A public health focus on infertility prevention, detection, and management

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In 2002, 2 million American women of reproductive age were infertile. Infertility is also common among men. The Centers for Disease Control and Prevention (CDC) conducts surveillance and research on the causes of infertility, monitors the safety and efficacy of infertility treatment, and sponsors national prevention programs. A CDC-wide working group found that, despite this effort, considerable gaps and opportunities exist in surveillance, research, communication, and program and policy development. We intend to consult with other federal agencies, professional and consumer organizations, the scientific community, the health care community, industry, and other stakeholders, and participate in the development of a national public health plan for the prevention, detection, and management of infertility. (Fertil Steril[®] 2008; \blacksquare : \blacksquare . ©2008 by American Society for Reproductive Medicine.)

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The desire to have children is powerful and widespread, but for a sizeable minority it is not easily fulfilled. Challenges to fertility arise from genetic abnormalities, infectious or environmental agents, delayed childbearing, behavior, and certain diseases. Awareness of the potential risks may lead some people to adopting corrective behaviors and maintain fertility. Many people, however, find themselves coping with infertility. The journey for those people who are infertile may begin with unrecognized health problems; continue with difficulties in obtaining services that often are not covered by health insurance; and even after success with physically demanding and expensive medical procedures, it may lead to unexpected adverse effects on the health and quality of life of the patients and their children. Each step of this journey is characterized by interactions among the physical

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Reprint requests: Maurizio Macaluso, M.D., Dr.P.H., Division of Reproductive Health, Centers for Disease Control and Prevention, Mailstop K-34, 4770 Buford Highway, Atlanta, GA 30341 (FAX: 770-488-6391; E-mail: mmacaluso@cdc.gov). and social environment, the biological background and behavior of individuals, and the health care system. On the population scale, these interactions create patterns of disease, utilization of services, and outcomes that are increasingly a topic of public debate. The range of issues raised by the debate includes identifying and managing risk factors for infertility, addressing racial and economic disparities in access to care, addressing the ethical and financial implications of medically assisted reproduction, and assessing the risks and benefits of such technologies. The purpose of this article is to outline the reasons why infertility is a public health concern and open a discussion about the role that the public health community can play in addressing the problem. This article is not intended to propose specific solutions but to propose a list of topics that should be discussed in a forum open to scientists in academic institutions, industry, and government agencies; health care professionals and their organizations; individuals and couples who are coping with infertility and their advocacy groups; and the general public. We hope that the article, and the discussion that it sparks, will create the momentum necessary to develop a national plan for infertility prevention, detection, and management. The broad objectives of such a plan include the reduction of the burden of infertility and impaired fecundity and the improvement of the quality of life of Americans who live with infertility, through better diagnosis, safe and effective treatment of infertility, and improved access to these services.

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INFERTILITY: AN EMERGING PRIORITY

Challenges to human fertility may arise from many conditions caused by genetic abnormalities, infectious or environmental agents, and certain behaviors. Natural aging processes also place a limit to human fertility. For some individuals, the fertility window closes earlier than expected. Recent trends toward postponing age at first pregnancy have highlighted the natural limits of fertility and accelerated the development and use of medical technology to overcome such limits. The proportion of first births to women aged 30 years and older has increased more than fourfold since 1975, from 5% to 24% in 2006. The absolute number of these births increased from more than 69,000 to approximately 405,000 during this period (1, 2). Although some perceive infertility as a qualityof-life issue, the American Society for Reproductive Medicine (ASRM) regards infertility as a disease (3). A U.S. Supreme Court opinion agreed with a lower court statement that reproduction is a major life activity and confirmed that conditions that interfere with reproduction should be regarded as disabilities, as defined in the Americans with Disabilities Act (4).

Prevalence

According to data from the National Survey of Family Growth (NSFG), in 2002 an estimated 7.3 million American women aged 15-44 years had impaired fecundity (i.e., had experienced difficulties conceiving or bringing a pregnancy to term during their lifetime) (5). Two million couples in the United States were infertile (i.e., had not conceived during the previous 12 months despite trying) (5). Although the focus of research and services has traditionally been on women (and, as a consequence, much of this article reflects it), fertility impairments may be just as common among men (6). The statistics cited above distinguish impaired fecundity from infertility. In this article we refer to infertility more broadly, including all fertility impairments. Recurrent pregnancy loss (miscarriage) is a component of impaired fecundity, distinct from infertility (ASRM, unpublished data) and is not included in this presentation.

Societal and behavioral shifts in the last quarter of the 20th century may have affected levels of infertility, although it is unclear whether the prevalence of fertility impairments has changed over time (7). In part because "baby boomers" (i.e., the generation born between 1946 and 1964) have steadily postponed the age at which they choose to conceive their first child, and in part because new technologies have made it possible for some couples to overcome infertility and have made news with spectacular outcomes such as high-order multiple births (8), Americans are increasingly aware of and concerned about infertility. It is unclear whether infertility disproportionately affects less privileged people in the United States. Although data from the NSFG do not show large disparities in infertility (5), social and racial disparities in health status and in the frequency of certain risk factors (e.g., sexually transmitted infections that may lead to infertility if untreated) would suggest that preventable causes of infertility disproportionately affect the less privileged. A recent report from the Coronary Artery Risk Development in Young Adults (CARDIA) study indicates that among non–surgically sterile women, African American women had a twofold increase in odds of reporting a history of infertility (9). Financial barriers limit access to diagnosis, evaluation, and treatment and may lead to selectively underestimating the frequency of infertility in the same population groups (10). Thus, it is difficult to interpret the available data. On the other hand, delaying childbearing may be more common among professionals and other higher-income groups, making these groups more vulnerable to the cumulative effect of causes of infertility, including the effect of aging. Different subgroups may have infertility of different etiology.

Causes and Prevention

We do not know what proportion of the infertility burden can be prevented, but it may be substantial. For example, tubal infertility affects 18% of the couples who try to overcome infertility by using assisted reproductive technology (ART) (11) and is typically the consequence of chronic pelvic inflammatory disease (PID), which can lead to tubal scarring. The latter can be prevented by early detection and treatment of sexually transmitted infections and, in particular, chlamydia infection (12). More than 1 million chlamydia cases are reported to the CDC annually (13). In 2006, reported chlamydia rates were eight times higher among African Americans than among whites, highlighting the large disparities in this important risk factor for infertility (13).

Other modifiable factors contribute to the burden of infertility. Although the proportion of male factor infertility due to varicocele is unknown, this common condition is reported in approximately half of the inpatient surgery services and approximately two thirds of office visits for male factor infertility in the United States (14). Varicocele is easily treated, although the impact of treatment on subsequent fertility is unclear (15). Environmental and occupational hazards account for an unknown proportion of infertility but are suspected causes of declining human sperm quality in industrialized countries (16). Although approximately 84,000 chemicals are in the workplace (2,000 new chemicals every year), information on reproductive toxicity is available only for a few thousand. A consensus workshop sponsored by The National Toxicology Program identified 43 chemicals and prioritized the need for field studies on the basis of available toxicology and numbers of workers potentially exposed (17). For example, it was estimated that more than 2 million workers are potentially exposed to the solvent 2-butoxy ethanol (17). The prioritized list was incorporated into the National Occupational Research Agenda (18). There is also increasing evidence that lifestyle factors, such as tobacco smoking and obesity, which cause chronic disease and disability later in life, can cause fertility impairment during the reproductive years (19, 20). The Surgeon General's Report on the Health Consequences of Smoking highlights numerous adverse reproductive effects of tobacco smoking, including infertility (21, 22). In women, tobacco smoking is associated with decreased fecundability (probability of conception in a month) in a dose-dependent fashion (23), with ovulatory dysfunction (24), and with early menopause (25, 26). Although the evidence is less consistent than with female infertility, among men, tobacco smoking is associated with lower volume of the ejaculate, lower sperm density, and worse morphology of the spermatozoa (27). Although the proportion of infertility that is due to tobacco smoking is unknown, infertility specialists are increasingly aware that exposure to tobacco products can cause infertility and interferes with its treatment (28) and that tobacco screening and cessation is an important component of infertility care (29). The metabolic disorder associated with the polycystic ovary syndrome has highlighted the link between overeating, insulin resistance, and the endocrine changes that reduce fertility in women with polycystic ovary syndrome (20). Obesity is associated with ovulatory and menstrual dysfunction and subsequent infertility, increased risk of miscarriage, and decreased effectiveness of ART (30). Obesity in men is associated with erectile dysfunction and decreased androgen production, but its effects on male fertility are not as clear (30).

In addition to infertility due to environmental exposures, specific medical conditions, and behaviors, fertility impairments resulting from the treatment of diseases may also be successfully addressed. For cancer, the negative effects of specific chemotherapy and radiation on fertility are well known. Thus, cancer patients need to be informed about the reproductive consequences of treatment and about options available to address them, such as sperm banking, relocation of the ovary away from the radiation field, or oocyte or embryo cryopreservation before the initiation of treatment (31-33). Other therapeutic interventions, including highly active antiretrovirals used for the treatment of individuals infected with HIV, may also interfere with reproduction (34, 35). Available ART procedures offer the promise of maintaining the ability to procreate among individuals who cope with life-threatening diseases and may experience infertility as a side effect of treatment.

A public health strategy focusing on primary prevention (e.g., through removal of risk factors for infertility such as those described above) would reduce the prevalence of infertility, improve health and quality of life, and avert the costs of infertility treatment, including the downstream costs produced by adverse outcomes of such treatment on mothers and children. For some causes of infertility, primary prevention is feasible. Chlamydia screening in women, preventing initiation of cigarette smoking in adolescents, facilitating smoking cessation among adults, and promoting physical activity and a healthy diet are all clinical services with proven efficacy and cost-effectiveness (37, 38), although their possible impact on infertility is yet to be determined. The public health community can play an important role by disseminating information, by advocating for the adoption of effective interventions by public health program and health care services, and by monitoring effectiveness through surveillance. Whereas primary prevention is important, infertility diagnosis and treatment are relevant to public health in their own merit. First, infertility is an area where health care costs are borne most often by the individual, creating significant economic and racial disparities. Second, early diagnosis and treatment of underlying medical conditions (secondary prevention) may lead to effective restoration of fertility. Third, infertility treatment, although generally safe, is associated with adverse health outcomes for the mother and the child; epidemiologic surveillance efforts are increasingly necessary to design and implement tertiary prevention programs (i.e., the prevention of adverse outcomes of infertility treatment). Finally, the treatment of infertility, as well as some of its outcomes, contributes to increasing the cost of health care for all.

Approaches to Infertility Treatment

According to the NSFG, in 2002 7.3 million, or 12% of women of childbearing age in the United States had ever received infertility services (including counseling and diagnosis) in their lifetime. More than 1.1 million women sought medical help to get pregnant in the previous year (5). Of these, approximately 74% received counseling, 59% underwent some testing, 46% received drug treatment, 13% underwent IUI, and 8% underwent surgery for blocked tubes, whereas 3% used ART (39).

Assisted reproductive technology has been used in the United States since 1981 to help women become pregnant, most commonly through IVF of human eggs followed by transfer of the embryos into the woman's uterus (11). Data from the National ART Surveillance System (NASS) indicate that in 2005 134,242 ART cycles were performed at 422 reporting clinics in the United States, resulting in 38,910 deliveries of one or more living infants and 52,041 infants (40). Although use of ART is still relatively rare as compared with the potential demand, use has doubled over the past decade, and ART-born infants now account for more than 1% of all U.S.-born infants and 18% of all multiple births (41). This proportion is larger in states where statutes mandate insurance coverage of infertility treatment (42).

The NSFG data reported above indicate that infertility treatment other than ART, such as ovarian stimulation followed by natural conception or IUI, is much more common than ART. Although the scientific literature indicates that the efficacy of these treatments is lower than that of ART (pregnancy rates generally below 15%; for a review of trials of ovarian stimulation and IUI, see reference 43), their higher frequency makes it likely that just as many or more children are conceived through these forms of infertility treatment. There is no population-based information on the success rates or on the adverse health outcomes that are associated with non-ART approaches to infertility treatment (39).

Fertility assistance may be necessary not only for couples who live with infertility but also for fertile couples for whom natural conception may pose health risks, such as HIV-discordant couples or those affected by cancer. Whereas there is

recognition that denying fertility services to such persons would be unethical (36), there is not yet a broad consensus as to which assisted reproduction procedures should be offered.

Adverse Outcomes of Infertility Treatment

Although infertility treatment, including ART, is generally safe, adverse outcomes have been described both in women undergoing ART and in infants born from these procedures (44). Ovarian hyperstimulation syndrome is a rare but very serious adverse effect of ART and ovarian stimulation (45). Multiple-gestation pregnancies are much more common after infertility treatment than after natural conception and increase the risk for maternal complications (46, 47). Multiple-birth infants are at increased risk for low birth weight, preterm delivery, infant death, and disability among survivors (46–51). Recent systematic reviews of the literature (52, 53) indicate that ART-conceived singletons also face increased risks for low birth weight, very low birth weight, preterm delivery, and fetal growth restriction. These findings have been confirmed in population-based studies in the United States (8, 54). For infertile women who have a good prognostic profile (i.e., a high expected probability of success with ART), perhaps the simplest and most effective strategy for reducing the risk of adverse ART outcomes is elective single embryo transfer (SET). Clinical trials have shown that a protocol consisting of a SET cycle, followed by a second SET cycle if the first fails, is associated with a cumulative probability of success that is similar to that of a single conventional ART cycle in which two embryos are transferred simultaneously (55-58). The SET protocol, however, carries a much lower risk of multiple delivery, with consequently lower risk of adverse maternal and child health outcomes (59). The cost-effectiveness of SET is not as clear for patients with less-than-optimal prognosis (60). More research is needed to understand the causes of adverse consequences unrelated to multiple ET, and the long-term effects of infertility treatment on infertile women and their children (44). As the number of young women who donate oocytes for use in ART is increasing, the potential health consequences of participation in these programs need to be evaluated. Economic and racial disparities may be present not only in the frequency of infertility impairment or access to treatment but also in treatment outcomes (61).

Costs

Given that one IVF cycle costs, on average, more than \$12,000 (62), IVF continues to generate controversy and debate, including questions about its cost-effectiveness, about the impact of maternal age and multiple births on cost, and about the extent of disparities in access to infertility services (63). On the other hand, the financial impact of involuntary childlessness, including the cost of treating depression and decreased work productivity, has not been fully evaluated (64). In addition to uncertainties about the financial impact of infertility and its consequences, there are inadequate data on the total direct costs of infertility treatment. These include not only the expenses associated with diagnosis and treatment but also those associated with maternal and infant outcomes, including some longer-term disability costs associated with multiple gestation, preterm delivery, and low birth weight. Lack of insurance coverage in many states makes the couple directly responsible for paying for the initial assessment and subsequent treatment, and out-of-pocket expenses for care that is not covered by insurance are more difficult to track than expenses that lead to insurance claims. By contrast, the cost associated with pregnancy and maternal and child health outcomes is covered by most health insurance policies and can be documented more accurately. According to preliminary calculations, which are likely to underestimate the true value, the cost of diagnosing and treating infertility and its sequelae exceeds \$5 billion per year.* Clearly, the cost would be higher if all couples affected by infertility sought care and treatment (65). Research into the cost-effectiveness of interventions for the primary prevention of infertility is developing rapidly (66-70). Any increase in the utilization and cost of infertility diagnosis and treatment services that may occur in the future will likely increase the cost-effectiveness of primary prevention interventions.

Alternatives to Treatment of Infertility

Whereas infertility treatment most often provides couples with the means to have their biological children, surrogacy, adoption, and child-free living are important alternatives. The risks, benefits, and costs of these alternatives are not immediately clear, and decision-making involves serious emotional responses. Consumers cannot easily find objective information on these topics, and the same racial and social disparities that affect access to treatment also affect access to information on alternatives to treatment. A public health approach to managing infertility should promote integration of counseling services on adoption and child-free living with the medical counseling of infertile couples.

Infertility as a Global Issue

Although the focus of this article is on infertility in the United States, the problem of infertility is global (71). Because the global focus of public health policies and programs has justifiably been on containing population growth and providing affordable, safe, and effective family planning services, the inability to procreate has not traditionally made it to the top

^{*}To compute a preliminary estimate of these costs, we used the annual numbers of infertility visits and non-ART treatment procedures estimated by the NSFG, the annual number of male infertility visits and ambulatory surgery visits for varicocele estimated by Meacham et al. (9), and the number of ART cycles registered in the NASS, the average costs per non-ART infertility treatment procedure reported in a large commercial database (Medstat; Thomson Reuters, New York, NY), and the estimate of the cost for ART cycles published by the ASRM. We also assumed that the number and distribution of term and preterm live-born infants were the same for ART and non-ART infertility treatment and applied the total medical care costs during the first 5 years of life associated with preterm and non-preterm live-born children estimated by the Institute of Medicine (40).

of the priority list in many developing nations. The Demographic and Health Surveys program estimates that 167 million ever-married women aged 15–49 years in developing countries (excluding China) were infertile in 2002 (72). Infertility rates exceed 30% in sub-Saharan Africa (72). In many countries the demand for infertility treatment and assisted reproduction is increasing with economic development.

Legal, Policy, and Ethical Issues

Infertility, like reproductive health in general, has multiple dimensions, ranging from the biomedical to the social. Associated legal aspects encompass reporting of outcomes, program management, insurance coverage, government funding of services, clinic and laboratory operation, and public health research (73). The President's Council on Bioethics recently concluded a thorough evaluation of technologies that affect the beginning of life and found that, although the fields of assisted reproduction, human genetics, and embryo research increasingly are converging, no comprehensive systems exist for ascertaining the impact of these technologies, and their practice is largely unregulated (74). On the other hand, some physicians in this field already feel under excessive scrutiny because special laws and regulations mandate embryology laboratory registration and accreditation and the reporting of procedures performed, in addition to the usual certification and licensing requirements common to other medical specialties. Laws and regulations addressing infertility will inevitably change at both federal and state levels to respond to new challenges. It is important for the public health community to engage stakeholders in examining the scientific evidence about the prevention, diagnosis, and management of infertility and work toward addressing significant gaps.

UNMET NEEDS AND OPPORTUNITIES FOR PUBLIC HEALTH ACTION

Several federal agencies carry out programs to address infertility, and state and local health departments play an important role. The CDC is fully engaged in infertility prevention and control (also see the Appendix): it conducts the National Survey of Family Growth; maintains the NASS, publishes the Annual ART Success Rates Report, and conducts research on ART; and studies the links between infertility treatment and birth defects, neurodevelopmental outcomes, and autism. It also maintains the National Biomonitoring Program, publishes The National Report on Human Exposure to Environmental Chemicals, carries out research on workplace hazards that may have effects on reproduction; studies the link between infertility and chronic disease; and supports the National Infertility Prevention Program, which funds chlamydia and gonorrhea screening and treatment services for low-income, sexually active young women throughout the United States. Despite the range and depth of these activities, a survey of the key areas of surveillance and epidemiologic research, prevention research, program development and evaluation, and public education reveals considerable

gaps and opportunities that public health agencies could address with appropriate resources. The CDC has the necessary range of expertise and established relationships with a number of government agencies, professional organizations, and advocacy groups that are potential stakeholders to develop a comprehensive plan for infertility prevention, detection, and management. The following, not necessarily in order of importance, are key areas where we recognize unmet needs or significant gaps, and represent opportunities for strengthening infertility prevention and management.

Surveillance

Current surveys and surveillance systems address important aspects of infertility but are deficient in multiple areas. Whereas current systems provide general population-based estimates of the prevalence of infertility, they do not provide estimates of the prevalence of particular types of infertility (e.g., tubal-factor infertility caused by infections). Racial, ethnic, and economic disparities in access to diagnosis and treatment are difficult to address and may lead to underestimating the burden of infertility in minorities, especially given the huge disparities in underlying factors such as gonorrhea and chlamydia infection. Because disparities in access to treatment may lead to additional disparities in health and quality of life, current systems may lead to a biased assessment of the overall impact of infertility in less-privileged groups. In addition, the emphasis of current systems on infertility in women limits our ability to assess the burden of infertility in men. There is even less adequate information on the role of common environmental, nutritional, behavioral, and lifestyle risk factors in infertility that can be obtained from population-based surveys or surveillance data. With respect to treatment and treatment outcomes, whereas current systems provide adequate estimates of the success rates of ART, there are no surveillance systems to measure the success rates of non-ART infertility treatments and no systems for measuring the adverse impact of any type of infertility treatment on maternal and child health outcomes.

Ongoing data collection systems need to be developed, maintained, and expanded to obtain valid population-based measures of the burden of infertility in women and men and to better understand sociodemographic, environmental, and behavioral correlates of infertility. This can be accomplished at least in part by strengthening and expanding existing data collection systems like the NSFG and the NASS. Infertility may also be a new focus of ongoing epidemiologic data collection systems, such as the Behavioral Risk Factors Surveillance System and the Pregnancy Risk Assessment and Monitoring System, which may provide more information on behavior and health outcomes. Information available through the 2003 revision of the birth certificate, which includes information on types of infertility treatment, needs to be evaluated and may become an important source of information on maternal and child health correlates of infertility treatment. New data collection systems may be needed to achieve

better coverage of specific population groups and issues. Ad hoc surveys may be needed to obtain qualitative and quantitative data relating to morbidity, treatment, outcomes, psychosocial impact, practice patterns, knowledge, behaviors, and attitudes. Data from these surveys need to be analyzed to understand whether combining the information gathered in these surveys can provide a more complete picture of infertility in the United States. Finally, appropriate mechanisms need to be put in place to maximize dissemination and utilization of surveillance data.

Research Issues

In-depth research studies are necessary to address some of the same issues that would be desirable to evaluate at the population level using surveillance systems. In the area of primary prevention, research into modifiable causes of infertility should be given high priority. Research is needed to elucidate the mechanisms through which specific medical conditions lead to infertility, given that detection and early treatment of these conditions may prevent infertility. Although the causal role of sexually transmitted diseases (STDs) on tubal infertility is well established, and randomized trials document that chlamydia screening prevents PID, how much the chlamydia screening program has impacted infertility is unclear. There is no information on whether interventions and programs aimed at reducing the prevalence of tobacco smoking and improving nutrition and physical activity have an impact on the prevalence of infertility. Finally, the link between infertility and chronic diseases and their treatment needs to be fully elucidated.

In the area of secondary prevention, there is inadequate information on the potential risks and benefits of early detection of fertility impairment (i.e., detection of conditions leading to infertility among individuals who are not trying to conceive or for individuals who are contemplating conception). Whereas the benefits of early detection may arise, for example, from increasing the probability of treatment success by detecting infertility at a younger age, an individual who does not intend to have a child may experience negative psychological effects of the awareness of a diagnosis that does not immediately represent a limitation and may not necessarily predict infertility in the future. Research is needed to evaluate the potential benefit of early detection and treatment of conditions leading to infertility, both among couples who are actively seeking a pregnancy and among individuals who may want a child in the future.

In the area of clinical outcomes research and tertiary prevention, there are few and limited economic studies assessing the cost-effectiveness of infertility treatment, the financial impact of treatment options, and the effect of insurance coverage on access to treatment and treatment outcomes. Because the promotion of elective SET may lead to a substantial reduction in the adverse effects and health care costs of ART-related multiple gestation, it is important to clarify the extent to which this practice can be proposed to patients with a variety of prognostic profiles and to identify biochemical and morphologic characteristics of oocytes and embryos that predict successful implantation and ultimately the birth of a healthy child. This research is critically needed to provide evidence in support of recommendations for the practice of infertility treatment and minimize the frequency and severity of adverse outcomes.

In the area of communication, there is very limited information on the needs and options for special populations who may seek infertility treatment or ART, such as cancer survivors, HIV-positive persons, and persons with known genetic conditions. There is essentially no information on the effect that disseminating information about fertility preservation and treatment options would have on attitudes, knowledge, and behavior among special populations.

These research themes need to be incorporated in the strategic research plans of governmental agencies and nongovernmental organizations and require a blend of basic science, clinical, and epidemiologic investigations and behavioral and social science research.

Programs, Policies, and Systems

A preliminary survey of current programs and policies at the national and state level reveals that there is no coordination of national and state-based surveillance efforts, that there is no national strategy for integrating infertility diagnosis and treatment in reproductive health services, including preconception care, and that insurance coverage varies greatly across states. In addition, there are no comprehensive guidelines on what information and counseling should be provided to infertile couples on issues ranging from prevention to the risks and benefits of treatment, adoption, and child-free living. Finally, there is only limited discussion of the impact that ethical and legal issues surrounding infertility treatment may have on public health policies and programs.

There is increasing awareness by the public, media, and policy makers that infertility and its management are important problems that Americans face today; but there is no comprehensive national plan to address the problem of infertility. A national plan would offer the opportunity to strengthen existing prevention programs and propose new strategies based on an understanding of preventable risk factors, as well as the opportunity to systematically review definitions and to identify gaps in diagnosis and treatment guidelines. For a national plan to be truly comprehensive and effective, it would have to be evidence based, consensus driven, and developed and promoted by a coalition of stakeholders.

Decision makers at all levels of government need to be informed and advised about needs and priorities in the areas of surveillance, research, and health care and about evidencebased strategies for addressing infertility. Policy to guide surveillance and research should pave the way for the development of prevention and management strategies. Systems and policies to facilitate the translation of research results

into prevention programs need to be developed. Programmatic and policy implications of surveillance and research results need to be considered and acted on as appropriate.

Professional organizations need to take the lead in the development of evidence-based practice guidelines, and the health care insurance system needs to be engaged in addressing specific forms of infertility or underlying conditions that require appropriate preventive care, diagnosis, and treatment.

Once comprehensive infertility prevention and management programs are developed, efforts need to be coordinated to ensure that they reach the people who most need them. Adherence to current recommendations to prevent infertility (e.g., screening and treatment of sexually transmitted infections that result in infertility, treatment of sexual partners, and promotion of primary prevention methods such as condom use) needs to be promoted by all stakeholders, including community organizations. Enhancement of scientific and programmatic capacity by states, territories, and tribal governments may be needed to enable health agencies to build the necessary coalitions and partnerships for translating research into public health programs, practices, and services for those who are at risk of, or suffering from, infertility.

Communication and Education

The implementation of a national plan needs to include a strong communication and public education program, targeting policy makers, providers, and the public. Evidencebased practice guidelines on the prevention, diagnosis, and treatment of infertility and on patient counseling need to be promoted to all health care providers. Appropriate training opportunities and aid materials should be developed and marketed. Adherence to current recommendations that help prevent infertility (e.g., screening and treatment of sexually transmitted infections that result in infertility) needs to be promoted and monitored. Evidence-based messages to inform the general public about the frequency, causes, signs, and consequences of infertility need to be disseminated. The general public needs to be educated on strategies that minimize the risk of infertility. Populations at risk for infertility and poor pregnancy outcomes need to be educated on their reproductive risks and options. Discussions about infertility need to be encouraged to reduce stigma, and appropriate messages should promote attitudes and behavior that facilitate early access to infertility diagnosis and treatment. Evidence-based recommendations on diagnostic and treatment options for couples and individuals need to be appropriately worded, made accessible, and disseminated. The dissemination of public information on the options for infertility management, including adoption and child-free living, needs to be explored. The communication program should expedite the dissemination of new research findings to the general public. The feasibility of integrating infertility education into existing national reproductive health education programs needs to be explored.

DEVELOPING A NATIONAL COMPREHENSIVE PUBLIC HEALTH PLAN FOR INFERTILITY PREVENTION, DETECTION, AND MANAGEMENT

The following is a list of possible aims that a broad coalition of stakeholders should consider in developing a national plan:

- To reduce the burden of infertility and reduced fecundity in the United States
 - o By promoting behaviors that maintain fertility
 - o By promoting prevention, early detection, and treatment of infections (such as chlamydia) and other medical conditions that lead to infertility
 - o By removing or reducing environmental threats to fertility
- To improve access to the diagnosis and treatment of infertility and eliminate disparities in infertility care
- To improve the efficacy and safety of infertility treatment
- To improve the quality of life of Americans who live with infertility

Engaging Partners and Mobilizing Support

Whereas public health agencies like the CDC and state and local health departments may respond to the challenges outlined above, developing a coherent national plan requires a broader range of stakeholders to set priorities and identify the resources necessary to make the plan effective. The CDC may play a role in facilitating the development of a national action plan, but ultimately it will be a broad coalition of interests that will own and implement the plan. Collaborative partnerships enable the CDC to tap into outside knowledge and expertise, address challenging public policy issues, and reach new populations. In the area of infertility, the potential partners of the CDC include other federal agencies, the scientific community, the health care community, insurance providers, employers, industry, advocacy groups, the general public, and of course, people who are coping with infertility. Ensuring that all of these partners' voices are heard can be difficult but is necessary to achieve success.

Setting Priorities

A coalition of public and private sector organizations working together needs to identify opportunities and set priorities for reducing the burden of infertility in the United States. The development of a comprehensive plan requires a coordinated, multidisciplinary approach to address infertility, from primary prevention to treatment and support.

Successful strategies to define and reach target groups (such as individuals at risk of developing infertility, or infertile patients) require the development and promotion of improved protocols, guidelines, and evidence-based practices, as well as rigorous evaluation of demonstration projects. It is incumbent upon policy makers, program planners, and consumers facing infertility to ensure the translation and application of research findings and population-based implementation of best practices nationwide.

Further development of public health and clinical interventions demands a partnership between public and private entities. Such system changes may be accomplished through formal and informal means—through laws, regulations, and community "standards of practice," as well as by altering the economic, social, and physical environment.

CALL FOR ACTION

The CDC will strengthen its effort to address infertility by engaging other federal agencies, professional and consumer organizations, industry, and the community at large in the development of a national public health plan for the prevention, detection, and management of infertility. The findings and recommendations contained in this article can serve as a platform to stimulate discussion. The national plan will identify public health priorities and recommend integration of existing programs and initiatives, as well as creation of new programs as deemed necessary. It will also outline plans for promoting the necessary changes in law and policies, in public health surveillance and research, and in the organization and financing of public health programs and health care systems. As a first step, the CDC invited potential partners from the public, private, and nonprofit arenas to participate in a Public Health Symposium on Infertility held in Atlanta on September 15-16, 2008. About 60 individuals from federal agencies, organizations representing local public health agencies, professional organizations, consumer organizations and other NGOs attended the meeting. The symposium ended with a collective intent to continue the conversation, form working groups on specific topics, and develop a draft national action plan.

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APPENDIX

Current Public Health Efforts Addressing Infertility at the CDC

The National Center for Birth Defects and Developmental Disabilities studies the links between infertility treatment and birth defects (in the National Birth Defects Prevention Study), infertility treatment and neurodevelopmental outcomes (using registry data from Denmark), and infertility treatment and autism (through the Study to Explore Early Development) (http://www.cdc.gov/ncbddd/bd/research).

The National Center for Chronic Disease Prevention and Health Promotion maintains the National ART Surveillance System and publishes the Annual ART Success Rates Report; maintains the Pregnancy Risk Assessment Monitoring System, which collects state-specific, population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy; collaborates with state health departments in the evaluation of adverse outcomes of ART; and conducts research on the effectiveness and safety of ART and on the link between infertility and chronic disease (http://www.cdc.gov/ reproductivehealth). It also implements the National Action Plan for Cancer Survivorship: Advancing Public Health Strategies, which specifically mentions infertility as a concern of cancer survivors, and recognizes the need for fertility preservation in this group (http://www.cdc.gov/cancer/survivorship/ what_cdc_is_doing/action_plan.htm).

The National Center for Environmental Health maintains the National Biomonitoring Program, which evaluates people's environmental exposures by measuring toxic substances or their metabolites in human specimens and publishes *The National Report on Human Exposure to Environmental Chemicals* (http://www.cdc.gov/exposurereport/). The National Center for Environmental Health also improves the technology for laboratory testing of steroid hormones to facilitate research and clinical assessment of conditions leading to infertility, and carries out research on the impact of pesticides, hormonally active agents, and other environmental/).

The National Center for Health Statistics conducts the National Survey of Family Growth (NSFG), which gathers information on family life, marriage and divorce, pregnancy, infertility, use of contraception, and men's and women's health. The NSFG is the only population-based source of information on the prevalence of infertility and receipt of infertility services other than ART (http://www.cdc.gov/nchs/ NSFG.htm). The National Center for Health Statistics also maintains the National Vital Statistics System (http:// www.cdc.gov/nchs/nvss.htm). The 2003 revision of the birth certificate includes questions on infertility treatment in the risk factors section. As of today, 19 states have incorporated these questions in their birth certificate.

The National Center for HIV/AIDS, Hepatitis, Sexually Transmitted Diseases and Tuberculosis Prevention supports the National Infertility Prevention Program, which funds and coordinates chlamydia screening and treatment services for low-income, sexually active young women attending family planning, STD, and other women's health care clinics (http://www.cdc.gov/std/infertility/ipp.htm). In addition, the Center supports prevention of gonorrhea, another important cause of PID, develops and publishes guidelines that identify the most effective STD treatments, monitors rates of these PID-causing infections, and facilitates treatment of sexual partners exposed to infection (http://www.cdc.gov/std).

The National Institute of Occupational Safety and Health has developed and implements the National Occupational Research Agenda, which includes a reproductive health component and carries out specific research on workplace hazards that may have effects on reproduction, including studies on cohorts of employees exposed to specific chemicals (boron, phthalates, Bisphenol-A, 1- and 2-bromopropane, methoxychlor, pesticides) and studies on the reproductive health of working men and women (http://www.cdc.gov/niosh/nora). The National Institute of Occupational Safety and Health also participates in the National Birth Defects Prevention Study, which studies the link between parental exposure and child outcomes.