



## Complete Summary

---

### GUIDELINE TITLE

Pregnancy outcomes after assisted reproductive technology.

### BIBLIOGRAPHIC SOURCE(S)

Allen VM, Wilson RD, Cheung A, Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada, Reproductive Endocrinology Infertility Committee. Pregnancy outcomes after assisted reproductive technology. J Obstet Gynaecol Can 2006 Mar;28(3):220-50. [117 references] [PubMed](#)

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
QUALIFYING STATEMENTS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
DISCLAIMER

## SCOPE

### DISEASE/CONDITION(S)

Pregnancy outcomes after assisted reproductive technology, including:

- Obstetrical complications
- Adverse perinatal outcomes
- Multiple gestations
- Structural congenital abnormalities
- Chromosomal abnormalities
- Imprinting disorders
- Childhood cancer

### GUIDELINE CATEGORY

Counseling  
Evaluation  
Screening

### **CLINICAL SPECIALTY**

Family Practice  
Medical Genetics  
Obstetrics and Gynecology  
Pediatrics

### **INTENDED USERS**

Advanced Practice Nurses  
Physician Assistants  
Physicians

### **GUIDELINE OBJECTIVE(S)**

- To review the effect of assisted reproductive technology (ART) on perinatal outcomes, to provide guidelines to optimize obstetrical management and counselling of Canadian women using ART, and to identify areas specific to birth outcomes and ART requiring further research
- To compare perinatal outcomes of ART pregnancies in subfertile women to those of spontaneously conceived pregnancies. Also, perinatal outcomes are compared between different types of ART

### **TARGET POPULATION**

Women using assisted reproductive technology

### **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Genetic/clinical counseling
2. Genetic testing for alterations in genes associated with cystic fibrosis (as indicated)
3. Ovarian stimulation
4. Provision of patient information concerning:
  - Increased risks and interventions associated with pregnancy after undergoing assisted reproductive technology (ART)
  - Psychosocial implications of ART
  - Options for prenatal screening
5. Prenatal diagnosis (chorionic villus sampling, amniocentesis)
6. Biochemical and sonographic screening
7. Long-term follow-up to evaluate the prevalence of imprinting disorders and cancers associated with ART

### **MAJOR OUTCOMES CONSIDERED**

- Incidence of obstetrical and perinatal complications
- Incidence of multiple gestations

- Rate of congenital abnormalities, chromosomal abnormalities, imprinting disorders, and childhood cancer

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Cochrane Library and MEDLINE were searched for English-language articles from 1990 to February 2005, relating to assisted reproduction and perinatal outcomes. Search terms included assisted reproduction, assisted reproductive technology, ovulation induction, intracytoplasmic sperm injection (ICSI), embryo transfer, and in vitro fertilization (IVF). Additional publications were identified from the bibliographies of these articles as well as the Science Citation Index. Studies assessing gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT) were excluded since they are rarely used in Canada. All study types were reviewed. Randomized controlled trials were considered evidence of the highest quality, followed by cohort studies.

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

#### Quality of Evidence Assessment\*

**I:** Evidence obtained from at least one properly designed randomized controlled trial.

**II-1:** Evidence obtained from well-designed controlled trials without randomization.

**II-2:** Evidence obtained from well-designed cohort (prospective or retrospective) or case-control analytic studies, preferably from more than one center or research group.

**II-3:** Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as

the results of treatment with penicillin in the 1940s) could also be included in this category.

**III:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

\*Adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam..

## **METHODS USED TO ANALYZE THE EVIDENCE**

Systematic Review

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Not stated

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Classification of Recommendations\***

- A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination
- B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.
- D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.
- E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

\*Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Periodic Health Exam.

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline has been reviewed by the Genetics Committee and the Reproductive Endocrinology and Infertility Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Board of the Canadian Fertility and Andrology Society (CFAS).

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The quality of evidence (**I-III**) and classification of recommendations (**A-E**) are defined at the end of the "Major Recommendations."

#### **Outcomes Associated with Untreated Infertility**

1. Spontaneous pregnancies in untreated infertile women may be at higher risk for obstetrical complications and perinatal mortality than spontaneous pregnancies in fertile women. Further research is required to clarify the contribution of infertility itself to adverse obstetrical and perinatal outcomes. **(II-2A)**
2. All men with severe oligozoospermia or azoospermia should be offered genetic/clinical counselling for informed consent and offered karyotyping for chromosomal abnormalities before attempting in vitro fertilization (IVF)–intracytoplasmic sperm injection (ICSI). They should be made aware of the availability of tests for Y chromosome microdeletion. Some patients may consider the option of donor insemination. **(II-3B)**
3. Couples exploring IVF-ICSI when the man has obstructive azoospermia should be offered genetic/clinical counselling for informed consent and offered genetic testing for alterations in genes associated with cystic fibrosis (CF) before attempting IVF-ICSI. **(II-2A)**

#### **Obstetrical, Perinatal and Long-Term Outcomes Associated with Assisted Reproductive Technology (ART)**

4. Pregnancies achieved by ovarian stimulation with gonadotropins and intrauterine insemination are at higher risk for perinatal complications, and close surveillance during pregnancy should be considered. It remains unclear if these increased risks are attributable to the underlying infertility, characteristics of the infertile couple, or use of assisted reproductive techniques. Multiple gestations remain a significant risk of gonadotropin treatment. **(II-2A)**

#### **Obstetrical Outcomes**

5. Pregnancies achieved by IVF with or without ICSI are at higher risk for obstetrical and perinatal complications than spontaneous pregnancies, and close surveillance during pregnancy should be considered. It remains unclear

- if these increased risks are attributable to the underlying infertility, characteristics of the infertile couple, or use of assisted reproductive techniques (ART). **(II-2A)**
6. Women undergoing ART should be informed about the increased rate of obstetrical interventions such as induced labour and elective Caesarean delivery. **(II-2A)**
  7. Couples suffering from infertility who are exploring treatment options should be made aware of the psychosocial implications of ART. Further research into the psychosocial impact of ART is needed. **(II-2A)**

## **Perinatal Outcomes**

### *Singleton Birth*

8. Singleton pregnancies achieved by assisted reproduction are at higher risk than spontaneous pregnancies for adverse outcomes, including perinatal mortality, preterm delivery, and low birth weight, and close surveillance during pregnancy should be available as needed. **(II-2A)**

### *Multiple Birth*

9. A significant risk of ART is multiple pregnancies. Infertile couples need to be informed of the increased risks of multifetal pregnancies. Although dichorionic twins are most common, the incidence of monochorionic twins is also increased. Risks of multiple pregnancies include higher rates of perinatal mortality, preterm birth, low birth weight, gestational hypertension, placental abruption, and placenta previa. Perinatal mortality in assisted conception twin pregnancies appears to be lower than in spontaneously conceived twin pregnancies. **(II-2A)**
10. When multifetal reduction is being considered for high-order multiple pregnancies, psychosocial counselling should be readily available. Careful surveillance for fetal growth problems should be undertaken after multifetal reduction. **(II-2A)**
11. To reduce the risks of multiple pregnancies associated with ART and to optimize pregnancy rates, national guidelines should be developed on the number of embryos replaced according to characteristics such as patient's age and grade of embryos. **(II-2A)**

## **Long-Term Outcomes**

12. Further epidemiologic and basic science research is needed to help determine the etiology and extent of the increased risks to childhood and long-term growth and development associated with ART. **(II-2A)**

## **Genetic and Structural Abnormalities Associated with Assisted Reproductive Technology**

### **Structural Congenital Abnormalities**

13. Discussion of options for prenatal screening for congenital structural abnormalities in pregnancies achieved by ART is recommended, including appropriate use of biochemical and sonographic screening. **(II-2A)**
14. Further epidemiologic and basic science research is needed to help determine the etiology and extent of the increased risks of congenital abnormalities associated with ART. **(II-2A)**

### **Chromosomal Disorders**

15. Couples considering IVF-ICSI for male-factor infertility should receive information, and if necessary formal genetic counselling, about the increased risk of *de novo* chromosomal abnormalities (mainly sex chromosomal anomalies) associated with their condition. Prenatal diagnosis by chorionic villus sampling (CVS) or amniocentesis should be offered to these couples if they conceive. **(II-2A)**
16. Further epidemiologic and basic science research is needed to help determine the etiology and extent of the increased risks of chromosomal abnormalities associated with ART. **(II-2A)**

### **Prenatal Diagnosis of Structural and Chromosomal Disorders**

17. Discussion of options for prenatal screening and testing for aneuploidy in pregnancies achieved by ART, adapted for maternal age and number of fetuses, is recommended, including appropriate use of biochemical and sonographic screening. **(II-2A)**

### **Imprinting Disorders**

18. The precise risks of imprinting and childhood cancer from ART remain unclear but cannot be ignored. Further clinical research, including long-term follow-up, is urgently required to evaluate the prevalence of imprinting disorders and cancers associated with ART. **(II-2A)**

### **Preimplantation Genetic Disorders**

19. The clinical application of preimplantation genetic diagnosis must balance the benefits of avoiding disease transmission with the medical risks and financial burden of in vitro fertilization (IVF). Further ethical discussion and clinical research is required to evaluate appropriate indications for preimplantation genetic diagnosis (PGD). **(III-B)**

### **Definitions**

#### **Quality of Evidence Assessment\***

**I:** Evidence obtained from at least one properly designed randomized controlled trial.

**II-1:** Evidence obtained from well-designed controlled trials without randomization.

**II-2:** Evidence obtained from well-designed cohort (prospective or retrospective) or case-control analytic studies, preferably from more than one center or research group.

**II-3:** Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.

**III:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

### **Classification of Recommendations \***

- A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination
- B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
- C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.
- D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.
- E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

\*Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Periodic Health Exam.

\*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.

\*\*Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.

### **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Appropriate obstetrical management and counseling of pregnant women after assisted reproductive technology

## POTENTIAL HARMS

Not stated

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Allen VM, Wilson RD, Cheung A, Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada, Reproductive Endocrinology Infertility Committee. Pregnancy outcomes after assisted reproductive technology. J Obstet Gynaecol Can 2006 Mar;28(3):220-50. [117 references] [PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2006 Mar

**GUIDELINE DEVELOPER(S)**

Canadian Fertility and Andrology Society - Professional Association  
Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

**SOURCE(S) OF FUNDING**

Society of Obstetricians and Gynaecologists of Canada

**GUIDELINE COMMITTEE**

Society of Obstetricians and Gynaecologists of Canada Genetics Committee  
Reproductive Endocrinology and Infertility Committee

**COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Principal Authors:* Victoria M. Allen, MD, MSc, FRCSC, Halifax NS; R. Douglas Wilson (*Chair*), MD, MSc, FRCSC, Philadelphia PA

*Contributing Author:* Anthony Cheung, MBBS, MPH, MBA, FRACOG, FRCSC, Vancouver BC

*Genetics Committee Members:* R. Douglas Wilson (*Chair*), MD, MSc, FRCSC, Philadelphia PA; Victoria M. Allen, MD, MSc, FRCSC, Halifax NS; Claire Blight, RN, Halifax NS; Valerie A. Désilets, MD, FRCSC, Montreal QC; Alain Gagnon, MD, FRCSC, Vancouver BC; Sylvie F. Langlois, MD, FRCPC, Vancouver BC; Anne Summers, MD, FRCPC, Toronto ON; Philip Wyatt, MD, PhD, North York ON

*Reproductive Endocrinology and Infertility Committee Members:* Paul Claman (*Chair*), MD, FRCSC, Ottawa ON; Anthony Cheung, MBBS, MPH, MBA, FRACOG, FRCSC, Vancouver BC; Gwen Goodrow, MD, FRCSC, Hamilton ON; Gillian Graves MD, FRCSC, Halifax NS; Jason Min, MD, FRCSC, Ottawa ON

**FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

**GUIDELINE STATUS**

This is the current release of the guideline.

**GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) from the [Society of Obstetricians and Gynaecologists of Canada Web site](#).

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416

## **AVAILABILITY OF COMPANION DOCUMENTS**

None available

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This NGC summary was completed by ECRI Institute on March 10, 2009. The information was verified by the guideline developer on March 25, 2009.

## **COPYRIGHT STATEMENT**

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

## **DISCLAIMER**

### **NGC DISCLAIMER**

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

[Copyright/Permission Requests](#)

Date Modified: 5/4/2009

