A NATIONAL PUBLIC HEALTH ACTION PLAN FOR THE DETECTION, PREVENTION, AND MANAGEMENT OF INFERTILITY

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A NATIONAL PUBLIC HEALTH ACTION PLAN FOR THE DETECTION, PREVENTION, AND MANAGEMENT OF INFERTILITY

EXECUTIVE SUMMARY

Because the desire to have one's own biological children can be strong and compelling, the effects of infertility for couples who are unable to conceive can be devastating. Infertility or its treatment can cause psychological stress, anxiety, and depression. Treatment of infertility may be medically invasive and may cause discomfort or, in some cases, may be associated with adverse health events for women and resulting offspring. Preventing infertility and the adverse consequences associated with its treatment are important concerns, given the goals of CDC, and public health in general, to reduce disease, premature death, injury, and disability in the population through prevention and health promotion. There is a clear need to identify public health priorities regarding infertility and its implications.

About 7.4% of married couples of reproductive age in the United States are infertile (defined as failing to become pregnant after one year of trying with the same partner), and about 12% of women of reproductive age have impaired fecundity (defined as difficulty in getting pregnant or carrying a child to term). Men also can experience impaired fertility. In a 2002 survey of U.S. men of reproductive age, 1.2% reported ever having an infertility problem.

Known or potential causes of infertility include genetic abnormalities, aging, acute and chronic diseases, treatments for certain conditions, behavioral factors, and exposure to environmental, occupational, and infectious agents. However, many questions about infertility remain unanswered. In addition, significant disparities exist by socioeconomic status, race, and ethnicity in the diagnosis, referral, and treatment of infertility. Furthermore, treatments for infertility can carry health risks. This document addresses these issues, focusing on the public health aspects of infertility detection, prevention, and management.

Description of the Plan

In consultation with many governmental and nongovernmental partners, the U.S. Centers for Disease Control and Prevention developed the National Public Health Action Plan for the Detection, Prevention and Management of Infertility. Addressing both male and female infertility, the plan outlines and summarizes actions needed to promote, preserve, and restore the ability of women in the United States to conceive, carry a pregnancy to term, and deliver a healthy infant. This goal extends beyond simply addressing the inability to conceive but also focuses on reducing the burden of impaired fecundity by promoting behaviors that maintain fertility; by promoting prevention, early detection, and treatment of medical conditions; and by reducing environmental and occupational threats to fertility. Given the public health focus of this action plan, promoting healthy pregnancy outcomes associated with treating and managing infertility is also important, as is improving the efficacy and safety of infertility treatment.

The document is organized into three chapters: “Detection of Infertility,” “Prevention of Infertility,” and “Management of Infertility.” Each chapter addresses the topic’s public health importance, existing challenges, and opportunities for action to decrease the impact of infertility on the public's health. The suggested opportunities provide federal and other government agencies, professional and consumer organizations, and other partners and stakeholders a foundation and platform to work together to decrease the burden of infertility in the United States.

INTRODUCTION

In general, infertility refers to the inability of a couple to achieve pregnancy after one year of trying. However, definitions for infertility vary, depending on the information available and the purpose for which the information is collected. For example, among women 35 years of age or older, clinicians may diagnose infertility after only six months of trying because the ability to conceive declines substantially with increasing age and because delaying the initiation of infertility interventions could limit their effectiveness. In contrast, demographers often define infertility as the inability of a noncontracepting, sexually active woman to have a live birth; this definition better meets the needs and constraints of demographic research, because of difficulty in collecting complete information about conception in studies of populations.[1] Thus, the available data may be limited by methodological constraints. For example, surveys have focused on married women as a proxy for a population having regular intercourse, and estimates derived from these studies might not be generalizable to wider populations. Furthermore, the true burden of infertility may be much higher than that reported because the statistics do not necessarily reflect those that may have stopped trying or had experienced infertility in the past.

Infertility can involve different presentations, such as resolved infertility (i.e., pregnancies occurring after one year of trying without medical intervention) and primary (i.e., never pregnant) or secondary infertility (failure to conceive after having previously delivered an infant without medical intervention). Furthermore, other conditions related to infertility are also important to consider when assessing the public health impact of infertility. *Fecundability* refers to the probability of becoming pregnant in a single menstrual cycle; couples with low probability are referred to as *subfertile*.[1] *Impaired fecundity* has been defined as difficulty in conceiving or in carrying a child to term.[2] Because this document draws on many different sources of information, we use these terms broadly and reference source material for more specific definitions, as needed.

Public Health Priority

Although the ability to have children is often taken for granted, a significant proportion of couples will experience infertility and many of its resulting social, economic, psychological, and physical effects. The ability to have children represents more than a quality-of-life issue. The World Health Organization and other professional organizations, such as the American Society for Reproductive Medicine, have defined infertility as a disease.[3,4] Early exposures (e.g., in utero or in childhood) could permanently reprogram men and women for fecundity or biologic capacity (e.g., gynecologic and urologic health or gravid health during pregnancy) and fertility outcomes (e.g., multiple births or gestational age at delivery), which could affect later adult onset diseases.[5,6] Thus, infertility could have public health implications beyond simply the ability to have children.

The U.S. Centers for Disease Control and Prevention (CDC) has long been concerned with the public health aspects of infertility, its causes, and prevention. CDC's activities related to infertility include the following:

- Surveillance to monitor the prevalence of infertility and the use, efficacy, and safety of infertility services and treatments, including assisted reproductive technology (ART) (defined as treatments that involve the handling of both eggs and sperm to establish a pregnancy).

- Research on the infectious, environmental, and occupational causes of infertility; links between chronic diseases and the treatment of chronic diseases and infertility; and links between infertility treatment and adverse perinatal and child outcomes, such as preterm delivery, birth defects, and developmental disabilities.
- Public health programs for the primary and secondary prevention of infertility, especially in the area of sexually transmitted diseases (STDs) and reproductive tract infections.

Infertility affects a substantial proportion of reproductive-aged women and men in the United States. Data from CDC's 2002 National Survey of Family Growth (NSFG) show that, among the surveyed population representative of married U.S. women 15–44 years of age, an estimated 7.4% of women (and thus their husbands) were affected by infertility (defined as failing to become pregnant after one year of trying with the same partner).[2] About 12% of all women 15–44 years of age had impaired fecundity. Prospective cohort studies with preconception enrollment of women upon discontinuing contraception found that approximately 10-36% of couples did not achieve pregnancy within 6 menstrual cycles of observation.[7,8] More than 1.1 million women of reproductive age sought medical help to get pregnant in the previous year, and 7.3 million had received infertility services, including counseling and diagnosis, in their lifetime.[2]

About 1.2% of men of reproductive age in 2002 reported ever being diagnosed with a male-related infertility condition.[9] About 2.2% of sexually experienced U.S. men 15–44 years of age reported seeking medical services to have a child in the past year, and 7.5% reported ever seeking assistance.[10] Environmental and occupational hazards account for an unknown proportion of infertility but are suspected causes of declining human sperm quality in industrialized countries.[11] Estimates of the proportion of infertility cases attributable to male- or female-specific factors in developed countries were derived in the 1980s by the World Health Organization; 8% of infertility cases were attributable to male factors, 37% to female factors, 35% to both the male and female, and 5% to an unknown cause (the remaining 15% became pregnant).[12]

The natural age limits of fertility in both women and men have become more apparent with the recent trend toward delaying childbearing in the United States.[13-15] The proportion of first births among women aged 30 years or older increased from 5% in 1975 to 26% in 2010.[16,17] The proportion of women experiencing infertility increases markedly with age, from 6.3% among married women 15–29 years of age to 9.4% among those 40–44 years of age.[2] As women age, the risk of infertility rises because of diminished egg quality and ovulatory function as well as an increase in disorders such as endometriosis, leiomyomata, and tubal disease.[18] Advanced paternal age also might contribute to infertility through reductions in the quality and quantity of sperm produced.[14,15] The combination of the high proportion of pregnancies in the United States that are unintended (approximately one-half)[19] and the rise in intended pregnancy at later ages, when infertility is increasingly common, indicates a basic need for improved education to inform those who may desire children in the future about family planning, infertility, and other reproductive health issues.

Services and treatments for infertility range from counseling and advice to medications and surgery. The 2002 NSFG showed that the most common medical services ever obtained by reproductive-aged women with current infertility problems were advice (25%), testing of her or her male partner (22%), or use of ovulation medications (16%).[20] Fewer women reported having used artificial insemination (a term sometimes used for the procedure in which sperm from a female's partner or a donor is placed into her reproductive tract – usually the uterus or cervix - for the purpose of producing a pregnancy) (6%), surgery or treatment for blocked tubes (4%), or ART (1%). Treatments for infertility can carry significant health risks to the mother and child. For example, a rare but serious risk of using drugs for ovulation induction is ovarian hyperstimulation syndrome (OHSS), which is characterized by enlargement of the ovary and an accumulation of fluid in the abdomen.[21] Infertility treatments have increased the rate of twin and higher-order multiple births, which put both mother and infants at higher risk for adverse health outcomes.[22,23] Furthermore, even singleton births resulting from ART are associated with increased risk for low birth weight (<2500 grams).[24] Births resulting from ART[25] or non-ART treatments (e.g., use of clomiphene citrate) may be at higher risk for birth defects.[26] Overall, the long-term health risks are not clear for women receiving treatment for infertility and children born as a result of ART and other treatment approaches are not clear.[27]

Development of the National Public Health Action Plan

In 2007, a CDC-wide ad hoc workgroup formed to examine the full scope of infertility activities across the agency. This workgroup conducted an assessment to identify gaps and opportunities in public health surveillance, research, communications, programs, and policy development, which led to the 2010 publication of a "white paper" outlining the need for a national plan, with a public health focus, on infertility prevention, detection, and management.[28] In September 2008, CDC also hosted a symposium, Infertility as a Public Health Issue, which was attended by about

60 stakeholders from federal agencies, professional and consumer organizations, academia, and the health care community. At the symposium, the causes, consequences, and potential interventions for infertility were reviewed.

The U.S. House of Representatives 2010 Committee on Appropriations Report requested that CDC develop a public health plan for the prevention, detection, and management of infertility:

> The Committee has included funding within Safe Motherhood/Infant Health for the development of a national public health action plan for the prevention, detection, and management of infertility. The development of this plan is critical to the efforts of more than two million women who battle this medical condition across the U.S. The Committee supports the goal of CDC's national plan to identify public health priorities and encourages the integration of existing programs and initiatives regarding infertility, as well as creation of new programs as deemed necessary.[29]

As a result, CDC developed this National Public Health Action Plan (hereafter referred to as "the Plan"), intended to facilitate collaborative activities within and outside the federal government to achieve the Plan's overall goal: to promote, preserve, and restore the ability of women in the United States to conceive, carry a pregnancy to term, and deliver a healthy infant. CDC consulted with a broad coalition of stakeholders through presentations, individual contact, and group discussions, including participants of the 2008 CDC infertility symposium, to draft the Plan.

CHAPTER 1:DETECTION OF INFERTILITY

Public Health Importance

The clinical detection of infertility is important for couples, since it can prompt the initiation of additional evaluations and possibly treatment. Similarly, public health surveillance will be most effective when there is a standard case definition that can be implemented in population-based data collection efforts. Currently no definitive test or case definition exists for infertility.[1,30] A range of definitions has been used, often based on a combination of the length of time that the couple has been attempting to conceive (or to produce a live birth) and the age of the woman. A standard, clear definition for identifying infertility is needed to ensure that couples needing testing and care can receive these without undue delay while also avoiding the over-treatment of couples who may have conceived without medical interventions.

Fully understanding the impact of infertility in the United States, as well as measuring progress toward reducing the burden of infertility, requires the ongoing collection, analysis, interpretation, and use of population-level data related to infertility. Information on four types of measures is needed on a recurring basis: 1) disease incidence and prevalence, 2) prevalence and impact of risk factors for infertility, 3) access, utilization, safety, efficacy, and quality of infertility services, and 4) economic and financial aspects of service delivery.

Measurement of disease incidence and prevalence at the population level requires surveillance of infertility and the conditions that may directly lead to it. Other key indicators that are important to monitor include recurrent pregnancy loss, male and female sterilization (as well as sterilization reversal), and resolved infertility. It is also important to estimate and track the size of the sub-populations that may need or potentially benefit from fertility preservation. Patients with cancer, autoimmune disorders, or bleeding or clotting disorders could use fertility preservation methods, which could include the use of drugs for protecting the ovaries during chemotherapy or cryopreservation of ovarian tissue, eggs or sperm, or of embryos following in vitro fertilization.

Surveillance of the risk factors for infertility should include data on sociodemographics (e.g., age, race/ethnicity, education, place of residence, and socioeconomic status), health behaviors (e.g., use of alcohol and tobacco), factors and behaviors that increase the risk of unhealthy weight (underweight or overweight) and STDs, adherence to screening and treatment recommendations related to risk factors, physical and mental health conditions (e.g., genetic disorders, STDs, obesity, depression, and cancer), environmental exposures, and occupational exposures (e.g., industry type, specific occupations, and identified chemicals or physical exposures in the workplace).

Collection of population-based data on access, use, and quality of infertility services requires key indicators related to screening, diagnosis, laboratory services, state infertility treatment mandates, and psychosocial determinants (e.g., fertility goals) as modifiers of service-seeking behavior, counseling, and treatment decisions.

Finally, estimating and tracking the economic and financial aspects of service quality involve the collection of data on service utilization and its cost, cost of successful infertility treatment, direct and indirect costs of untreated infertility and treated infertility (regardless of the reproductive outcome), cost-effectiveness of alternative treatment strategies, economic impact of reducing barriers to diagnosis and treatment, and long-term health care costs of adverse maternal and child outcomes from infertility treatment.

The Challenge

Clinical detection and surveillance

Clinical detection and public health surveillance of infertility should be based on standard diagnostic criteria and a case definition, respectively. Appropriate clinical and behavioral indicators for both are needed to improve the detection of infertility in the population. The clinical diagnosis of infertility must be evidence based to allow for effective prevention and management of the condition. Public health surveillance of infertility depends on the systematic, recurring collection and management of accurate data. Ideally, surveillance systems capturing data on infertility will use standard case definitions that can be applied across multiple data systems. Furthermore, for surveillance to be maximally effective and useful, data collected must characterize types of infertility as well as associated risk factors and outcomes.

CDC surveillance systems (see Appendix) include ongoing, population-based surveys, such as the National ART Surveillance System and the NSFG, that collect data on a variety of reproductive behaviors, infertility treatments, and outcomes. The current systems all have several challenges, such as the lack of standardized information across systems and the use of a single case definition. For example, methods for quantifying infertility and subfecundity can differ by data source. Also, information is lacking on many key indicators, such as prevalence of specific types of infertility, the success rates and use of infertility treatments other than ART, and adverse maternal and child health outcomes associated with infertility treatment. Surveillance could be improved by also collecting information on time to pregnancy or current duration of unprotected intercourse in population-based surveys or on birth certificates. Registries of individual cases (e.g., registries of egg donors, patients treated with specific classes of fertility drugs, or cancer patients who use fertility preservation methods) could provide a data source to better assess infertility in the population, including safety and effectiveness of treatment. Current surveillance systems do not include measures of all relevant indicators and thus cannot provide a comprehensive assessment of the magnitude of incidence, prevalence, risk factors, and outcomes associated with infertility.

Scientific and Programmatic Opportunities

1. Develop and validate standard case definitions for population-based and clinical surveillance of infertility.

Development of standard case diagnoses and definitions for infertility and related factors would provide uniform measures for use in clinical practice and public health surveillance. These standard definitions could improve the synthesis of information and ultimately lead to improved evidence-based guidelines and recommendations for detecting, preventing, and managing infertility.

2. Improve the surveillance of infertility and related factors.

Population-based surveys could be developed or existing systems augmented to facilitate the measuring and monitoring of infertility as well as associated risk factors and outcomes. For example, by increasing the sample sizes related to the use of infertility treatment, adding new survey questions, and extending the survey to include older women and men, the NSFG could be used to evaluate the impact of national policies and programs. Infertility questions also could be added to other large population-based surveys (see Appendix) that presently collect data relevant to understanding health conditions and factors that may affect fertility. Similarly, to improve the value of surveillance of ART outcomes, technical solutions for linking multiple records of ART in the National ART Surveillance System should be explored to facilitate the evaluation of ART effectiveness on a per-patient, rather than on a per-cycle, basis. This enhancement would strengthen the ability to evaluate the short- and long-term effects of ART use on maternal and infant outcomes. Finally, the development of new surveillance systems to monitor the use and outcomes of non-ART treatments for infertility should be explored.

CHAPTER 2: PREVENTION OF INFERTILITY

Public Health Importance

Many questions remain about the prevention of infertility. Although unknown, the proportion of infertility that may be preventable is suspected to be substantial.[28] Established and possible causes of infertility include genetic abnormalities, aging, certain acute and chronic diseases, behavioral risk factors (e.g., body weight and smoking),[31] and exposure to certain environmental, occupational, and infectious agents. One example of a recognized preventable risk factor for infertility is untreated STD. In particular, infection with *Chlamydia trachomatis* increases the risk of pelvic inflammatory disease,[32-34] which if left untreated, can cause structural or functional fallopian tube damage known as tubal factor infertility. Tubal factor infertility, which may be caused by *Chlamydia trachomatis* or by other infections, such as *Neisseria gonorrhoeae*, is estimated to affect as many as 18% of women using ART for treating infertility.[23] In addition, substantial racial disparities have been identified in the occurrence of chlamydial infection; prevalence among non-Hispanic blacks is approximately five times higher than among non-Hispanic whites.[35] Racial disparities also exist in chronic conditions that affect fertility, such as fibroids.[36] Public health can help address infertility by monitoring the condition and its associated risk factors in the population and by identifying, informing, and implementing effective prevention and management strategies.

The Challenge

Understanding the causes of infertility

To develop and implement effective public health interventions, the field needs to have standard case definitions for both infertility and its causes. Although much is understood about the causes of infertility, additional research would help elucidate the causes and proportion of infertility cases attributable to specific risk factors and medical conditions. However, research on infertility is inherently complicated. First, three different subjects are potentially involved: the woman, the man, and the fetus or infant. Second, infertility is generally diagnosed only when a woman attempts to become pregnant; those not actively trying to conceive will typically not have the opportunity to be diagnosed or evaluated for infertility. Current surveillance systems are not designed to identify the spectrum of women and men who may be infertile.

Research is needed on methods for the early identification and amelioration of conditions that are precursors to infertility. A research agenda could include a range of outcomes—from basic science to public health—to target the early detection of infertility by developing and evaluating methods for detecting impaired fertility in both women and men at earlier ages and at earlier stages.

Research is required to better understand many known and potential causes of infertility, including the following:

- Reproductive aging (e.g., determining the predictors and correlates of early depletion of the ovarian reserve, and the effects of age on semen quality and reproductive function).
- Determining sensitive developmental windows (e.g., in utero or puberty) for factors affecting fertility in order to identify the optimal time of intervention.

- Infectious diseases (e.g., the proportion of cases of tubal factor infertility attributable to infectious diseases and the role of specific infections, such as chlamydia, gonorrhea, mycoplasmas, trichomoniasis, bacterial vaginosis, tuberculosis of the reproductive tract, microbial organisms associated with reproductive tract infections, and mumps).
- Chronic conditions and diseases, including endocrine and metabolic diseases (e.g., primary ovarian insufficiency, polycystic ovary syndrome (PCOS), hypothalamic amenorrhea, menstrual cycle defects, endometriosis, uterine leiomyomata, thyroid disorders, and metabolic syndrome), diabetes, autoimmune disorders, meiotic aneuploidy, cystic fibrosis, varicocele, testicular disorders, and multiple sclerosis.
- Behavioral factors (e.g., diet, exercise, psychological stress, caffeine consumption, tobacco and alcohol use, weight gain or loss, nutritional disorders, and illicit or prescription drug use).
- Iatrogenic causes (e.g., chemotherapy for testicular and ovarian cancer and antiretroviral therapy for HIV/AIDS).
- Occupational and environmental hazards (e.g., radiation, injury, repetitive motion or posture, injury, and natural and synthetic chemicals and compounds with hormonal activities [e.g., endocrine disrupters]).
- Genetic influences.
- Transgenerational and in utero effects.
- Other causes (e.g., autoimmune or immune-mediated disorders).

Public health interventions for prevention

Public health interventions to prevent infertility must be based on evidence from research. This translation of science into public health practice requires the development of systems and policies to incorporate research results into prevention programs. The prevention of infertility should be integrated into a broader agenda for reproductive health promotion for both men and women. Programs, interventions, strategies, and other methods for preventing infertility must be developed and evaluated. Examples of these activities include the following:

- Comprehensive approaches to STD screening, treatment, prevention, and education to reduce infertility and to address economic and racial disparities in access to STD prevention and treatment, in use of infertility services, and in treatment outcomes.[37,38]
- Interventions to reconcile the messages for preventing infertility and for preventing unintended pregnancy among youth.
- Chronic disease prevention and health promotion programs to reduce the incidence and severity of diseases, such as diabetes and PCOS and PCOS-related infertility.
- Methods to measure reproductive potential (including markers of ovarian reserve and semen analyses) and preserve fertility before, during, or after medical therapies that could lead to iatrogenic infertility.
- Measures to protect the reproductive health of workers (who may be exposed to environmental and occupational hazards) by translating research findings, technologies, and information into evidence-based practice.
- Methods to accurately assess environmental and occupational exposures, including laboratory biomonitoring, control technologies, screening tools, and interventions.
- Programs aimed at lowering the risk of infertility by preventing the use of illicit drugs and tobacco, improving nutrition, and promoting adequate levels of physical activity.

- Research to determine the cost effectiveness and cost benefit of programs aimed at preventing infertility.

Scientific and Programmatic Opportunities

1. **Expand the knowledge base on infertility prevention through collaborative efforts to identify, prioritize, and address research gaps.**

Research on preventing infertility requires collaboration from a range of disciplines, including basic science, epidemiology, and the clinical, behavioral, and social science fields. Addressing our gaps in understanding the causes of infertility and increasing opportunities for prevention must involve collaborative efforts by both governmental and nongovernmental organizations to focus on the effects—on both female and male fertility—of age, behavioral risk factors, chronic conditions and diseases and their treatment, genetic disorders, and exposure to environmental, occupational, and infectious agents.

2. **Expand laboratory capacity and services to help address knowledge gaps about environmental, occupational and infectious causes of infertility.**

Methodological improvements in infertility research would improve understanding of how environmental, occupational and infectious exposures might adversely affect fertility. For example, it is essential to increase the capacity of public health laboratories to conduct biomonitoring of chemicals or their metabolites in human specimens (e.g., blood, urine, or hair).

3. **Increase awareness of the prevalence and causes of infertility.**

Scientific knowledge should be rapidly disseminated and translated into public health programs and evidence-based practices. Educational programs should be developed and conducted to expand awareness among youth and adults about the prevalence and causes of infertility. These programs should be integrated with other reproductive health promotion activities and should be culturally and age-appropriate to maximize their impact.

4. **Develop and promote evidence-based behavioral and clinical approaches for preventing infertility.**

Efforts should focus on the design, evaluation, and implementation of programs, interventions, strategies, clinical services, and other methods for addressing the known causes of infertility, including the reduction of behaviors that increase the risk of infertility.

5. **Support and improve access to quality services, including screening, diagnosis, and treatment services for known causes of infertility.**

Further integration of infertility services into primary care settings would facilitate widespread access to screening, testing, and counseling on infertility. In particular, economic and racial disparities in access to infertility services and treatment outcomes could be reduced by enhancing the provision of these services at public health and other clinics that target underserved populations and by ensuring appropriate referral, as needed. Improving the quality of services provided could require additional training of public health providers.

CHAPTER 3: MANAGEMENT OF INFERTILITY

Public Health Importance

According to the 2002 National Survey of Family Growth (NSFG), 12% of women in the United States 15–44 years of age had ever used one or more infertility services.[2] This percentage likely underestimates the true burden of infertility, since it does not include men or those who have not sought services. Although most infertility services do not involve ART,[20,22] the prevalence of its use has been increasing. The number of ART cycles (which are primarily in vitro fertilization [IVF] cycles) performed in the United States nearly doubled between 1999 and 2008, and ART procedures were used for >1% of total births in the United States in 2008.[23]

Fertility treatments can pose health risks for women and their offspring. For example, the use of drugs to induce ovulation can lead to OHSS, which is characterized by ovarian enlargement and which, in serious cases, can be life-threatening. Infertility treatments, including both ART procedures and non-ART procedures in which medications are used to stimulate ovulation, are associated with an increased risk of multiple-order births, which carry health risks for women and infants and increased costs.[23]

Infertility treatment can also be expensive, and there are disparities in access to and use of services. The average cost of a single cycle of IVF in the United States has been estimated at more than $12,000.[28] Currently, 15 states have laws requiring that insurance policies cover some level of infertility treatment.[39] Clinics in states that do not mandate insurance coverage of IVF transfer more embryos on average and thus have higher rates of twin and triplet pregnancies than clinics in other states.[40] Economic, regional, and racial/ethnic disparities in access to and use of infertility services are clearly present.[37,38] Furthermore, even in states with more equitable access to care because of insurance mandates, racial/ethnic differences have been found in the rate of adverse health outcomes following infertility treatments.[38]

Improving the management of infertility requires additional research to 1) identify and reduce exposure to treatment regimens that pose increased risk for adverse outcomes, 2) address issues related to both the clinical and social ethics implications, as well as the financial costs of medically assisted reproduction, and 3) eliminate disparities in access to safe and effective treatment.

The Challenge

New safe and effective treatment strategies need to be developed, as well as research to improve the safety and efficacy of current regimens. These strategies include regimens for ovulation induction, adjuvant therapy for enhancing the success rates of IVF, regimens for preventing OHSS, methods for preserving the integrity of oocytes and embryos, lower-cost ART methods, and treatments for recurrent pregnancy loss. The safety and efficacy of the use of donors for infertility management (e.g., oocyte donation, oocyte cryopreservation, sperm donation, reproductive tissue donation, and gestational surrogacy) should be evaluated for donors, donees, and children conceived. In addition, the long-term effects of infertility treatments on adults—as well as on children conceived as a result of the treatment—need to be assessed.

Additional research is needed to improve the effectiveness of communication with diverse populations of women and men requiring medical intervention to conceive. Psychological and behavioral research could help improve our understanding of issues such as the effect of infertility on well-being and quality of life; psychosocial determinants (e.g., fertility goals) of service-seeking behavior; decision making around the issue of infertility and approaches for single adults and couples trying to have children; and the impact of multiple gestation and adverse pregnancy outcomes on parents and children.

Studies should examine the cost-effectiveness of different treatment methods (e.g., pharmaceutical management versus single embryo transfer versus higher-order embryo transfer), including the costs of patient outcomes (e.g., multiple births). These investigations could use insurance data as well as data from other sources. For example, with adequate protection of the security and confidentiality of the data, studies could use insurance and hospitalization datasets to monitor the costs related to treating infertility, including hospitalization costs, out-of-pocket expenses, and days of work lost.

Efforts are needed to determine the best methods for providing equitable access to infertility services among those in need while minimizing adverse and costly health outcomes, such as those associated with multiple births.

Infertility management practices would be improved by engaging public and private payers for those services, conducting cost analyses, and developing guidelines and recommendations for providers of infertility services. Guidelines should be based on scientific evidence on the safety and effectiveness of infertility services and treatments and should take into account multiple considerations. Some infertility services, such as gestational surrogacy and egg or sperm donation, raise complex ethical, legal, and social questions, including ones about coercion, payment for surrogates or donors, and ability to follow up with donors to assess possible long-term effects on their mental and physical health. These guidelines may also include counseling on alternatives for achieving parenthood (i.e., adoption) or choosing to live without children. It is essential to balance one thing—the appropriate use of infertility management technologies that allow extension of the age at which conception, carrying a pregnancy to term, and delivery may now be achieved—against another: public health and societal interests in preventing adverse health outcomes and excessive health care costs.

Scientific and Programmatic Opportunities

1. Monitor and evaluate the short- and long-term safety of infertility interventions.

Research and enhanced surveillance should focus on the safety, efficacy, and use of different infertility services and treatments for managing male and female infertility. These efforts would improve our understanding of the possible short-term effects of infertility treatment (e.g., OHSS) as well as the possible long-term effects of infertility treatment on men and women (regardless of the success of the treatment) and on any children conceived as a result of the treatment.

2. **Eliminate disparities in access to high-quality infertility services, including diagnosis, referral, and treatment.**

Efforts should focus on reducing disparities in access to, use of, and outcomes related to infertility services. Integration of infertility services into primary care settings that target underserved populations could help reduce the economic and racial disparities in access to infertility treatment.

3. **Promote the development, adoption, evaluation, and implementation of evidence-based guidelines and recommendations that address the prevention, diagnosis, and clinical management of infertility.**

Evidence-based guidelines and recommendations for providing infertility services should be further developed and promoted, and their use and impact should be evaluated. They should be based on scientific evidence and should be comprehensive in addressing the numerous—and often complex—issues that surround the management of infertility, including complications associated with infertility treatment (e.g., higher-order multiple births and OHSS), and bioethical and cost considerations.

4. Develop educational programs to increase awareness of the safety and effectiveness of treatments for infertility.

Efforts should be directed toward ensuring that health professionals engaged in the treatment of infertility have adequate resources and training to educate patients and the public about the benefits and risks of the infertility services available.

CONCLUSION

This National Public Health Action Plan for the Detection, Prevention, and Management of Infertility identifies many opportunities for minimizing the population burden of infertility, including its causes. The Plan highlights scientific and programmatic opportunities to strengthen the public health approach to detecting, preventing, and managing infertility. Decreasing the public health burden of infertility in the United States will require action by and collaboration among many partners, including federal, state, and local health and human services agencies, as well as the scientific community, health care providers, insurance providers, employers, industry, nonprofit organizations, consumer-based organizations, and individuals who are coping with infertility. Collaborative efforts among these parties should increase the efficiency with which opportunities identified in this report are addressed. The development of this plan is the first step toward improving our understanding of the causes, challenges, and adverse effects of infertility and its treatments.

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APPENDIX: SURVEILLANCE SYSTEMS AND OTHER SOURCES OF DATA

The following is a summary of surveillance systems and other sources of data that either currently collect, or could be augmented to collect, data relevant to infertility and reproductive health.

Behavioral Risk Factor Surveillance System

http://www.cdc.gov/brfss/index.htm

CDC coordinates the Behavioral Risk Factor Surveillance System, a state-based system of health surveys on health risk behaviors, preventive health practices, and health care access primarily related to chronic disease and injury. Data are collected monthly via telephone survey in the 50 states, the District of Columbia, Puerto Rico, the U.S. Virgin Islands, and Guam. States use the system's data to identify emerging health problems, establish and track health objectives, and develop and evaluate public health policies and programs.

Birth Records

http://www.cdc.gov/nchs/births.htm

CDC's National Center for Health Statistics cooperates with the states to maintain the National Vital Statistics System, a federal compilation of births and other vital statistics data. Birth certificates contain maternal and paternal information (e.g., education, race, and age) as well as information on the infant (e.g., birth date, plurality, sex, birth weight, congenital anomalies, and complications of labor and delivery). The 2003 revision of the standard birth certificate includes information on the use of infertility treatment and may become an important source of information on its maternal and child health correlates.

Infertility Prevention Project

http://www.cdc.gov/std/infertility/ipp.htm

CDC, in collaboration with the Office of Population Affairs, supports the national Infertility Prevention Project, which seeks to prevent sequelae leading to infertility by promoting and providing chlamydia and gonorrhea screening and treatment services for low-income, sexually active women attending a range of public health clinic settings. The surveillance component of this project gathers data on the number of chlamydia and gonorrhea tests performed, the basic demographics of the subject screened, the test characteristics (e.g., technology used and specimen type), and the context of the visit during which the test was administered. These data contribute to the preparation of CDC's annual *Sexually Transmitted Disease Surveillance* report.

National ART Surveillance System

https://www.artreporting.org/Scripts/Greeting.asp

In collaboration with the Society for Assisted Reproductive Technology, CDC supports the National ART Surveillance System, a Web-based system for reporting ART data. This surveillance system captures more than 95% of the estimated ART procedures performed annually in the United States. The system collects data on the client's medical history (such as infertility diagnoses), clinical data on the ART procedure, and data on resulting pregnancies and births.

National Health and Nutrition Examination Survey

http://www.cdc.gov/nchs/nhanes.htm;

CDC's National Center for Health Statistics began the National Health and Nutrition Examination Survey program as a series of surveys focusing on different population groups or health topics in the early 1960s; the surveys became a continuous program in 1999. The surveys use household and private interview methods each year to collect health and nutrition information on a nationally representative sample of non-institutionalized civilians. The health interview topics include current health status, medical conditions, reproductive health (i.e., pregnancy history, lactation, use of contraception, and men's and women's health conditions), health insurance coverage, use of health care services, lifestyle behaviors (including sexual, illicit drug, alcohol, and tobacco use behaviors), occupational history, and environmental exposure to chemicals.

Reports on Environmental Health

CDC's National Center for Environmental Health produced the *National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population 1999-2002* (http://www.cdc.gov/nutritionreport/), a first-of-its-kind report that provides a snapshot of the U.S. population's nutritional status by age, sex, and race/ethnicity. This report improves our understanding of the levels of biochemical indicators of diet and nutrition in the general U.S. population and in selected subpopulations, such as children, women of childbearing age, and minorities.

The National Center for Environmental Health also produced the *National Report on Human Exposure to Environmental Chemicals* (http://www.cdc.gov/exposurereport/), which uses biomonitoring (e.g., measurement of concentrations of chemicals or their metabolites in human samples, such as blood or urine) to provide an ongoing assessment of the U.S. population's exposure to environmental chemicals. Among the chemicals assessed are hormonally active agents, including bisphenol A, phthalates, pesticides, and persistent organic chemicals.

National Survey of Family Growth

http://www.cdc.gov/nchs/NSFG.htm

CDC's National Center for Health Statistics conducts the NSFG to collect national estimates of the prevalence of infertility and impaired fecundity, as well as estimates of the use of infertility services. The survey gathers information on family life, marriage and divorce, pregnancy, infertility, use of contraception, and men's and women's health. Survey results are used to plan health services and health education programs and to conduct statistical studies of families, fertility, and health. CDC's Division of Cancer Prevention and Control has recently added questions to the survey to help researchers investigate the associations between cancer history and various factors, including the use of infertility services. CDC's Division of STD Prevention has added questions on recent chlamydia screening to address adherence to current Infertility Prevention Project guidelines.

National Occupational Hazard Survey and National Occupational Hazard and Exposure Survey

http://www.cdc.gov/noes/

CDC’s National Institute for Occupational Safety and Health conducted the National Occupational Hazard Survey and the National Occupational Exposure Survey in 1972–1974 and 1981–1983, respectively. These surveys have been used extensively to identify substances of common exposure and are the only comprehensive assessments of general industry that estimate the number of workers potentially exposed to chemical agents. However, these databases are outdated and of limited use because they indicate only potential exposure.

Pregnancy Risk Assessment Monitoring System

http://www.cdc.gov/prams/

CDC and state health departments conduct the Pregnancy Risk Assessment Monitoring System, which collects state-specific, population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy. The goal of this system is to improve the health of mothers and infants by reducing adverse outcomes, such as low birth weight, infant mortality and morbidity, and maternal morbidity. Data collection in selected states now includes use of infertility treatment; these data may provide additional useful information on the association of infertility and infertility treatment with adverse perinatal health outcomes.

STD Surveillance

http://www.cdc.gov/std/stats/

In compiling its annual *Sexually Transmitted Disease Surveillance* report, CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention receives case report data for nationally notifiable STDs (i.e., chlamydia, gonorrhea, and syphilis), which are collected and compiled by the STD control programs and health departments in all 50 states, the District of Columbia, selected cities, U.S. dependencies and possessions, and independent nations in free association with the United States. Because of incomplete diagnosis and reporting, the number of STD cases reported to CDC is less than the actual number of cases occurring in the U.S. population. CDC also collects data from projects that monitor STD prevalence in various settings, including regional Infertility Prevention Projects, the National Job Training Program, the Indian Health Service, the STD Surveillance Network, the Gonococcal Isolate Surveillance Project, and national surveys carried out by federal and private organizations. The annual *Sexually Transmitted Disease Surveillance* report serves as a reference document for policy makers, program managers, health planners, researchers, and others who are concerned with the public health implications of these diseases.