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Infant and maternal health monitoring using a combined Nordic database on ART and safety

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Abstract

Objective. To evaluate infant and maternal health after assisted reproductive technology (ART), using data on over 90 000 ART children and their mothers in Denmark, Finland, Norway and Sweden. Data have been combined and will be compared with a control group of spontaneously conceived children and their mothers. The overall aim of this project is to evaluate the safety of ART. The size of the cohort should enable estimation of the prevalence of rare conditions such as birth defects, cancers, neurological impairments and imprinting diseases in the ART population compared to control children. Outcome data on the mothers of ART children can be used to study risks during pregnancy and obstetric complications after ART. *Methods.* A personal identification number given to all Nordic residents allows cross-linkage of the national health registers and enables long-term follow-up of ART children. The medical birth registers in the Nordic countries make it possible to cross-link data from mother and child. When a child is identified as conceived by ART, we can obtain a list of all International Classification of Diseases (ICD) codes ever registered on that specific child. *Conclusion.* Combining the Nordic ART and health registers is a complicated but feasible task. The main strengths of this ongoing study are the size of the cohort of ART children and their mothers and the possibility to follow the children through the health registers. The limitations are related to the national differences in reporting and recording of data together with the heterogeneity of data.

Abbreviations: ART, assisted reproductive technology; ICD, international classification of diseases; EIM, European IVF Monitoring group; ESHRE, European Society for Human Reproduction and Embryology; CoNARTaS, Committee on Nordic ART and Safety; IVF, in vitro fertilization; ICSI, intracytoplasmatic sperm injection; FER, frozen embryo replacement; IUI, intra-uterine insemination; BMI, body-mass-index; OI, ovulation induction; PIN, personal identification number; eSET, elective single embryo transfer; SET, single embryo transfer; SGA, small for gestational age; PGD, pre-implantation genetic diagnosis.

Introduction

From the early days of assisted reproductive technology (ART) treatments, the Nordic countries have used national reporting systems to collect data on such treatments. National ART monitoring systems were gradually established as a consequence of the expanding use of ART in order to evaluate quality and safety, including possible health consequences of the reproductive technology (1,2). The national registers have already been widely used for research on follow-up on maternal and infant health and the largest published cohort of ART children analyzed to date includes almost 32 000 Swedish children (3). Although large cohorts of ART children have been analyzed, national datasets may still be too limited in sample size to evaluate the risk of rare outcomes such as specific birth defects or rare diseases. Additionally, surveillance of very large populations may be of value to assess the safety of new ART procedures, such as vitrification and oocyte freezing, because it could allow a more rapid accumulation of data (4,5).

Five years ago, the European IVF Monitoring group (EIM), which is a committee under the European Society for Human Reproduction and Embryology (ESHRE), decided to assess the possibility of using the Nordic ART registers to pool outcome data for research on infant and maternal health after ART (2). However, one of the challenges in pooling Nordic ART data is the heterogeneity of the collected data, as major differences in the type and level of information recorded in each Nordic country prevail. To implement the decision by ESHRE, the Committee on Nordic ART and Safety (CoNARTaS) was established. The aim of the Nordic database on ART and safety is to provide a continuous large-scale Nordic monitoring system that can maintain and secure the reporting of safety and quality aspects of ART treatments. The Nordic database on ART and safety contains data on all ART pregnancies, deliveries and children born after in vitro fertilization (IVF), intracytoplasmatic sperm injection (ICSI) and frozen embryo replacement (FER) in Denmark, Finland, Norway and Sweden.

The main objective of the present paper is to provide a systematic description of the ART registers in the four Nordic countries regarding structure, reporting systems, coverage and data quality. The primary aim is to disseminate the knowledge of the many possibilities of using register data in epidemiological research. The second aim is to clarify the strengths and limitations of pooling health data from different countries.

The Nordic ART registers

In the Nordic countries each resident receives a unique personal identification number shortly after birth or at the time of immigration. A personal identification number allows cross-linking of national health registers and makes it possible to follow a woman/couple receiving ART treatment from one clinic to another. The medical birth registers in the Nordic countries allow cross-linkage between mother and child. When a child is registered as conceived by ART, it is possible to obtain a list of all International Classification of Diseases (ICD) codes ever registered on that specific child. This applies for in-patient health care and in the recent years also for out-patient health care.

The IVF clinics in all four Nordic countries are responsible for reporting to their national ART register. The reporting to the registers is mandatory in all countries. In Norway, ART treatments that result in a pregnancy are reported to the ART register. In Finland, only data on women who give birth after ART treatment are included. In Denmark, the reporting to the ART register is based on individual treatment cycles and thus this register also includes data on those treatment cycles that did not result in pregnancy or birth. In Sweden, the ART registration used to be based on ART births but this has recently been changed to an individual treatment cycle registration system. Apart from Sweden, the national health authorities run the ART registers as well as the majority of all other national health registers and they are legally responsible for the registers and their maintenance and updating. In Sweden, the IVF medical doctors themselves have been responsible for the national ART registration since 2007, when the registration converted into a treatment cycle-based system.

In the following, we describe each Nordic ART register in relation to time period, volume and type of data recorded. Table 1 lists the Nordic ART and health registers contributing with data to the Nordic database on ART and safety. In Table 2, examples are given of the similarities and differences regarding the specific data recorded in the Nordic ART registers. Table 3 shows the number of ART children and mothers, as well as the control children and mothers included in the database. Table 4 describes the national ART legislation in Denmark, Finland, Norway and Sweden.

The Danish ART registration

The structure of the Danish ART register has been described in detail previously (6). The ART register was established in 1994 and until 2007 included information on more than 23 000 children conceived after IVF, ICSI and FER (Table 3). Every treatment cycle is reported with details on both clinical and laboratory data as well as data on outcome in terms of pregnancies. Continuous evaluation of the ART register secures updating and addition of new variables when relevant (Table 2). A major update of the ART register occurred in January 2007, when more data were included and non-ART infertility treatments such as intra-uterine insemination (IUI) were added. After the latest update, the ART register now also includes information on important lifestyle factors such as smoking and body mass index (BMI).

The Finnish ART registration

Finland has three different data sources that can be used for research purposes:

- The national data collection for IVF statistics started in 1992. Each ART clinic has to report the numbers and

Table 1. National health registers and International Classification of Diseases (ICD) revisions used for the Nordic database on ART and safety. The years indicate when the specific health registers were initiated and the time periods during which each country has used the different revisions of the ICD.

	Denmark	Finland	Norway	Sweden
ART register	1994	1992	1988	1982
Medical Birth Register	1960	1987	1967	1973
Hospital Discharge Register	1976	1967	1997	1987
Causes of Death Register	1950	1936	1951	1952
Register of psychiatric illnesses	1969	No	No	No
Register of congenital anomalies	No	1963	No	1964
Cancer Register	No	1953	1951	1958
ICD-8	Until 1994	Until 1986	Until 1987	Until 1986
ICD-9	Never used	1987–1995	1988–1998	1987–1996
ICD-10	Since 1994	Since 1996	Since 1999	Since 1997

Table 2. Data recorded in the Nordic ART registers according to country. The years indicate from when the specific information was recorded.

	Denmark	Finland[1]	Norway	Sweden
IVF	1994	1992	1988	1982
ICSI	1994	1993	1988	1982
FER	1994	1992	1996	1982
Preimplantation genetic diagnosis (PGD)	2006	2001	No	No
Insemination	2006	2006	No	No
Stimulation regimen	1994	1992	No	1982[2]
Type of drugs used	2006	No	No	No
Number of oocytes aspirated	1994	1992	No	2007
Number of embryos transferred	1994	1992	1988	2001
Number of embryos cryopreserved	1994	No	No	2007
Infertility diagnosis	1994	1992	2002	No
Duration of infertility	2006	No	2002	No[3]
Ultrasound week 7	1994	No	1988	2001

[1] Aggregated data only.

[2] Information only on whether the cycle is natural or stimulated.

[3] Duration of infertility registered in the Medical Birth Register.

results of IVF and ICSI treatments (since 1992) and IUI treatments (since 2007) to the National Institute for Health and Welfare. As a result of the first ART legislation, the data collection has been mandatory since September 2007. Only aggregated data are collected in the national ART reporting system (7). All clinics are requested to keep a local register on all couples/women receiving ART treatment. The national ART reporting system cannot be used for follow-up due to the lack of individual data, but the local registers can be pooled for research purposes.

- Since October 1990, the Medical Birth Register in Finland has collected information on ART treatments and, since 2004, also information on inseminations and ovulation inductions. It is not possible to distinguish between the different in vitro techniques, e.g. IVF vs. ICSI.
- Due to reimbursement of ART treatments, the Social Insurance Institution also collects data on ART treatment cycles and ovulation induction (with or without IUI).

The Norwegian ART registration

The fertility clinics in Norway report pregnancies conceived by assisted fertilization to the Medical Birth Register of Norway. Only data on fertility-treated women who become pregnant are recorded. Assisted fertilization is defined as fertilization in vitro, notably in vitro fertilization (IVF) or intracytoplasmatic sperm injection (ICSI). The register does not include information on pregnancies after ovulation induction (OI) or IUI. The database is considered to be virtually complete from 1988 onwards. The record gives information on the method used for fertilization (IVF or ICSI) and whether the transferred embryos were fresh or thawed after cryopreservation. Date of embryo transfer, number of

Table 3. Number of children and mothers from Denmark, Finland, Norway and Sweden included in the Nordic database on ART and safety. Data were collected until 31 December 2007.

	Denmark	Finland	Norway	Sweden	Total
Data sampling period	*1995–2007*[1]	*1992–2007*	*1988–2007*[2]	*1982–2007*	
ART children, total (*n*)	23 474	19 065	17 451	32 819	92 809
ART singletons (*n*)	14 568	12 950	10 612	23 417	61 547
ART twins (*n*)[3]	8 608	5 683	6 347	8 856	29 494
ART triplets (*n*)	298	424	458	524	1 704
ART quadruplets (*n*)	0	8	34	22	64
Control children, total (*n*)	95 643	76 260	69 804	131 489	373 196
Control singletons (*n*)	92 525	74 553	67 922	128 451	363 451
Control twins (*n*)[3]	3 016	1 672	1 838	2 983	9 509
ART mothers (*n*)	17 009	14 122	12 308	24 632	68 071
Control mothers (*n*)	82 663	71 854	62 271	127 224	344 012
ART born in 2007 (*n*)	2 695	1 982	1 798	3 136	
IVF/ICSI born in 2007 (*n*)	2 298	1 289	1 518	2 291	
FER born in 2007 (*n*)	361	695	280	845	
Children[4] born in 2007 (*n*)	64 847	58 915	59 632	105 966	

n=number of children.

[1] The Danish ART register was established in 1994 but because of incomplete registration the first year data were not included until 1995.

[2] The Norwegian ART registration was established in 1984 but because of incomplete registration data were not included until 1988.

[3] Does not include the twins from the secondary twin control group.

[4] ART + non-ART + spontaneously conceived.

Table 4. ART legislation in the four Nordic countries.

	Denmark	Finland	Norway	Sweden
Donation of semen	+	+	+	+
Donation of oocytes	+	+	−	+
Donation of embryos	−	+	−	−
Fertility treatment of lesbians	+	+	+	+
Fertility treatment of single women	+	+	−	−
ICSI	+	+	+	+
FER	+	+	+	+
Preimplantation genetic diagnosis (PGD)	+	+	−	+
Surrogacy	−	−	−	−
Age limit fertility treatment	40 (public) 45 (private)	no official limit[1]	39 (public) 44 (private)	no official limit

Legal (+), illegal (−).

[1] ART is only allowed if a pregnancy is not considered to involve any health risk for the woman or child due to the woman's age or health.

embryos replaced and the number of fetuses with ongoing heart activity confirmed by ultrasound during the first trimester are also reported. Specific indications for fertility treatment and the duration of infertility have been recorded since 2002 (Table 2).

The Swedish ART registration

Until 2006, Sweden used two parallel reporting systems. One was the annual reporting from all IVF clinics to the National Board of Health and Welfare. This was based on summary data with information on the number of cycles per different in vitro technology, number of embryos transferred, and pregnancy and delivery outcomes. The other reporting system, run by the National Board of Health and Welfare in cooperation with the Swedish Society for Obstetrics & Gynecology and the Swedish Pediatric Society (during later years by the National Board of Health and Welfare alone), collected personal identification number (PIN) codes from all women who had given birth after ART treatment. These PIN codes were then cross-linked with five different National Health Registers: the Medical Birth Register, the National Patient Register (previously named the Hospital Discharge Register), the Cancer Register, the Causes of Death Register and the Register of Congenital Malformations (Table 1). Since 2007 the two parallel systems have been replaced by the 'IVF

Quality Register', which is administered by the profession of IVF medical doctors. The IVF Quality Register is based on individual treatment cycles and also includes data on those treatment cycles that did not result in pregnancy or birth.

Major national scientific contributions on infant health based on the Nordic ART registers

Danish studies

In Denmark, the ART register and the other national health registers have been the basis for follow-up studies of both singletons and twins born after ART. The major findings extracted from the Danish registers were that the characteristics of the parents and the multiplicity of pregnancies rather than ART determine the fetal risk of ART pregnancies. The neonatal outcome of IVF/ICSI twins was comparable to that of non-IVF/ICSI twins when considering dizygotic twins only. Furthermore, it has been shown that ART twins have the same risk for neurological sequelae as both their spontaneously conceived peers and ART singletons (8). Using the ART register, an evaluation of the usability of the national prenatal screening program for trisomy 21, specifically concerning ART children, has also been possible. This has resulted in considerations regarding differentiated screening recommendations for ART children because the blood concentration of pregnancy-associated plasma protein-A in ART has been found to be decreased when compared with that of pregnancies conceived spontaneously (9). Further longitudinal cohort studies on ART have combined national register data with follow-up questionnaires. These studies addressed the crude delivery rate after ART, IUI, spontaneous conception and adoption in a large infertile cohort. Using this approach it was possible to show that almost 70% of the women initiating fertility treatment at a tertiary hospital center had given birth to at least one child five years after referral (10).

Finnish studies

Since the establishment of the Finnish ART monitoring system in the early 1990s, studies from Finland have addressed multiple issues regarding ART. One important issue has been the evolution of elective single embryo transfer (eSET) into clinical practice (11). Evidence of the safety of frozen embryo transfer has been provided together with analyses showing that eSET combined with cryopreservation is more effective and less expensive than double embryo transfer (12,13). Follow-up studies of ART children using register data have shown that the postnatal health of ART children is worse than that of spontaneously conceived peers. Growth of ART children was found to be behind that of control children during the first three years of life but the psychomotor development was similar (14). However, along with change of practice with an increased number of single-embryo transfers, the perinatal outcome has improved (15,16). Single embryo transfer (SET) pregnancies may be associated with improved neonatal outcome and this was analyzed combining birth register data and IVF register data in a single hospital. These results indicated that subject- and infertility-related mechanisms other than the number of transferred embryos influence the neonatal outcome of singleton IVF pregnancies (16). The Finnish ART register has also been used to conduct analyses on the costs of ART, showing that there are additional health care costs in ART singletons compared with control neonates (17). The register data can also be used to study IVF service system and the characteristic of the treated women (18).

Norwegian studies

To differentiate between maternal and specific treatment-related causes of poorer outcome in ART children, the Norwegians have used their ART register data to compare the perinatal outcome of ART children with that of their spontaneously conceived siblings. In their sibling analyses they were able to show that birthweight, gestational age, and the risk of preterm birth as well as small for gestational age (SGA) did not differ significantly among siblings of women who had conceived both spontaneously and after assisted reproduction (19). It has been shown that there is an increased risk of placenta praevia and that the increased risk could be related to the reproductive technology, while the increased risk of breech delivery in ART pregnancies seemed to be mediated through a higher maternal age and a lower parity in ART pregnancies (20,21). With the use of data from the Medical Birth Register, it has also been shown that the initially high rates of cesarean section in ART pregnancies were gradually approaching the rates of cesarean section in the spontaneously conceived pregnancies in the general population over 20 years (21). A recently published study has shown that the triplet incidence rate in Norway has more than doubled in the last 40 years, even after excluding ART pregnancies. The study also showed that the risk of perinatal death in triplets was 10 times higher relative to singletons and had not changed over 40 years, independent of the introduction of ART (22).

Swedish studies

The cross-linkage between the Swedish ART register and several national health registers has allowed Swedish researchers to make multiple analyses of the delivery and neonatal outcomes as well as the long-term outcomes of ART treatments, assessing the safety for both women undergoing fertility treatment and children born after different in vitro procedures. Sweden has thus been a Nordic and indeed an international pioneer in using national register data for comprehensive cohort studies of now almost 32 000 ART children (3).

The major findings have been a moderately increased risk of birth defects and cancer after ART, compared with spontaneous conception, and also of preterm birth and its sequelae (23). Trends over time have demonstrated that the very substantial reduction of the number of embryos replaced with eSET as the norm since 2004 has resulted in a dramatic reduction in the number of multiple deliveries. This has reduced the prevalence of children born preterm and its sequelae, such as cerebral palsy. Also, fewer women now have obstetric complications such as preeclampsia (3,24). In contrast, the risk of birth defects has remained unchanged. No difference in the risk of adverse outcomes has been observed when comparing IVF and ICSI (25).

Swedish studies have also been among the first to show that cryopreservation does not adversely influence infant development (26). Another major finding in the Swedish studies has been that infertility per se (parental factors) plays an important role in the adverse outcome in ART singletons. By adjusting for duration of unwanted childlessness, most of the differences between ART and spontaneously conceived children decreased or disappeared (27).

Structure of the Nordic database on ART and safety

ART children

Each country contributes data from their national ART register and relevant data from other national health registers. Outcome data are collected on all children born after ART from the year each national ART register was initiated until 31 December 2007 (Table 3).

Spontaneously conceived children

To evaluate the influence of ART on child morbidity, a control group of both singletons and multiples born after spontaneous conception has also been enrolled in the Nordic database on ART and safety. Each country contributes a control group fourfold the size of their ART population. A second control group of all non-ART twins, who are not already included in the first control group, has also been enrolled in the Nordic database on ART and safety.

Legal aspects of linking register data from the four Nordic countries

Permission to work with health data was obtained from the national health authorities in each country. When needed, ethical approvals were obtained. In the establishment of the Nordic database on ART and safety, all personal identification numbers are encrypted and serial numbers containing information on country, as well as status of ART or non-ART, are given to each mother and child. A file containing the link between the personal identification numbers and the serial numbers is kept by the national health authorities in each country to correct the data if necessary and to allow future follow-up.

Limitations and methodological concerns when pooling data from the four Nordic ART registers

Pooling of data from the different Nordic ART registers is complicated by dissimilarities in the national datasets from each of the participating countries. None of the registers includes complete data on fertility treatments such as ovulation induction with or without IUI during the study period. Recording of the diagnosis of infertility, duration of infertility and information on lifestyle factors such as smoking and BMI were not initially recorded in the registers (Table 2). Some of the data, such as on infertility (Sweden), smoking (all countries) and BMI (all countries excluding Norway), can be linked from the medical birth registers, but this applies only to treatments that result in childbirth. Furthermore, when conducting analysis on specific types of in vitro methods, not all data can be pooled, as some countries cannot differentiate between the different in vitro methods in the first part of the study period.

In some of the Nordic countries, ART registration, especially in the early years, was restricted to treatments resulting in a delivery only. There is therefore an incomplete description of the maternal population and a lack of information about the unsuccessful fertility treatments that did not result in a pregnancy or a delivery.

Since the establishment of national ART registers, some Nordic countries have recorded information on treatment regimes, medication and laboratory procedures (Table 2). Nevertheless, major differences in the level of parameters and details reported to the ART registers exist between the four countries. As for the other national health registers, not all four countries record out-patient hospital treatments and none of the countries did so during the entire study period. In Finland, out-patient treatments have been recorded since 1998 and when validating data it was concluded that less than 1% of data was missing. In Sweden, out-patient treatments have been recorded since 2005 but data have not been validated. For Denmark this is also the case, with data having been recorded since 1994. Norway does not have a national registration system for out-patient treatments. It is important to keep these differences in mind when evaluating the prevalence of psychiatric and neurological morbidity among the ART children, as most of these diagnostic procedures take place in pediatric or neurological out-patient clinics.

The four Nordic countries have all used the International Classification of Diseases system, but different editions (ICD-8, -9 and -10) during different periods (Table 1). Hence the cross-country pooling of data necessitates a comprehensive standardization of data. Some countries have used national non-ICD systems for recording specific categories of diseases. Surgical procedures are coded in all countries using the Nordic Classification of Surgical Procedures, but there is some national variation in single codes. When systems other than ICD-classification systems have been used, data are not included in the Nordic database on ART and safety. This results in an incomplete data contribution on specific categories of diseases and procedures for some countries. Furthermore, differences in the national ART legislations also contribute to the heterogeneity of data (Table 4).

Children with more than one main diagnosis constitute another obstacle and require a specific diagnosis ranking system, where some diagnoses are superior to others. Although such ranking systems do not exist, they are needed to allow evaluation of the overall morbidity of the children. Missing data and different sources of error are a reality in all health registers but we have no reason to assume an unequal distribution of missing data between the ART and non-ART population. However, it should be emphasized that the spontaneously conceived control group will also include children born after hormone stimulation with or without IUI. These children cannot be identified in the Nordic database on ART and safety.

Discussion

The Nordic ART and health registers have long been used to conduct epidemiological studies on follow-up of infant and maternal health after ART. To date, Sweden has contributed with the world's largest national cohort of ART children, showing that ART children have a higher risk of birth defects than children born after spontaneous conception (25). By establishing a cohort of more than 90 000 ART children through this Nordic collaboration, it is possible to estimate the prevalence of rare but important disorders such as specific birth defects, neurological impairments and imprinting diseases in both ART and non-ART populations.

The oldest ART children are currently in their mid- or late twenties, making research on both pubertal and reproductive issues possible. As the database will include data from two to three decades of ART, it should be possible to conduct analyses on the consequences of major changes in clinical practices and laboratory procedures. Hence the database will be a useful tool to evaluate the consequences of the implementation of different treatment strategies such as eSET and cryopreservation of embryos.

Assessment of the safety of new laboratory procedures, such as vitrification, as well as the shift towards transfer of blastocysts will be possible. The vitrification technique is being taken up very rapidly worldwide and the safety data on this new procedure are very limited (4,5,28). Similarly, there is an ongoing trend towards transfer of blastocysts, which have been associated with an increase in the rate of monozygotic twins as well as a small increase in the risk of congenital malformations and prematurity (29). Another example is the use of non-ejaculated sperm for male infertility, which is also under debate; concerns have been raised about these aspects of assisted reproduction (30). Thus, international fusion of database recordings could be valuable in achieving an appropriate sample size of ART children to enable studies on the safety of emerging technologies.

The control group of spontaneously conceived children was fourfold the size of the ART children, which is estimated to be large enough to represent the background population on prevalences of diseases, birth defects, etc. The control group consists of both singletons and multiples and is matched on mother's parity, and year and month of birth. The decision to match on mother's parity (primipara vs. multipara) was made because there is a large difference in this characteristic between the mothers of the ART population and the mothers of the control population. To perform analyses restricted to ART twins, a second control group of all non-ART twins, who are not already included in the first control group, has also been enrolled in the Nordic database on ART and safety. This was done because the proportion of twins born after assisted reproduction is much larger than the proportion of twins after spontaneous conception, and there would therefore be too few spontaneously conceived twins in the ordinary control group to enable analyses restricted to twins.

Overall, the Nordic database on ART and safety will provide a substantial national and international contribution to future research and knowledge on safety aspects related to ART and evaluation of both short- and long-term health outcomes among children conceived by ART as well as their mothers. It is our intention to update the database every five years with new data from the four Nordic countries. Therefore, the value of the Nordic database on ART and safety is expected to increase over time, primarily because the annual number of children conceived after ART is increasing every year, and also because more details regarding the treatment procedures will be included as each country continuously develops and improves its national ART registration.

The research potential on Nordic ART data also includes the possibility to conduct sibling analyses when identifying and linking siblings conceived after the same or different ART method or comparing siblings where one child is conceived after ART and the other is conceived spontaneously (20,31). This approach enables a situation where the maternal characteristics, and thereby the influence on child outcome, are kept steady while evaluating the influence of the different in vitro techniques or modes of conception.

Combining the Nordic ART and health registers is a complicated but feasible task. It is important to acknowledge the limitations of pooling data from the Nordic ART and health registers regarding the differences in recording procedures, details of data and coverage of the registers. The collaboration of the Nordic countries allows benchmarking of the Nordic ART populations and an evaluation of the national changes over time concerning both technical procedures and the changes in treatment methods and strategies.

The perspective of the common Nordic database on ART and safety is a continuous inclusion of other European countries with the ultimate aim of collecting outcome data on all ART children born in Europe. This might only be feasible if more standardized ART data registration systems are developed throughout Europe. To date, the European IVF Monitoring group (EIM) has been the only European collaboration in collecting ART data (2). The Committee of Nordic ART and Safety is potentially another example of an international collaboration to secure continuous research on the morbidity of ART children and their mothers, thereby contributing to the ongoing assurance of the quality and safety of ART for many years to come.

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