. Data used to estimate country-specific relative case rates were extrapolated from World Tourism Organization estimates of annual numbers of U.S. travelers to specified countries (*5*). Estimated relative case rates were determined by dividing the individual country-specific case rate by the median individual country-specific case rate.

Definitions

The following definitions are used in this report:

- **U.S. residents:** Persons living in the United States, including civilians and U.S. military personnel, regardless of legal citizenship.
- **Foreign residents:** Persons who do not meet the definition of U.S. residents.
- **U.S. civilians:** U.S. residents, excluding U.S. military personnel.
- **Laboratory criteria for diagnosis:** Demonstration of malaria parasites on blood film or by PCR.
- **Confirmed case:** Symptomatic or asymptomatic infection that occurs in a person in the United States or one of its territories who has laboratory-confirmed (by microscopy or PCR) malaria parasitemia, regardless of whether the person has had previous episodes of malaria while in other countries. A subsequent episode of malaria is counted as an additional case if the indicated *Plasmodium* species differs from the initially identified species. A subsequent episode of malaria occurring in a person while in the United States could indicate a relapsing infection or treatment failure resulting from drug resistance if the indicated *Plasmodium* species is the same species identified previously.

This report also uses terminology from recommendations of the World Health Organization (*6*). Definitions of the following terms are included for reference:

- **Autochthonous malaria:**
  - — **Indigenous.** Mosquitoborne transmission of malaria in a geographic area where malaria occurs regularly.
  - — **Introduced.** Mosquitoborne transmission of malaria from a person with an imported case in an area where malaria does not occur regularly.
- **Imported malaria:** Malaria acquired outside a specific area. In this report, imported cases are those acquired outside the United States and its territories.
- **Induced malaria:** Malaria acquired through artificial means (e.g., blood transfusion or by using shared common syringes).
- **Relapsing malaria:** Recurrence of disease after it has been apparently cured. In malaria, true relapses are caused by reactivation of dormant liver-stage parasites (hypnozoites) found in *P. vivax* and *P. ovale*.
- **Cryptic malaria:** A case of malaria for which epidemiologic investigations fail to identify a plausible mode of acquisition. (Cryptic malaria cases are primarily identified in countries where malaria is not endemic.)

Laboratory Diagnosis

Early and prompt diagnosis of malaria requires that physicians obtain a travel history from every febrile patient. Malaria should be included in the differential diagnosis of every febrile patient who has traveled to a malarious area. If malaria is suspected, a Giemsa-stained film of the patient's peripheral blood should be examined for parasites as soon as possible. Thick and thin blood films must be prepared correctly because diagnostic accuracy depends on blood-film quality and examination of the film by experienced laboratory personnel (*7*).† Certain reference laboratories and health departments have the capacity to perform PCR diagnosis of malaria, although PCR diagnosis generally is reserved for cases for which blood-film diagnosis of malaria or species determination is inadequate.

Results

General Surveillance

For 2006, CDC received 1,564 reports of cases of malaria occurring among persons in the United States and its territories, representing a 2.4% increase from the 1,528 cases reported with a date of onset in 2005 (*7*). A total of 713 cases occurred among U.S. residents, and 217 cases occurred among foreign residents; resident status was not known for 634 cases. The number of cases increased during 1980–2000 among U.S. residents; however, during 2001–2006, the number of cases plateaued (Table 1).

† To obtain confirmatory diagnosis of blood films from questionable cases and to obtain appropriate treatment recommendations, contact either the state or local health department or CDC's Malaria Branch (770-488-7788).

Plasmodium Species

Of the 1,564 cases reported in 2006, the infecting *Plasmodium* species was identified and reported in only 991 (63.4%) cases. *P. falciparum* and *P. vivax* make up the majority of infections and were identified in 61.8% and 27.7% of infected persons of known species infection, respectively. The number of reported cases of *P. falciparum* and *P. vivax* remained relatively stable during 2004–2006 (Table 2). Among 909 cases for which both the region of acquisition and the infecting species were known, *P. falciparum* accounted for 65.8% of infections acquired in Africa, 22.5% in the Americas, 9.3% in Asia, and 4.5% in Oceania (Table 3). Infections attributed to *P. vivax* accounted for 4.3% acquired in Africa, 58.3% in the Americas, 61.5% in Asia, and 72.7% in Oceania.

Region of Acquisition and Diagnosis

All cases were reported as imported cases. Of 1,140 imported cases for which the region of acquisition was known, 793 (69.6%) were acquired in Africa, 205 (18.0%) in Asia, 120 (10.5%) in the Americas, and 22 (1.9%) in Oceania (Table 3). West Africa accounted for 563 (71.0%) cases acquired in Africa, and India accounted for 121 (59.0%) cases acquired in Asia. In the Americas, a combined total of 82 (68.3%) cases were acquired in Central America and the Caribbean (The Bahamas, Belize, Costa Rica, Dominican Republic, El Salvador, Guatemala, Haiti, Honduras, Jamaica, and Nicaragua), followed by 27 (22.5%) cases in South America (Bolivia, Brazil, Ecuador, Guyana, Peru, and Suriname) and 11 (9.2%) cases in Mexico. Information regarding region of acquisition was missing for 424 (27.7%) imported cases. Among U.S. civilians, a small but steady increase (16%) in cases acquired in Asia occurred from 2005 to 2006.

In the United States, six state health departments accounted for 47.8% of the reported cases: California (n = 185), New York City (n = 174), Texas (n = 129), Georgia (n = 90), New Jersey (n = 87), and Illinois (n = 82) (Figure 1). Compared with 2005, the states with the most significant change in number of reported malaria cases in 2006 were Georgia and Alaska. The number of cases reported in Georgia increased from 54 cases in 2005 to 90 cases in 2006, and Alaska reported an increase from eight cases in 2005 to 23 cases in 2006; all cases occurred among U.S. military personnel, all of whom had traveled to Afghanistan.

Imported Malaria by Resident Status

Of 930 imported malaria cases of known resident status, 713 (76.7%) occurred among U.S. residents, and 217 (23.3%) occurred among residents of other countries. Of the 713 imported cases, 511 (71.7%) were acquired in Africa, 116 (16.3%) were acquired in Asia, and 42 (5.9%) were acquired in Central America and the Caribbean (Table 4). Of the 217 imported cases among foreign residents, 131 (60.4%) were acquired in Africa. Of patients with foreign cases for whom purpose of travel was known, 76 (58%) identified as being a recent immigrant or refugee, and 22 (17%) reported visiting friends and relatives in the United States.

Relative Case Rates Among U.S. Residents

In 2006, the countries with the lowest estimated case rates of malaria among U.S. travelers (among countries that reported cases) were The Bahamas and Jamaica, both of which had been considered nonendemic countries but experienced malaria outbreaks in 2006 (Figure 2). Examples of other countries with low estimated relative case rates include Mexico, Vietnam, Costa Rica, and Thailand. For many of these countries, malaria risk areas are concentrated in small parts of the country. Examples of countries with estimated relative case rates in the middle range include India, Honduras, Haiti, and Kenya, which have malaria transmission occurring more homogenously throughout the country. Estimated relative case rates were highest in countries in West Africa and Oceania, including Nigeria, Ghana, Papua New Guinea, and Vanuatu. These high estimated case rates not only reflect widespread transmission areas but also likely reflect higher transmission intensity.

Interval Between Arrival and Illness

Both the interval between date of arrival in the United States and onset of illness and the infecting *Plasmodium* species were known for only 622 (39.8%) of the imported malaria cases (Table 5). Symptoms began before arrival in the United States for 40 (6.4%) persons and after arrival for 582 (93.6%) persons. Clinical malaria occurred <30 days after arrival in 384 (89.5%) of the 429 persons with *P. falciparum* cases and in 69 (54.3%) of the 127 *P. vivax* cases (Table 5). Six (1.0%) of 622 persons became ill with an infection with *P. vivax* or *P ovale* ≥1 year after returning to the United States.

Imported Malaria Among U.S. Military Personnel

In 2006, 50 cases of imported malaria were reported among U.S. military personnel. Information on infecting species was known for 38 cases: 33 cases of *P. vivax*, four cases of *P. falciparum*, and one case of *P. malariae*. Among the 38 cases with known infecting species, 33 patients had reported taking chemoprophylaxis, of whom 19 (57.5%) had taken the correct CDC-recommended antimalarial drug for the specific region of travel; only one patient reported adherence to the prescribed drug regimen. These cases were reported by state health departments and do not include all cases reported through malaria surveillance activities conducted by the U.S. Department of Defense.

Chemoprophylaxis Use Among U.S. Civilians

Information concerning chemoprophylaxis use and travel area was known for 602 (90.8%) of the 663 U.S. civilians who had imported malaria. Of these 602 patients, 405 (67.3%) had not taken any chemoprophylaxis. Of the 197 patients who did report taking malaria chemoprophylaxis, 58 (29.4%) had not taken a CDC-recommended drug for the area visited, whereas 131 (20.9%) had taken a CDC-recommended drug (*7*). Data for the specific drug taken were missing for the remaining eight (4.1%) travelers. A total of 58 (44.3%) patients receiving CDC-recommended chemoprophylaxis reported taking mefloquine; 36 (27.5%) had taken doxycycline; 25 (19.1%) had taken atovaquone-proguanil; and eight (6.1%) who had traveled only in areas where chloroquine-resistant malaria has not been documented had taken chloroquine. Of the 131 persons taking a CDC-recommended malaria chemoprophylaxis for the travel region, only 52 (40.0%) reported adherence to the prescribed drug regimen.

Malaria Infection After Recommended Prophylaxis Use

A total of 220 patients (including 136 U.S. civilians, 41 persons in the U.S. military, eight foreign residents, and 35 persons for whom information regarding status was missing) contracted malaria after taking a recommended antimalarial drug for chemoprophylaxis. Of these, 76 (34.5%) reported complete adherence with the drug regimen, and 104 (47.3%) reported nonadherence; adherence was unknown for the remaining 40 (18.2%). Information regarding infecting species was available for 178 (80.9%) patients who had taken a recommended antimalarial drug; the infecting species was undetermined for the remaining 42 patients.

Cases Caused by *P. vivax* or *P. ovale*

Among the 220 patients who received a diagnosis of malaria after recommended chemoprophylaxis use, 70 (31.8%) had cases that were caused by *P. vivax*, and 10 (4.5%) had cases caused by *P. ovale*. Among the 80 total cases of *P. vivax* or *P. ovale*, 41 (51.2%) occurred >45 days after arrival in the United States. These cases were consistent with relapsing infections and do not indicate primary prophylaxis failures. Information on 19 cases was insufficient (i.e., missing data regarding symptom onset or return date) to assess whether the infection was a relapse infection. A total of 20 cases occurred ≤45 days after the patient returned to the United States; 10 each caused by *P. vivax* and *P. ovale.* Nine of the 20 patients did not adhere to their malaria chemoprophylaxis regimen; information regarding drug regimen adherence was missing for four cases. Seven patients reported adherence with an antimalarial chemoprophylaxis regimen. Of these seven, three patients had traveled to Africa, two of whom reported taking atovaquone-proguanil as malaria chemoprophylaxis and one who reported taking doxycycline. Two patients had traveled to Asia; one had traveled to India and had taken primaquine, and one had traveled to Iraq and taken mefloquine for chemoprophylaxis. The remaining two patients had traveled to Central America and South America; one patient had traveled to Peru and took doxycycline, and one had traveled to Honduras and taken mefloquine for chemoprophylaxis. Possible explanations for these cases include inappropriate dosing, unreported nonadherence to the regimen, malabsorption of the drug, or emerging parasite resistance.

Cases Caused by *P. falciparum* and *P. malariae*

Ninety-four cases of malaria were reported among persons who had taken a recommended antimalarial drug for chemoprophylaxis, including 78 cases of *P. falciparum* and 16 of *P. malariae.* Of the 78 *P. falciparum* cases among those who reported taking a recommended antimalarial drug, all except one case was acquired in Africa. Forty-three (55.1%) patients reported nonadherence to the antimalarial drug regimen; adherence information was not available for 14 cases. In 21 (26.9%) cases, patients reported adherence with malaria chemoprophylaxis, all of whom had traveled to Africa. Fourteen patients reported taking mefloquine, three doxycycline, one primaquine, and three took atovaquone-proguanil. Of the 16 *P. malariae* cases, 11 were

acquired in Africa, four in Asia, and one in the Caribbean. Five patients reported nonadherence to the antimalarial drug regimen, and no adherence information was available for five cases. For the remaining six cases, patients reported adhering to the drug regimen; three took mefloquine, two took doxycycline, and one took atovaquone-proguanil.

Cases of Mixed-Species Infection

Among the 220 patients who had taken a recommended malaria chemoprophylaxis, four had a mixed *Plasmodium* species infection. Three patients had traveled to Africa, two of whom had a mixed infection of *P. vivax* and *P. falciparum,* and one who had *P. vivax* and *P. ovale* infections. All three patients had taken atovaquone-proguanil for malaria chemoprophylaxis; however, one had not completed the drug regimen, and no adherence information was available for the remaining two. The patient with the fourth mixed-infection case (*P. ovale* and *P. falciparum*) had traveled to Papua New Guinea and also did not complete the malaria chemoprophylaxis drug regimen.

Purpose of Travel

Purpose of travel to areas in which malaria is endemic was reported for 617 (86.5%) of the 713 U.S. civilians with imported malaria. Though travelers could report multiple reasons for travel, the largest proportion (50.9%) represented persons who had visited friends or relatives in malarious areas; the second and third highest proportions, 9.9% and 7.4%, represented persons who had traveled as missionaries or as tourists, respectively (Table 6).

Malaria in Children

Of the 1,445 cases for whom age was known, 280 (19.4%) cases occurred in persons aged <18 years. Among these, 113 (40.4%) cases occurred among U.S. civilian children, 78 (27.9%) occurred among children of foreign citizenship, and for 89 (31.8%) cases, resident status was unknown.

Ninety-four (83.1%) of the cases among U.S. civilian children for whom country of exposure was known were attributable to Africa. Of the 113 cases among U.S. civilian children, six (5.3%) of the children were aged <24 months, 24 (21.2%) were aged 24–59 months, 40 (35.4%) were aged 5–12 years, and 24 (21.2%) were aged 13–17 years. Among 75 patients for which reason for travel was known, 74 were reported as visiting friends and relatives; the remaining patient was reported as a being a tourist. Among the 88 cases for whom chemoprophylaxis information was known, 30 (34%) patients reported taking chemoprophylaxis, of whom 18 (60%) had taken a correct regimen; only three (16.7%) reported complete adherence.

Malaria During Pregnancy

A total of 17 cases of malaria were reported among pregnant women in 2006, representing 3.4% of cases among women. Eight (47.0%) of the 17 cases occurred among U.S. civilians, five of whom had traveled to Africa and three of whom had traveled to countries in Central America and South America. The five women who traveled to Africa were reported as visiting friends and relatives; the three women who traveled to Central America and South America were reported as being tourists. Of the eight cases of malaria reported among U.S. civilian pregnant women, only one (12.5%) woman reported taking malaria chemoprophylaxis; however, she reported taking an inappropriate medication. No information was available on the birth outcomes of the pregnant women.

Deaths Attributed to Malaria

Six deaths attributable to malaria were reported in 2006 and are described in the following case reports:

Case 1

On March 20, a man aged 47 years from Thailand arrived in New York City and developed fever and lethargy. He had a medical history of alcoholic cirrhosis, ascites, spontaneous bacterial peritonitis, and diabetes. On March 21, the patient was admitted to the hospital and had symptoms of a chronically ill person, with fever, jaundice, and a distended abdomen. The initial diagnosis was hepatic encephalopathy and spontaneous bacterial peritonitis; peripheral blood smears were ordered to determine whether a concurrent malaria infection was present. The patient was intubated, received mechanical ventilation, and was treated with ceftriaxone, ampicillin/sulbactam, clindamycin, and dexamethasone. The blood smear was positive for *P. malariae* by microscopy, which was subsequently confirmed by PCR. Doxycycline and quinidine gluconate were added to the regimen within 24 hours of admission. The patient experienced renal failure and died on March 25, 2006.

Case 2

On March 30, a woman aged 65 years returned to Arizona from a 17-day tour of Kenya and Tanzania. Malaria prophylaxis had been prescribed, but the entire regimen was not completed. On June 7, the woman experienced fever and chills. On June 9, she sought treatment at an

emergency room; she was evaluated, received intravenous fluids, and was sent home. On June 12, the patient returned to the hospital with the same symptoms as well as nausea and syncope. A peripheral blood film revealed *P. falciparum* infection; the patient was administered oral quinine and doxycycline. On June 13, she experienced a decreased level of consciousness, necessitating intubation and mechanical ventilation. She died the same evening.

Case 3

On June 29, a girl aged 2 years who recently had emigrated from Nigeria was hospitalized in Boston, Massachusetts, for fever, vomiting, diarrhea, and scleral icterus. Peripheral blood films obtained on admission were positive for *P. falciparum,* with 1.4% parasitemia; she was administered oral atovaquone-proguanil. On June 30, her parasitemia increased to 26.7%, and she was transferred to the pediatric intensive care unit for an exchange transfusion and continuous quinidine infusion plus intravenous clindamycin. By July 2, the parasitemia had resolved, but the patient experienced acute respiratory distress syndrome. The patient was intubated and mechanical ventilation was initiated; she died on July 3, 2006.

Case 4

On July 28, a man aged 59 years returned from a month-long trip to Ghana. The patient also traveled regularly to India twice per year for mission work; his most recent trip had been in January 2006. He did not take malaria prophylaxis routinely while in India and did not take malaria prophylaxis while traveling to Africa. The evening he returned to the United States, he experienced a high fever and went to an urgent care center, where he received a diagnosis of community-acquired pneumonia and was treated with azithromycin. The patient's symptoms persisted and progressed to include vomiting and melena. He sought medical attention again on August 1; a peripheral blood film revealed *P. falciparum* with 10% parasitemia. He was administered oral mefloquine and transferred to a hospital intensive care unit (ICU), where he was treated with quinine and doxycycline. Within 24 hours, he experienced respiratory distress and was intubated. Quinidine gluconate was recommended, and exchange transfusion was initiated; however the patient died before quinidine gluconate could be administered. The patient died on August 3, 2006.

Case 5

On October 17, a woman aged 75 years who was a resident of India arrived in Arizona to attend a family wedding. On October 19, she was taken to the hospital because of fever, disorientation, and decreased level of consciousness. Her medical history included a neurogenic bladder, necessitating self-catheterization, and cerebral malaria. The initial diagnosis was pyelonephritis, and she was treated with intravenous ceftriaxone in the ICU. On October 20, a peripheral blood film revealed *P. falciparum;* quinine and doxycycline were added to the treatment regimen. The patient experienced renal failure and acute respiratory distress syndrome and was intubated on the October 23. She experienced a nosocomial blood stream infection, and antibiotics were continued; however, her condition continued to deteriorate. The patient was discharged to hospice care and died on November 11, 2006.

Case 6

Case 6 was reported as case 2 in the CDC malaria surveillance report published in 2007 (*7*). However, the actual date of onset was April 19, 2006, not 2005 as previously reported.

On April 19, a man aged 55 years was taken to an ED with a 4-day history of fever, emesis, and epigastric pain. He was a resident of the United States but had traveled to Uganda, his country of origin, for 3 months and had returned on April 12. He had not taken malaria prophylaxis. On admission, he had sinus tachycardia and a temperature of 100.3°F (37.9°C). Routine laboratory analysis was significant only for thrombocytopenia (platelet count: 19,000/μL). A differential diagnoses list was generated, including malaria, dengue fever, and Chikungunya fever; no additional evaluations were performed. The patient's symptoms improved with antiemetics, normal saline, and pain control. He was discharged with a tentative diagnosis of dengue fever. Four days later, on April 23, he died abruptly. Samples sent to CDC were positive for *P. falciparum* by PCR but negative for other suspected pathogens.

Discussion

A total of 1,564 cases of malaria were reported to CDC for 2006, representing an increase from the total number of cases reported in 2005. The number of cases with no information regarding residential status or clinical information increased from 2005 to 2006, from 325 unidentified cases to 634 unidentified cases (*7*). Excluding the cases with no information on residence status, the percentage of U.S. resident cases was relatively stable from 2000 to 2006.

Although during 2002–2006, the number of cases acquired from specific regions overall was stable, the proportion of cases from Asia increased slightly but steadily.

Flux in the number of cases acquired in a specific region can be affected by many factors, including the amount of transmission occurring in the region, adherence to preventive measures (e.g., mosquito avoidance and chemoprophylaxis) by travelers, the purpose of travel that predominates in that country (e.g., business travel or adventure travel), and the volume of travel to those countries.

Of the 1,564 imported cases, 634 (40.5%) cases did not have information available regarding residential status, and 424 (27.1%) did not have information regarding travel history. An increase in the number of cases that do not have residential and clinical information available decreases the accuracy with which the data reflect trends in malaria surveillance in the United States. Vigilance needs to be exercised by local and state health departments, health-care providers, and other health personnel to provide accompanying information regarding malaria cases when submitting cases through the various reporting systems to CDC.

In the Caribbean region, the endemic transmission of malaria ended in the mid-1960s, except in the island of Hispaniola, which includes the countries of Dominican Republic and Haiti (*8*). In 2006, three cases of malaria in the United States were reported from the Caribbean region; two in U.S. travelers and one in a foreign visitor. Two of the three cases were acquired from Jamaica and one from The Bahamas (Great Exuma Island); all were caused by *P. falciparum*. Although these countries were not considered risk areas for malaria, the islands remained at risk for reintroduction because of the tropical climate, presence of viable vectors, and close proximity to countries where malaria is still endemic. As a result, CDC issued recommendations on June 16, 2006, and December 4, 2006, for chloroquine chemoprophylaxis for persons traveling to Great Exuma, The Bahamas, and Kingston, Jamaica, respectively. Through several interventions, including active case finding and treatment and mosquito-control strategies, the outbreak in Great Exuma seemed to be controlled. CDC rescinded chemoprophylaxis recommendations for travelers to Great Exuma on September 19, 2006 (*9*). However, additional cases have occurred in travelers, and chemoprophylaxis recommendations have been reinstated. In Jamaica, similar strategies to contain the outbreak have been used; however, rare cases continue to be identified in Kingston.[§] Fortunately, these occasional cases do not present a substantial ongoing risk to travelers, and routine chemoprophylaxis is no longer recommended. Both of these outbreaks demonstrate the importance of the constant vigilance of health-care providers and rapid response by public health officials for effective containment strategies to avoid widespread reintroduction of malaria in nonendemic areas.

U.S. military personnel usually are on long-term prophylaxis for malaria to adequately protect them for the duration of their deployment in malaria-endemic regions. In regions where *P. vivax* or *P. ovale* infections predominate, primaquine is recommended in addition to the chemoprophylactic regimen to prevent relapsing malaria infection (*10*). The U.S. Army recommends that U.S. soldiers being deployed in regions where *P. vivax* infections predominate should take mefloquine or doxycycline as the primary prophylactic drug, followed by primaquine for 2 weeks before their return to the United States (*11,12*). In 2006, 19 of 25 soldiers who had long-term (≥1 year) deployments in Afghanistan had not taken primaquine terminal prophylaxis after their course of doxycycline as prescribed by the U.S. Army. Of the remaining six soldiers who had taken both doxycycline and primaquine chemoprophylaxis, only one soldier reported adherence to the entire regimen.

One purpose of malaria surveillance is to identify prophylaxis failures that might indicate emergence of drug resistance. However, approximately 82% of imported malaria cases among U.S. residents for whom information regarding prophylaxis use was available occurred among persons who were either not taking prophylaxis or were taking a non-CDC recommended prophylaxis regimen. Based on available information, the majority of patients who apparently received an appropriate medication and had onset of symptoms within 45 days, reported nonadherence with their chemoprophylactic regimen or provided insufficient information to make a determination regarding adherence. Because CDC does not actively seek serum drug levels from patients who report adherence with a recommended regimen, differentiating among inaccurate reporting of adherence, malabsorption of the antimalarial drug, and emerging drug resistance is not possible. No conclusive evidence indicates a single national or regional source of infection in this group of patients or the failure of a particular chemoprophylactic regimen. Health-care providers are encouraged to contact CDC quickly when chemoprophylaxis failure is suspected to enable CDC to measure serum drug levels of the antimalarial drugs in question and parasite from the patient to evaluate for possible drug resistance.

Of the six fatal cases that occurred in the United States in 2006, four of the patients reported taking no chemoprophylaxis while traveling to areas where malaria is endemic; information on chemoprophylaxis use for the remaining two cases was not available. One patient sub-

[§] Additional information on the malaria outbreak in Jamaica is available from the World Health Organization at http://www.who.int/csr/don/2007_02_09/en/index.html.

stantially delayed seeking care, five had substantial delays in establishing a diagnosis, and three patients experienced a delay in receiving appropriate treatment. These findings underscore the importance of patients adhering to correct chemoprophylaxis and promptly seeking medical care if symptoms develop, as well as the importance of physicians considering malaria in the differential diagnosis of fever in a person who has returned from travel. A previous review of deaths attributed to malaria in the United States indicated that failure to take or adhere to recommended antimalarial chemoprophylaxis, promptly seek medical care for posttravel illness, and promptly diagnose and treat suspected malaria all contributed to fatal outcomes (*13*).

As in previous years, people who traveled to visit friends and relatives experienced the majority of malaria cases in 2006. Foreign-born U.S. civilians need to be aware that acquired immunity wanes quickly when malaria exposure is interrupted and that they need to take prophylaxis when returning to malarious areas. Additionally, children of foreign-born U.S. civilians who are born in the United States are not immune to malaria and are highly vulnerable to infection (*14*). In this summary, approximately three fourths of the children with malaria whose reason for travel was to visit friends and relatives abroad had not been taking any chemoprophylaxis or had been taking an incorrect medication for chemoprophylaxis.

Seventeen cases were reported in pregnant women, a 21% increase from 2005. Among U.S. civilians who were pregnant, only one of eight women (12.5%) reported taking chemoprophylaxis. This proportion is much lower than the percentage of total U.S. civilians with malaria who took chemoprophylaxis. Malaria during pregnancy among women who are not immune poses a high risk for both maternal and perinatal morbidity and mortality (*15*). Pregnant travelers should be counseled to avoid travel to malarious areas. If deferral of travel is impossible, these women should be informed that the risks from malaria greatly outweigh those associated with prophylaxis and that safe chemoprophylaxis regimens are available and should be emphasized. Information for pregnant travelers is available at http://wwwn.cdc.gov/travel/contentmalariapregnantpublic.aspx.

Signs and symptoms of malaria are often nonspecific, but fever usually is present. Other symptoms include headache, chills, increased sweating, back pain, myalgia, diarrhea, nausea, vomiting, and cough. For prompt diagnosis, malaria must be included in the differential diagnosis of illness in a febrile patient with a history of travel to a malarious area. Clinicians should ask all febrile patients for a travel history, including international visitors, immigrants, refugees, migrant laborers, and other international travelers.

Prompt treatment of suspected malaria is essential because persons with *P. falciparum* infection are at risk for experiencing life-threatening complications soon after onset of illness. Ideally, therapy for malaria should be initiated immediately after the diagnosis has been made. Treatment should be determined on the basis of the infecting *Plasmodium* species, the probable geographic origin of the parasite, the parasite density, and the patient's clinical status (*15*). If malaria is suspected but cannot be confirmed or malaria is confirmed but species determination is not possible, antimalarial treatment that is effective against *P. falciparum* should be initiated. Resistance of *P. falciparum* to chloroquine occurs worldwide, with the exception of a limited number of geographic regions (e.g., Central America). Therefore, therapy for presumed *P. falciparum* malaria should entail the use of a drug effective against such resistant strains (*16*).

The findings in this report are subject to at least two limitations. First, although malaria is a notifiable disease in the United States, malaria case counts are obtained through passive surveillance systems and from individual reporting from health-care professionals treating persons with malaria. Therefore, only cases that are diagnosed by health-care or laboratory workers and reported to state and local health departments and to CDC are included, possibly resulting in an underestimate of disease incidence. Second, the completeness of reporting to the surveillance system might vary by reporting group and by year, which limits the amount of information that can be learned from each case.

Health-care providers should be familiar with prevention, recognition, and treatment of malaria and are encouraged to consult appropriate sources for malaria prevention and treatment recommendations (Table 7). Physicians seeking assistance with the diagnosis or treatment of patients with suspected or confirmed malaria should call CDC's Malaria Branch (telephone: 770-488-7788; Monday–Friday, 8:00 AM–4:30 PM EST); call CDC's Emergency Operations Center (telephone: 770-488-7100) during evenings, weekends, and holidays (ask to page person on call for Malaria Branch); or visit CDC's website at http://www.cdc.gov/malaria/diagnosis_treatment/treatment.htm. These resources are intended for use by health-care providers only.

Detailed recommendations for the public for preventing malaria are available online at http://wwwn.cdc.gov/travel/contentdiseases.aspx#malaria. In addition, biannually, CDC publishes recommendations in *Health Information for*

International Travel (commonly referred to as *The Yellow Book*) (*17*), which is available and updated frequently on CDC's website at http://wwwn.cdc.gov/travel; *The Yellow Book* also can be purchased online from Elsevier at http://www.elsevierhealth.com or by telephone (800-545-2522).

CDC provides assistance for diagnostic parasitology through DPDx (Laboratory Identification of Parasites of Public Health Concern), a project developed and maintained by CDC's Division of Parasitic Diseases. DPDx (available at http://www.dpd.cdc.gov/dpdx) provides free Internet-based laboratory diagnostic assistance (i.e., telediagnosis) to laboratorians and pathologists in suspected parasitic disease cases, such as malaria. Digital images captured from diagnostic specimens can be submitted for consultation through e-mail. Telediagnosis assistance by CDC is available during regular business hours. Because laboratories can transmit images to CDC and obtain a rapid response (with average time ranging from minutes to several hours) to their inquiries, this system allows efficient diagnosis of challenging cases and rapid dissemination of information. As of January 2008, approximately 49 public health laboratories in 46 states and Puerto Rico had the ability to perform telediagnosis. Implementation of telediagnosis at public health laboratories receives full assistance from CDC, including training of personnel in digital imaging techniques. The DPDx website also contains reference material with images, text, and videos on approximately 100 different species of parasites with information (including laboratory diagnosis, geographic distribution, clinical features, treatment, and life cycles) available for each parasite.

Acknowledgments

This report is based, in part, on data reported from state, territorial, and local health departments; health-care providers; and laboratories.

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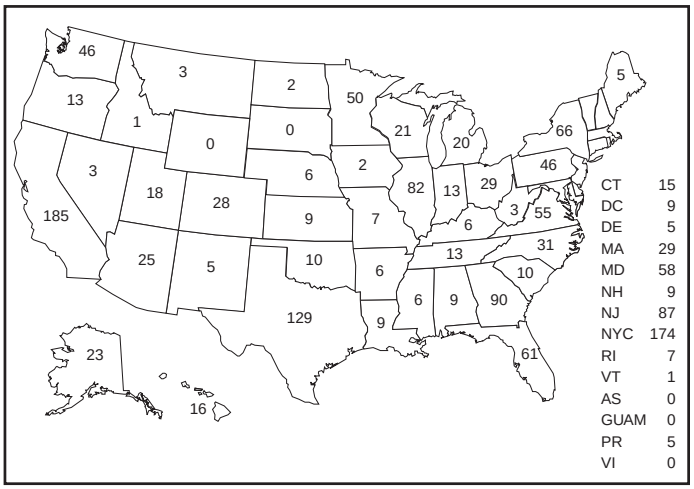
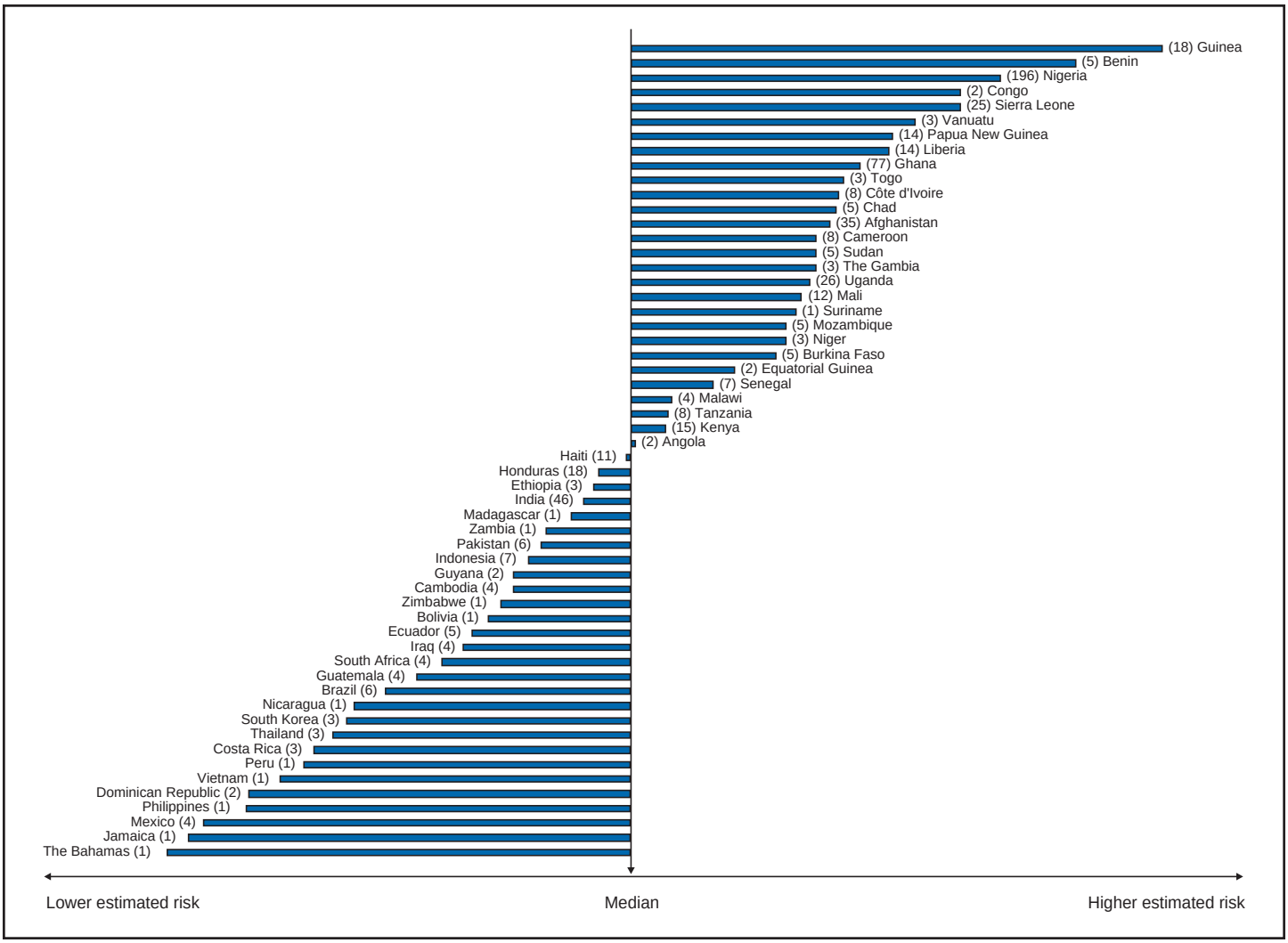
FIGURE 1. Number of malaria cases,* by state in which the disease was diagnosed — United States, 2006



*N=1,561. No state was reported for three cases.

FIGURE 2. Number of imported malaria cases and estimated relative case rates* among U.S. civilians, by country of acquisition — United States, 2006



* Using estimates of travel volume for U.S. travelers to each country from which cases of malaria were acquired, and the number of cases among U.S. travelers attributable to each country, a case rate was estimated for each country. Data used to estimate country-specific relative case rates were extrapolated from World Tourism Organization estimates of annual numbers of U.S. travelers to specific countries (*6*). Relative case rates were determined by dividing the individual country-specific case rate by the median individual country-specific case rate. The number of cases of malaria among U.S. civilian travelers attributable to each country is displayed next to the country name in parentheses. Note that certain risk estimates are based on small numbers of cases.

TABLE 1. Number of malaria cases* among U.S. and foreign residents and U.S. military personnel — United States, 1976–2006

Year	U.S. military personnel	U.S. civilians	Foreign civilians	Status not recorded	Total
1976	5	178	227	5	**415**
1977	11	233	237	0	**481**
1978	31	270	315	0	**616**
1979	11	229	634	3	**877**
1980	26	303	1,534	1	**1,864**
1981	21	273	809	0	**1,103**
1982	8	348	574	0	**930**
1983	10	325	468	0	**803**
1984	24	360	632	0	**1,016**
1985	31	446	568	0	**1,045**
1986	35	410	646	0	**1,091**
1987	23	421	488	0	**932**
1988	33	550	440	0	**1,023**
1989	35	591	476	0	**1,102**
1990	36	558	504	0	**1,098**
1991	22	585	439	0	**1,046**
1992	29	394	481	6	**910**
1993	278	519	453	25	**1,275**
1994	38	524	370	82	**1,014**
1995	12	599	461	95	**1,167**
1996	32	618	636	106	**1,392**
1997	28	698	592	226	**1,544**
1998	22	636	361	208	**1,227**
1999	55	833	381	271	**1,540**
2000	46	827	354	175	**1,402**
2001	18	891	316	158	**1,383**
2002	33	849	272	183	**1,337**
2003	36	767	306	169	**1,278**
2004	32	775	282	235	**1,324**
2005	36	870	297	325	**1,528**
2006	50	663	217	634	**1,564**

*A case was defined as symptomatic or asymptomatic illness that occurs in the United States or one of its territories in a person who has laboratory-confirmed malaria parasitemia (by microscopy or polymerase chain reaction), regardless of whether the person had previous attacks of malaria while in other countries. A subsequent attack of malaria occurring in a person is counted as an additional case if the demonstrated *Plasmodium* species differs from the initially identified species or if it is indicated as a relapsing infection demonstrating the same species identified previously. A subsequent attack of malaria occurring as a result of drug resistance or other treatment failure is not counted as an additional case.

TABLE 2. Number of malaria cases, by *Plasmodium* species — United States, 2004, 2005, and 2006

Plasmodium species	2004		2005		2006	
	No.	(%)	No.	(%)	No.	(%)
P. falciparum	656	(49.5)	742	(48.6)	613	(39.2)
P. vivax	315	(23.8)	337	(22.1)	275	(17.6)
P. malariae	47	(3.5)	54	(3.5)	46	(2.9)
P. ovale	27	(2.0)	38	(2.5)	47	(3.0)
Mixed	17	(1.3)	12	(0.8)	10	(0.6)
Undetermined	262	(19.8)	345	(22.6)	573	(36.6)
Total	**1,324**	**(100)**	**1,528**	**(100)**	**1,564**	**(100)**

TABLE 3. Imported malaria cases, by country of acquisition and *Plasmodium* species — United States, 2006

Country of acquisition	*Plasmodium* species						
	P. falciparum	*P. vivax*	*P. malariae*	*P. ovale*	Unknown	Mixed	Total
Africa	**522**	**34**	**34**	**37**	**159**	**7**	**793**
Angola	1	0	0	0	1	0	**2**
Benin	2	1	0	0	4	0	**7**
Burkina Faso	4	0	3	0	0	0	**7**
Cameroon	14	3	0	0	6	1	**24**
Chad	3	1	0	0	1	0	**5**
Congo	3	1	1	3	3	1	**12**
Côte d'Ivoire	11	1	0	3	5	0	**20**
Democratic Republic of Congo	0	0	0	1	0	0	**1**
Egypt	1	0	0	0	0	0	**1**
Equatorial Guinea	0	0	0	0	4	0	**4**
Eritrea	0	0	0	1	0	0	**1**
Ethiopia	0	4	1	0	4	0	**9**
Gambia	2	0	0	0	1	0	**3**
Ghana	85	4	6	4	17	0	**116**
Guinea	21	0	2	1	6	0	**30**
Kenya	15	0	2	1	5	0	**23**
Liberia	20	0	1	2	6	0	**29**
Madagascar	0	0	1	0	0	1	**2**
Malawi	4	0	0	0	1	0	**5**
Mali	13	0	0	0	2	0	**15**
Mozambique	3	0	0	1	2	0	**6**
Niger	3	0	1	0	0	0	**4**
Nigeria	202	8	5	11	50	2	**278**
Senegal	15	0	0	0	0	0	**15**
Sierra Leone	28	1	0	0	3	1	**33**
Somalia	0	0	1	0	0	0	**1**
South Africa	3	0	0	0	2	0	**5**
Sudan	2	2	0	0	3	0	**7**
Tanzania	4	0	1	0	3	0	**8**
Togo	4	0	0	0	2	0	**6**
Uganda	24	5	5	4	11	0	**49**
Zambia	2	0	0	0	0	0	**2**
Zimbabwe	1	0	0	0	1	0	**2**
West Africa, unspecified	14	1	1	0	8	0	**24**
East Africa, unspecified	0	0	0	1	0	0	**1**
Africa, unspecified	18	2	3	4	8	1	**36**
Asia	**19**	**126**	**7**	**1**	**50**	**2**	**205**
Afghanistan	0	34	0	0	8	0	**42**
Burma (Myanmar)	0	1	0	0	0	0	**1**
Cambodia	3	0	0	0	1	0	**4**
China	1	0	0	0	0	0	**1**
India	9	75	4	1	32	0	**121**
Indonesia	4	2	0	0	2	0	**8**
Iraq	0	1	1	0	2	0	**4**
Korea (South)	0	3	0	0	1	0	**4**
Pakistan	1	6	1	0	0	0	**8**
Philippines	1	0	0	0	0	0	**1**
Saudi Arabia	0	0	0	0	1	0	**1**
Thailand	0	2	1	0	2	2	**7**
Vietnam	0	1	0	0	0	0	**1**
Asia, unspecified	0	1	0	0	1	0	**2**
Central America and the Caribbean	**25**	**44**	**1**	**1**	**11**	**0**	**82**
Bahamas	1	0	0	0	0	0	**1**
Belize	0	0	0	1	0	0	**1**
Costa Rica	0	2	0	0	1	0	**3**
Dominican Republic	2	0	0	0	1	0	**3**
El Salvador	0	1	0	0	0	0	**1**

TABLE 3. (*Continued*) Imported malaria cases, by country of acquisition and *Plasmodium* species — United States, 2006

Country of acquisition	*Plasmodium* species						
	P. falciparum	*P. vivax*	*P. malariae*	*P. ovale*	Unknown	Mixed	Total
Central America and the Caribbean (cont'd.)							
Guatemala	0	11	0	0	5	0	**16**
Haiti	14	0	1	0	0	0	**15**
Honduras	5	29	0	0	2	0	**36**
Jamaica	2	0	0	0	0	0	**2**
Nicaragua	1	1	0	0	2	0	**4**
North America	**0**	**7**	**0**	**0**	**4**	**0**	**11**
Mexico	0	7	0	0	4	0	**11**
South America	**2**	**19**	**1**	**2**	**3**	**0**	**27**
Bolivia	0	1	0	0	0	0	**1**
Brazil	0	10	0	1	2	0	**13**
Ecuador	1	4	0	0	0	0	**5**
Guyana	1	1	0	0	1	0	**3**
Peru	0	1	1	0	0	0	**2**
Suriname	0	1	0	0	0	0	**1**
South America, unspecified	0	1	0	1	0	0	**2**
Oceania	**1**	**16**	**0**	**0**	**4**	**1**	**22**
Papua New Guinea	1	12	0	0	3	1	**17**
Vanuatu	0	4	0	0	1	0	**5**
Unknown	**44**	**29**	**3**	**6**	**342**	**0**	**424**
Total	**613**	**275**	**46**	**47**	**573**	**10**	**1,564**

TABLE 4. Number of imported malaria cases among U.S. and foreign residents, by region of acquisition — United States, 2006*

Area or region	United States		Foreign		Total	
	No.	(%)	No.	(%)	No.	(%)
Africa	511	(71.7)	131	(60.3)	**642**	**(69.0)**
Asia	116	(16.3)	52	(24.0)	**168**	**(18.1)**
Central America and the Caribbean	42	(5.9)	25	(11.5)	**67**	**(7.2)**
South America	18	(2.5)	3	(1.4)	**21**	**(2.3)**
North America	4	(0.5)	2	(0.9)	**6**	**(0.6)**
Oceania	17	(2.4)	1	(0.5)	**18**	**(1.9)**
Unknown†	5	(0.7)	3	(1.4)	**8**	**(0.9)**
Total	**713**	**(100)**	**217**	**(100)**	**930**	**(100)**

*Persons for whom U.S. or foreign status is not known are excluded.
†Region of acquisition is unknown.

TABLE 5. Number of imported malaria cases, by interval between date of arrival in the country and illness onset and by *Plasmodium* species* — United States, 2006

Interval (days)	*P. falciparum*		*P. vivax*		*P. malariae*		*P. ovale*		Mixed		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<0†	32	(7.4)	5	(3.9)	1	(3.1)	2	(7.4)	0	(0)	**40**	**(6.5)**
0–29	384	(89.5)	69	(54.3)	22	(68.7)	14	(51.9)	7	(100)	**496**	**(79.7)**
30–89	13	(3.0)	16	(12.6)	6	(18.7)	4	(14.8)	0	(0)	**39**	**(6.3)**
90–179	0	(0)	14	(11.0)	3	(9.4)	2	(7.4)	0	(0)	**19**	**(3.0)**
180–364	0	(0)	19	(15.0)	0	(0)	3	(11.1)	0	(0)	**22**	**(3.5)**
≥365	0	(0)	4	(3.1)	0	(0)	2	(7.4)	0	(0)	**6**	**(1.0)**
Total	**429**	**(100)**	**127**	**(100)**	**32**	**(100)**	**27**	**(100)**	**7**	**(100)**	**622**	**(100.0)**

*Persons for whom *Plasmodium* species, date of arrival in the United States, or date of onset of illness is unknown are not included.
†Persons with cases in this row had onset of illness before arriving in the United States.

TABLE 6. Number of imported malaria cases among U.S. civilians, by purpose of travel at time of acquisition — United States, 2006

	Imported cases	
Purpose of travel	**No.**	**(%)***
Visiting friends/relatives	363	(50.9)
Tourism	71	(9.9)
Missionary or dependent	53	(7.4)
Business representative	41	(5.7)
Student/teacher	26	(3.6)
Peace Corps volunteer	5	(0.7)
Air crew/sailor	4	(0.6)
Other/mixed purpose	18	(2.5)
Unknown	132	(18.5)

* Percentages do not equal 100% because travelers can identify multiple reasons for purpose of travel.

TABLE 7. Sources for malaria prophylaxis, diagnosis, and treatment recommendations

Type of information	Source	Availability	Telephone number, website, or e-mail address
Prophylaxis	CDC Travelers' Health website (includes online access to *Health Information for International Travel [The Yellow Book]*)	24 hours/day	http://www.cdc.gov/travel
Prophylaxis	*Health Information for International Travel* (*The Yellow Book*)	Order from: Elsevier, Health Sciences Division Order Fulfillment 11830 Westline Industrial Drive St. Louis, MO 63146	800-545-2522 or http://www.elsevier.com
Prophylaxis	CDC Malaria Risk Map	24 hours/day	http://www.cdc.gov/malaria/features/risk_map.htm
Diagnosis	CDC, Division of Parasitic Diseases website: Laboratory Identification of Parasites of Public Health Concern (DPDx)	24 hours/day	http://www.dpd.cdc.gov/dpdx
Diagnosis	CDC, Division of Parasitic Diseases diagnostic CD-ROM (DPDx)	Order by e-mail from CDC, Division of Parasitic Diseases	dpdx@cdc.gov
Treatment*	CDC Malaria Branch	8:00 A.M.–4:30 P.M. EST, Monday–Friday	770-488-7788*
Treatment*	CDC Malaria Branch	4:30 P.M.–8:00 A.M. EST, on weekdays; all day on weekends and holidays	770-488-7100* (Telephone number for CDC Director's Emergency Operations Center. Ask a staff member to page the person on call for the Malaria Branch.) http://www.cdc.gov/malaria/diagnosis_treatment/treatment.htm.

* Telephone number is for health-care professionals only.

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