Evidence-based pre-pregnancy counseling for oocyte Donation pregnancies: a systematic review and guide for physicians

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REVIEW

Evidence-Based Pre-Pregnancy Counseling for Oocyte Donation Pregnancies: a Systematic Review and Guide for Physicians

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Abstract

It is well known that oocyte donation (OD) pregnancies are associated with higher complication rates compared to autologous pregnancies. However, evidence-based information for pre-pregnancy counseling designed for health care workers is scarce. Therefore, a systematic literature search was performed to find articles that address pre-pregnancy counseling before OD.

A systematic search was conducted in September 2020 in various databases, including PubMed and Embase. Nine (systematic) reviews and meta-analyses were included that reported on pre-pregnancy advice in OD pregnancies.

Studies are consistent in documenting a higher risk for hypertensive disorders, cesarean section, preterm birth, postpartum hemorrhage, and low birth weight. Based on these complications, pre-pregnancy advice is mentioned in all included systematic reviews to prevent complications in the next pregnancy. All studies recommend counseling women on the increased risk of complications during OD pregnancy. Other recommendations include the prophylactic use of aspirin in pregnancy and restriction to single embryo transfer. Individualized appropriate surveillance and management strategies should be considered for every patient achieving pregnancy by OD.

In conclusion, we provide a summary of the most important outcomes in OD pregnancies, and thereby offer a guide for pre-pregnancy counseling.

Keywords Oocyte donation · Pregnancy · Pregnancy complications · Pre-pregnancy counseling

Introduction

It is well known that OD pregnancies are associated with a high rate of adverse pregnancy outcomes. Over the past ten years, many reviews [1–6] and systematic reviews [7–18] have been published focusing on the outcomes of OD pregnancies. Indeed, OD pregnancies are accompanied by a higher risk for hypertensive disorders, cesarean section, and bleeding complications, compared to naturally conceived (NC) pregnancies or pregnancies after in vitro fertilization (IVF) [7, 11, 14, 19]. Yet, since the first procedure in 1984, thousands of OD procedures have been performed worldwide [20, 21]. Nowadays, with postponing pregnancy as a worrisome trend and the average age of first childbirth approaching 30 years, the number of OD procedures is still increasing [21].

Numerous health professionals encounter OD pregnancies, but are possibly not aware of the high risk of complications since the information for the counseling of couples is scarce. The importance of pre-pregnancy counseling though is illustrated by a case with severe preeclampsia in the pregnancy after oocyte donation of the partner (ROPA) as part of shared lesbian motherhood [22]. Here, the significance and possible consequences of pre-pregnancy counseling before OD pregnancy are emphasized. In this review, we therefore aim to guide the pre-pregnancy counseling before the conception of an OD pregnancy. A systematic literature search was performed to obtain studies that address pre-pregnancy counseling before OD. We provide a summary of the most important outcomes in OD pregnancies and thereby offer a guide for pre-pregnancy counseling, including the effect of OD on pregnancy and fetal or neonatal outcomes. Finally, we advise on the (future) possibilities in care to reduce the complication risks in OD pregnancy.

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Methods

Study Selection

A systematic search was conducted in September 2020 in collaboration with an experienced research librarian in the following databases: PubMed, Embase, the Cochrane Library, Emcar, Web of Science, PsychINFO, and Academic Search Premier. The search strategy consisted of the major medical subject headings (MeSH) terms pregnancy, pregnancy complications, fertility, oocyte donation, family planning services, and reproduction. Furthermore, the MeSH terms for health care outcome assessment, fetal death, infant mortality, maternal mortality, and stillbirth were used. The search strategy is detailed in online resource 1. The titles and abstracts identified were independently screened by two review authors (KB and MH). If the studies were considered potentially relevant, the full-text article was read. Disagreements were solved by discussion and consensus. References of relevant publications were searched for additional relevant published studies. We included (systematic) reviews and meta-analyses that reported on pre-pregnancy advice in OD pregnancies. Non-review and mini-review articles were excluded, as were studies that focused on patients with Turner syndrome.

Quality Assessment

Risk of bias (ROB) assessment of the individual studies is a recommendation in the PRISMA [23]. To determine the methodological quality of the included systematic reviews in our study, we checked whether the reviews performed such a ROB assessment of the individual studies and whether this ROB was presented and discussed in the review.

Data Extraction

The selected studies were independently screened for pre-pregnancy advice by two review authors (KB and MH). The following data were extracted from the studies: year of publication, journal of publication, inclusion criteria for review, number of studies included, the total number of patients, and pregnancy outcome. Pre-pregnancy and pregnancy care advice for OD pregnancy mentioned in the studies was noted.

Results

Study Selection

The conducted search identified 452 studies; 9 articles were included in this review (Fig. 1). As the latest systematic review dates from August 2019, more recent original studies in the search have been checked for additional pre-pregnancy advice. In July 2020, a descriptive review of Berntsen et al. [24] was published, highlighting some recommendations for OD pregnancy. We added these recommendations, mostly compliant with the advice given in the included reviews, in Table 3.

Study Characteristics

The number of included studies in the reviews ranged from 7 [16] to 35 [14]. This broad range could be explained by the range in the year of publication (2011–2019), and by the analysis of different outcomes. Three reviews assessed obstetric complications, such as hypertensive disorders [10, 11, 13], while three other reviews examined neonatal outcomes, such as low birth weight and preterm birth [15–17]. The remaining three reviews investigated both obstetric and neonatal outcomes [12, 14, 18]. Overall, the assessed outcomes could be of influence in the approach of the given recommendations, which indicates the importance of including both reviews with obstetric and neonatal outcomes in OD pregnancies. Furthermore, the control groups differed between the reviews. All reviews included other autologous assisted reproductive techniques (ART), such as non-donor IVF, as a control group, and four reviews added NC pregnancies as a control as well [10, 11, 14, 15]. Table 1 shows an overview of the characteristics of the included reviews.

Quality Assessment

The majority of included systematic reviews performed a ROB assessment of the individual studies according to the PRISMA guideline [11–15, 17, 18]. Three reviews performed a sensitivity analysis according to methodological quality [11, 12, 15]. Three other reviews stated that, based on the ROB assessment, their results should be interpreted with caution [13, 14, 17]. Two reviews however lacked any assessment for the ROB across the included studies [10, 16]. Furthermore, the review by Pecks et al. [10] was not a systematic review and also did not assess the ROB of the included individual studies. Publication bias was reported by five reviews [11–13, 15, 17], two of the reviews made use of the Egger's test [13, 17].

As the results of all reviews were consistent, and as this review aims to offer a pregnancy guide for OD based on reported advice, we valued the recommendations of each review equally.

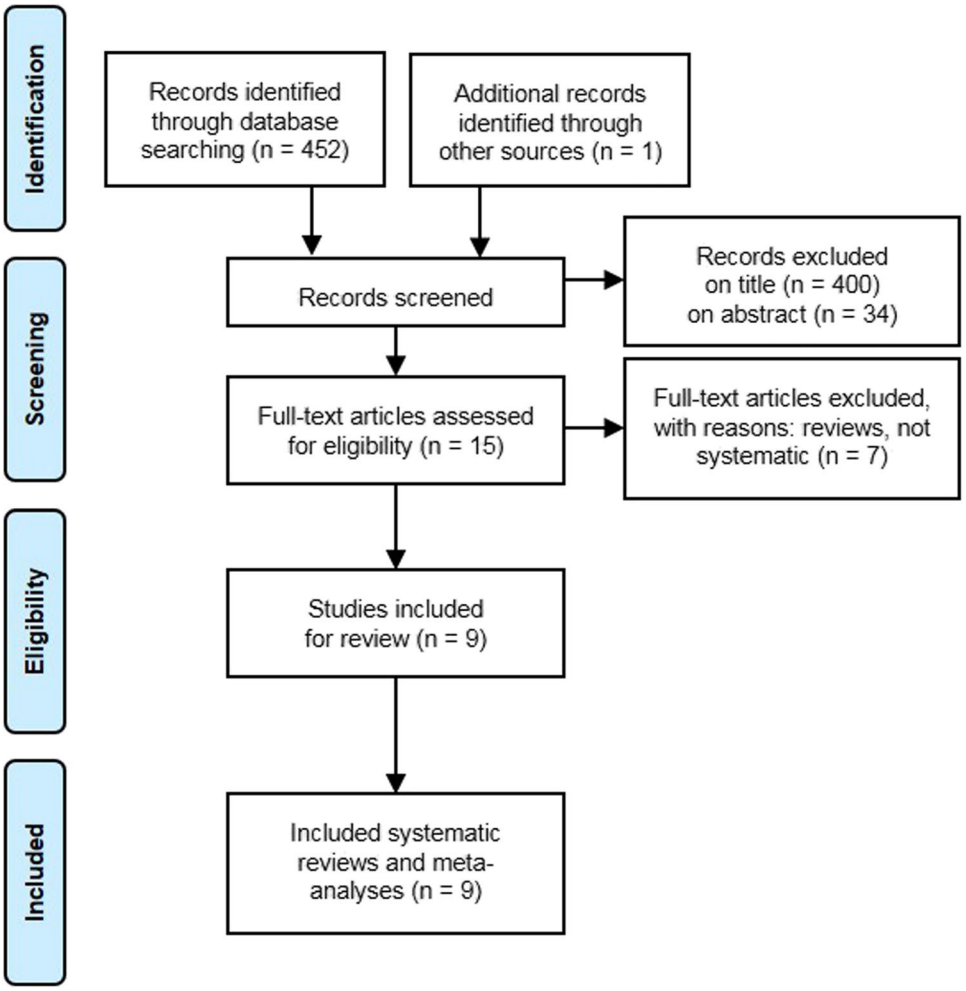

Fig. 1 Flowchart of the literature search

Narrative Synthesis

The included systematic reviews describe numerous recommendations based on the higher complication rate in OD pregnancies with the intention to reduce the complication risk [10–18]. Table 2 summarizes the results of the maternal and fetal complications presented in the systematic reviews. In general, OD pregnancies have a higher complication rate in comparison to autologous pregnancies, including IVF, intracytoplasmic sperm injection (ICSI), intrauterine insemination (IUI), and NC pregnancies. Studies are consistent in documenting a higher risk for hypertensive disorders, including pregnancy-induced hypertension and preeclampsia [9–12, 14, 18], and cesarean section [12, 14, 18] in OD pregnancies compared to autologous pregnancies. Moreover, preterm birth [12, 14–16, 18] and postpartum hemorrhage are more common in OD pregnancies [14]. In addition, a fetus small for gestational age [12] and low birth weight of the neonate [12, 14–16, 18] are more often documented in OD pregnancies compared to autologous pregnancies.

Based on these complication rates, pre-pregnancy advice is mentioned in all systematic reviews to prevent recurrence in future pregnancies. The given advice is summarized in Table 3. All studies recommend counseling women pre-pregnancy on the increased risk of maternal and fetal complications in OD pregnancy. Jeve et al. [12] and Storgaard et al. [14] suggest starting aspirin in a low dose in pregnancy to reduce the risk of preeclampsia. Storgaard et al. [14] and Moreno-Sepulveda et al. [18] advise restricting to single embryo transfer.

Discussion

In this review, we systematically searched the literature to provide a summary of the most important outcomes in OD pregnancies, and thereby offer a guide for pre-pregnancy counseling. Considering the high incidence of complications during OD pregnancies, all assessed studies advise

Table 1 Overview of included (systematic) reviews

Author	Year	Journal	Inclusion criteria	Studies included	Number of patients	Pregnancy outcome
Pecks [10]	Jan 2011	Dtsch Arztebl Int	OD versus autologous ART (IVF, ICSI, IUI) or NC	11	644 OD 2320 autologous	Pregnancy-induced hypertension
Masoudian [11]	Nov 2015	AJOG	OD versus autologous ART (IVF, ICSI, IUI) or NC	19	86,515 pregnancies	Preeclampsia, pregnancy-induced hypertension
Jeve [12]	Feb 2016	BJOG	OD versus autologous IVF/ICSI	11	81,752 cycles Primary outcome analysis: 970 OD 10,569 IVF/ICSI	Pregnancy complications, primary outcome: hypertensive disorders
Blázquez [13]	March 2016	J Assist Reprod Genet	OD versus autologous IVF	11	26,302 cases	Preeclampsia
Storgaard [14]	Sept 2016	BJOG	OD versus autologous IVF/ICSI or NC	35	1592 OD 29,447 IVF/ICSI 1,048,919 NC	Obstetric and neonatal complications (e.g. hypertensive disorders, preterm birth, gestational diabetes, birth weight)
Adams [15]	Nov 2016	J Develop Origins of Health and Disease	OD versus autologous IVF or NC	23	201,628 OD 432,361 autologous	Neonatal outcomes (e.g. birth weight, preterm birth, birth defects)
Mascarenhas [16]	Sept 2017	Eur J Obs & Gyn and Repr Bio	Fresh or frozen OD versus autologous IVF	7	19,885 OD 188,498 IVF	Perinatal outcomes (preterm birth, birth weight)
Al Shammary [17]	Aug 2019	JOGC	OD versus autologous ART (IVF, ICSI, IUI, sperm donation, hormonal modulation)	19	78,022 OD 563,106 autologous ART	Birth weight, gestational age
Moreno-Sepulveda [18]	Aug 2019	J Assist Reprod Genet	Singleton OD versus singleton autologous IVF	23	58,597 OD 351,766 IVF	Maternal and perinatal outcomes (e.g. hypertensive disorders, preterm birth, birth weight, gestational diabetes)

OD, oocyte donation; *ART*, assisted reproductive technique; *IVF*, in vitro fertilization; *ICSI*, intracytoplasmic sperm injection; *IUI*, intrauterine insemination; *NC*, naturally conceived

offering pre-pregnancy counseling [10–18]. We suggest that this pre-pregnancy counseling is performed by a multidisciplinary team of healthcare professionals, who have expertise in handling diagnostic and therapeutic dilemmas before, during, and after pregnancy. The counseling will inform patients about the potential risks, as summarized in Table 2 before they start the OD procedure. However, evidence that this counseling will contribute to the reduction of complications in OD pregnancies is lacking.

The use of low-dose aspirin to reduce the risk of preeclampsia in OD pregnancy was suggested by Jeve et al. [12], Storgaard et al. [14], and more recently by Berntsen et al. [24]. This advice is based on the ASPRE study [25] that showed a reduction of the incidence of preeclampsia in high-risk patients with the prophylactic use of 150 mg acetylsalicylic acid daily. However, OD pregnancy was not included as a risk factor in this study. The effect of low-dose aspirin in OD recipients was only studied by Weckstein et al. [26], though the primary outcome of this study was the clinical pregnancy rate in patients with an endometrial thickness of less than 8 mm, and there was no documentation on pregnancy complications [26].

Single embryo transfer to achieve OD pregnancy is recommended by several studies [14, 18, 24, 27] because the risk of a twin pregnancy is increased with a double embryo transfer [28]. Two recent studies documented a higher level of obstetric complications in OD twin pregnancies compared with autologous IVF and NC twin pregnancies [29, 30]. Boria et al. [29] showed that twin OD pregnancies are associated with a higher risk of preterm birth compared to

Table 2 Main results of the included reviews from the search categorized by pregnancy outcome

	OR or RR (95% CI)	OD %	Autologous IVF/ICSI %	NC %	First author
Hypertensive disorders	OR 3.92 (3.21–4.78)	35	17		Jeve [12]
	OR 2.30 (1.60–3.32)	13.0–39.3	1.9–23.3	2.1–3.8	Storgaard [14]
	OR 2.63 (2.17–3.18)				Moreno [18]
> 40 years; hypertensive disorders	OR 2.33 (1.21–4.49)	23	10		Jeve [12]
Pregnancy-induced hypertension	OR 3.00 (2.44–3.70) versus ART OR 7.94 (1.73–36.36) versus NC				Masoudian [11]
	OR 3.08 (2.26–4.19)	17	5		Jeve [12]
	OR 3.87 (2.61–5.74)	30.6	10		Pecks [10]
	OR 2.16 (1.79–2.62)				Moreno [18]
Preeclampsia	OR 2.90 (1.98–4.24)	10	3		Jeve [12]
	OR 2.11 (1.42–3.15)	9.3–16.9	3.2–11.5	2.4–3.8	Storgaard [14]
	OR 2.54 (1.98–3.24) versus ART OR 4.34 (3.10–6.06) versus NC				Masoudian [11]
	OR 3.12 (2.56–3.85)	17.2	5.7		Blázquez [9]
	OR 2.64 (2.29–3.04)				Moreno [18]
Severe preeclampsia	OR 3.22 (2.30–4.49)				Moreno [18]
Small for gestational age	OR 1.81 (1.26–2.60)	9	5		Jeve [12]
	No significant difference				Storgaard [14]
Low birth weight < 2500 g	OR 1.53 (1.16–2.01)	8.2–13.5	3.4–11.2	3.2–3.4	Storgaard [14]
	OR 1.34 (1.12–1.60)	10.1–14.4	9		Mascarenhas [16]
	RR 1.18 (1.14–1.22)				Adams [15]
	No significant difference				Al Shammary [17]
	OR 1.25 (1.20–1.30)				Moreno [18]
Very low birth weight < 1500 g	OR 1.51 (1.17–1.95)				Mascarenhas [16]
	RR 1.24 (1.15–1.35)				Adams [15]
	OR 1.37 (1.22–1.54)				Moreno [18]
Cesarean section	OR 2.71 (2.23–3.30)	88	33		Jeve [12]
	OR 2.20 (1.85–2.60) versus IVF OR 2.38 (2.01–2.82) versus NC	31.4–85	25.3–56.0	16.3–17.5	Storgaard [14]
	OR 2.28 (2.14–2.42)				Moreno [18]
Preterm birth < 37 weeks	OR 1.34 (1.08–1.66	19	9		Jeve [12]
	OR 1.75 (1.39–2.20)	10.0–24.3	5.9–18.9	4.4–5.0	Storgaard [14]
	OR 1.45 (1.20–1.77)	10.8–15.9	9		Mascarenhas [16]
	RR 1.26 (1.23–1.30)				Adams [15]
	No significant difference				Al Shammary [17]
	OR 1.57 (1.33–1.86)				Moreno [18]
Early preterm birth < 32 weeks	OR 2.14 (1.40–3.25)				Mascarenhas [16]
	OR 1.80 (1.51–2.15)				Moreno [18]
Postpartum hemorrhage	OR 2.40 (1.49–3.88) versus IVF	4.2–17.3	0–9.4	5	Storgaard [14]
Intra uterine death	No significant difference				Jeve [12]
Gestational diabetes	No significant difference				Jeve [12] Storgaard [14]
	OR 1.27 (1.03–1.56)				Moreno [18]

OR, odds ratio; *RR*, relative risk; *CI*, confidence interval; *OD*, oocyte donation; *IVF*, in vitro fertilization; *ICSI*, intracytoplasmic sperm injection; *NC*, naturally conceived; *ART*, assisted reproductive techniques; *g*, grams

autologous twin pregnancies (OR 3.2; 95% CI 1.15–8.86; $p = 0.025$), even after adjustment for maternal age. In a larger cohort study, Guilbaud et al. [30] did not find a significant difference for preterm birth in OD twin pregnancy. Yet, they did show a significantly higher risk for pregnancy-induced hypertension (OR 3.1; 95% CI 1.4–6.6) and preeclampsia

Table 3 Pre-pregnancy and pregnancy care advice for oocyte donation (OD)

Pecks [10]	Close monitoring of the pregnancy Pregnancy under the care of obstetricians specializing in fetal-maternal medicine
Masoudian [11]	Pre-pregnancy counseling about risks compared with other assisted reproductive techniques or natural conception Closer surveillance after 20 weeks of gestation for the development of hypertensive disorders
Jeve [12]	Pre-pregnancy counseling about the risks, and that the risk is independent of age or multiple pregnancies Consider an individualized surveillance and management strategy The use of low-dose aspirin in OD pregnancies in the absence of any other risk factor requires further evaluation Oocyte cryopreservation for future fertility is suggested as an alternative for avoiding OD in selected cases
Blázquez [13]	Pre-pregnancy counseling about the risks Provide strict obstetrical surveillance
Storgaard [14]	Prophylactic dose of aspirin should be considered for OD pregnancies Pre-pregnancy counseling about the risks Only a single embryo should be transferred into the woman conceiving by OD
Adams [15]	Pre-pregnancy counseling about the risks
Mascarenhas [16]	Additional resource allocation for obstetric and neonatal units to cope with the increased demand of OD
Al Shammary [17]	Pre-pregnancy counseling about the risks, and clinical management of OD pregnancies
Moreno-Sepulveda [18]	Pre-pregnancy counseling about the risks, and that these risks are regardless of age or multiple pregnancies Perform a complete medical evaluation Obstetricians must implement adequate monitoring strategies during prenatal, labor, and postnatal care The use of serial ultrasounds to diagnose small for gestational age and fetal growth restriction Transfer of a single embryo during OD cycles
Berntsen [24]	Only single embryo transfer should be used in OD pregnancies and with an upper maternal age limit of 45–50 years Treatment with low-dose aspirin commencing early in pregnancy and continuing until 37 weeks of gestation

(OR 2.5; 95% CI 1.1–5.7) in OD twin pregnancy compared to autologous twin pregnancies, adjusted for maternal age, geographic origin, parity, and chorionicity. Still, the results in both studies did not translate into adverse neonatal outcomes [29, 30].

Jeve et al. [12] recommend individualized appropriate surveillance and management for every patient achieving pregnancy by OD. This is in concordance with the advice in the European Society of Human Reproduction and Embryology (ESHRE) guideline for premature ovarian insufficiency with regard to OD pregnancies [31]. They state that OD pregnancies are high risk and should be managed in an appropriate obstetric unit. Therefore, women and their partners should be encouraged to disclose the origin of their pregnancy with their obstetric team. Indeed, it is of importance to realize that the cases represented in the studies described in this review are evidently disclosed OD cases, but there are probably numerous unreported cases. One retrospective study in Ireland reported the nondisclosure of OD pregnancies, and observed less than one-third of OD pregnancies (30.2%; $n=32/106$) had unambiguous documentation, one-third (33%; $n=35/106$) had no documentation, and the remainder (36.8%; $n=39/106$) had a code only familiar to their obstetrician [32].

Next to informing patients on the increased risk for pregnancy complications after OD, the risks of the reproductive technique should also be taken into account. Research has shown that IVF has an increased risk for multiple pregnancies, spontaneous miscarriage, and ovarian hyperstimulation syndrome (OHSS) [33]. Moreover, the IVF treatment could cause adverse events because of the use of hormonal medication or because of oocyte retrieval. In a retrospective study including 4052 oocyte retrievals for OD, complications (intra-abdominal bleeding, severe pain, ovarian torsion) occurred in 0.42% of patients. Moderate to severe OHSS occurred in 0.87% of patients, but only with the use of recombinant human chorionic gonadotrophin [34]. Other studies have shown that the rates of serious complications due to oocyte retrieval vary between 0.02 and 0.3% for intra-abdominal bleeding, 0.01 and 0.6% for pelvic infection, and 0.08 and 0.13% for ovarian torsion [35–37].

Originally, the indication to perform OD was premature ovarian insufficiency [38]. Nowadays, the indication has been extended to other forms of infertility, including menopausal women [39], diminished ovarian reserve to multiple failed IVF attempts [40], and patients with a genetic trait precluding the use of their own oocytes [41]. Considering the menopausal and, consequently, older women, it is well established that pregnancy complications are significantly increased in women with advanced maternal age, mostly defined as age over 45 years [42]. Older women have a higher risk for cesarean delivery, gestational diabetes, hypertensive disorders, preterm labor, postpartum hemorrhage, and many other complications. Since OD and advanced maternal age, together and separately, create a significantly increased risk for preeclampsia, additional advice would be to offer an accurate pre-pregnancy analysis of the cardiovascular risk of women of 45 years or older who wish

to conceive through OD. This advice is supported by the opinion of the Ethics Committee of the American Society for Reproductive Medicine, recommending medical testing determining cardiovascular and metabolic health for women of advanced reproductive age (>45 years) and also psychosocial screening [27]. If medical conditions that further increase the obstetrical and neonatal risks are present, and if women are over 55 years of age, even with no underlying medical problems, OD should clearly be discouraged. Finally, the Ethics Committee states that it is ethically permitted to refuse OD to women of advanced reproductive age based on concerns over the health and well-being of the woman and offspring [27].

Directly associated with the higher maternal age is increased paternal age. There is a lack of information about the effect of paternal age on fertility and pregnancy. Recently, a relation has been shown with a higher incidence of miscarriages [43] and adverse outcomes in the offspring, such as psychiatric disorders, stillbirth, and several birth defects [44]. OD pregnancies form an ideal model to determine the effect of paternal age on reproductive outcomes, as oocyte donors are usually young women [5]. According to a systematic review that covered a total of 12,538 OD cases, no significant correlation was found between advanced paternal age and the rate of fertilization, embryonic cleavage development, implantation, pregnancy, miscarriage, or live birth [5]. Possibly, the development of these early pregnancy complications is determined by a combination of both the maternal and the paternal age, as in OD pregnancy the negative effects of advanced paternal age are compensated by the (often very) young donor. Moreover, a recent individual patient data meta-analysis, that included 2637 OD cycles, concluded that advanced paternal age is not associated with higher rates of aneuploidy in embryos derived from OD [45]. However, the age of the donor, not the recipient, is related to the risk of aneuploidy and should be taken into consideration during prenatal aneuploidy screening.

Since the past decade, the use of frozen-thawed embryo transfers in ART has increased [46, 47]. Recently, two meta-analyses demonstrated that frozen embryo transfer results in lower risks of preterm delivery, small for gestational age, and low birth weight compared to fresh embryo transfer. However, frozen embryo transfer was related to increased risks of hypertensive disorders, large for gestational age, and postpartum hemorrhage [48, 49]. Mascarenhas et al. [16] compared fresh embryo transfer after OD with fresh embryo transfer after autologous IVF and showed that the risk of (early) preterm birth and (very) low birth weight is significantly increased in pregnancies achieved by fresh OD. However, when frozen OD and IVF transfers were compared, only early preterm birth and very low birth weight were significantly higher in the achieved OD pregnancies [16]. In a more recent retrospective cohort study, including 15,937 pregnancies resulting from ART, pregnancies with autologous oocytes showed a higher preeclampsia rate after frozen versus fresh embryo transfer

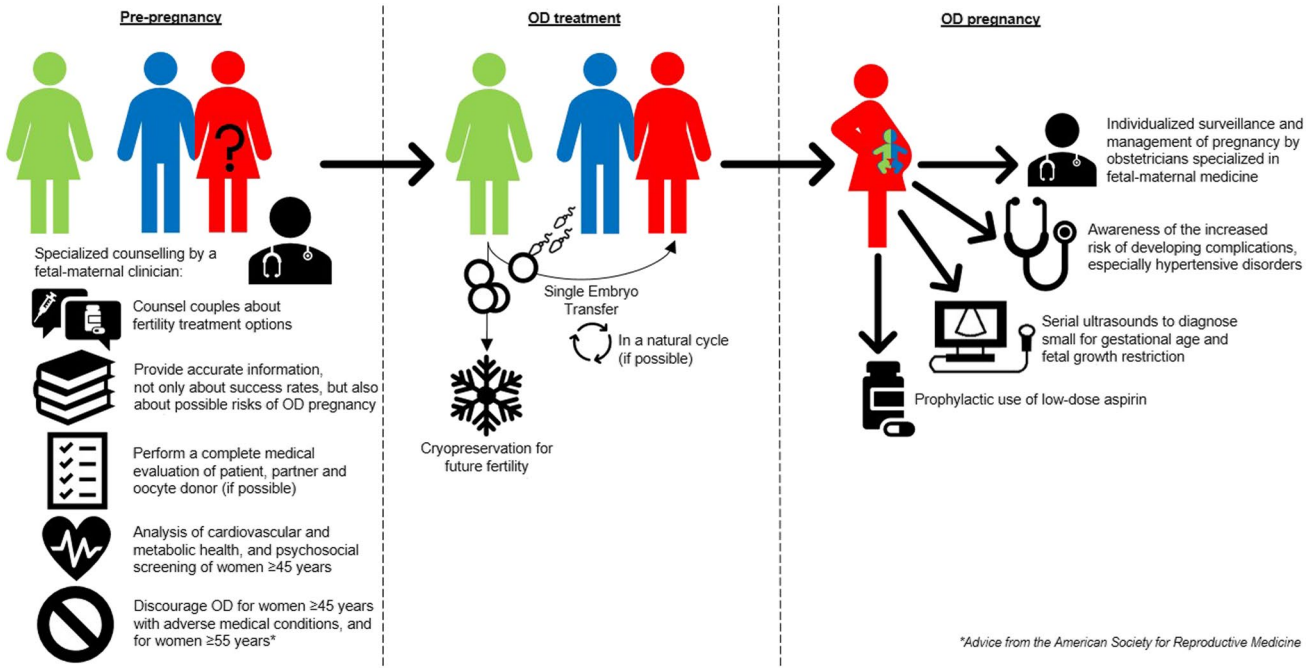

Fig. 2 Summary of advice for oocyte donation (OD) sorted by the following stages: pre-pregnancy counseling, OD treatment, and OD pregnancy

(OR = 2.17; 95% CI 1.67–2.82). With regard to OD pregnancies, no significant difference was found in the rate of preeclampsia between frozen ($n = 269$) and fresh ($n = 643$) embryo transfer [50]. Another retrospective cohort study with 433 patients conceiving through OD (fresh $n = 353$; frozen $n = 80$) showed that, despite a high prevalence of preeclampsia, the freezing–thawing process did not cause more risks than the fresh embryo transfers with regard to preterm preeclampsia, term preeclampsia or pregnancy-induced hypertension [9]. Hence, at this moment we do not advise restricting to either fresh or frozen embryos for OD pregnancies.

For transfer of the embryo, a natural or artificial endometrial cycle of the recipient can be used. Possibly, the absence of the corpus luteum in artificial cycles may play a role in the increased risk for hypertensive disorders [46]. This corpus luteum not only produces estrogen and progesterone but also vasoactive agents, such as relaxin and vascular endothelial growth factor (VEGF). These agents are hypothesized to be important for placentation, and abnormal early placentation is critical for the development of preeclampsia. As relaxin and VEGF are not replaced in an artificial cycle program, this is related to a deficiency of these vasoactive agents compared with a natural cycle [46]. We could assume that this effect is also seen in OD pregnancies, though studies are lacking. Moreover, since OD is mostly indicated for premature ovarian insufficiency or menopausal women [40], most women achieving pregnancy through OD will not have a natural cycle. Hence, embryo transfer using an artificial cycle is needed, lacking luteal vasoactive support.

Usually in standard pre-pregnancy counseling, also the effect of the underlying cause of infertility on pregnancy is discussed. However, the underlying cause to perform OD is very diverse. An obstetric healthcare worker should think about counseling on the effect on pregnancy, for example in relation to advanced maternal age, premature ovarian insufficiency, Turner syndrome, and preceding gonadotoxic treatment, including radiotherapy, chemotherapy, and surgery. It falls beyond the scope of this manuscript to describe the maternal risks for every underlying indication, but it is necessary to individualize the pre-pregnancy counseling considering these risks.

Conclusion

There are several publications on the clinical outcomes of OD pregnancy, showing an increased risk for various obstetric and neonatal complications. Although all the (systematic) reviews included in the current study give an advice on pre-pregnancy counseling in OD pregnancy, there is low or no evidence on the reduction of pregnancy complications. However, considering the increased risk of OD, it is necessary to provide experience-based and comprehensive pre-pregnancy counseling to patients undergoing OD. In most cases, these patients will have no alternative method to conceive. Therefore, alertness toward the risk profile of OD pregnancies is necessary, and an individualized appropriate surveillance and management strategy should be considered for OD treatment and care throughout pregnancy and labor. We have summarized our advice in Fig. 2.

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Author Contribution M.L. van der Hoorn came up with the idea for the article. M.L. van der Hoorn and K. van Bentem performed the literature search, data analysis, and drafted the work. All authors critically revised the work.

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Code Availability Not applicable.

Declarations

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Conflict of Interest The authors declare no competing interests.

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