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ARTICLE

Cost-effectiveness of hysteroscopy screening for infertile women

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Jenneke Cornelia Kasius attended the medical school and started her scientific carrier at the University Medical Center Utrecht, The Netherlands. She obtained her medical degree in 2009 and continued her research for a PhD. In 2010 she started to combine her research with clinical work at the department of gynaecology and obstetrics at the St Antonius Hospital, Nieuwegein and started her official residency in gynaecology and obstetrics at the Twee StedenZiekenhuis, Tilburg. Significance of hysteroscopy screening prior to assisted reproduction, since when she has been continuing her residency at the University Medical Center Utrecht.

Abstract This study assessed the cost-effectiveness of office hysteroscopy screening prior to IVF. Therefore, the cost-effectiveness of two distinct strategies – hysteroscopy after two failed IVF cycles (Failedhyst) and routine hysteroscopy prior to IVF (Routinehyst) – was compared with the reference strategy of no hysteroscopy (Nohyst). When present, intrauterine pathology was treated during hysteroscopy. Two models were constructed and evaluated in a decision analysis. In model I, all patients had an increase in pregnancy rate after screening hysteroscopy prior to IVF; in model II, only patients with intrauterine pathology would benefit. For each strategy, the total costs and live birth rates after a total of three IVF cycles were assessed. For model I (all patients benefit from hysteroscopy), Routinehyst was always cost-effective compared with Nohyst or Failedhyst. For the Routinehyst strategy, a monetary profit would be obtained in the case where hysteroscopy would increase the live birth rate after IVF by ≥2.8%. In model II (only patients with pathology benefit from hysteroscopy), Routinehyst also dominated Failedhyst. However, hysteroscopy performance resulted in considerable costs. In conclusion, the application of a routine hysteroscopy prior to IVF could be cost-effective. However, randomized trials confirming the effectiveness of hysteroscopy are needed. RBMOnline

KEYWORDS: assisted reproduction, cost-effectiveness, hysteroscopy, infertility, IVF

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Introduction

Despite progressing improvement of IVF, the maximum implantation rate per embryo transferred usually does not exceed 30% (Andersen et al., 2008). Even if both ovum retrieval and fertilization occur successfully in the process of IVF, there is a large unexplained drop between embryo transfer and occurrence of pregnancy. Implantation failure presents a major clinical challenge and is a cause of considerable stress to patients and their carers in assisted reproductive technology. Next to the physiological and physical burden that comes with every IVF cycle, implantation failure also adds up to the considerable costs associated with fertility treatment (Bouwmans et al., 2008). If progress is to be made in improving implantation rates, a greater understanding of the factors that determine successful implantation is required.

Implantation failure could be due to the embryo, uterine environment or a combination of both. Even minor uterine cavity abnormalities, such as endometrial polyps, small submucous myomas, adhesions and septa, are considered to have a negative impact on the chances of conceiving through IVF (Rogers et al., 1986). The prevalence of unsuspected intrauterine abnormalities, diagnosed by hysteroscopy prior to IVF, has been described to be 11—45% (Balmaceda and Ciuffardi, 1995; Demirol and Gurgan, 2004; Doldi et al., 2005; Fatemi et al., 2010; Hinckley and Milki, 2004; Oliveira et al., 2003; Rama Raju et al., 2006; Sala la et al., 1998; Shamma et al., 1992). Therefore, it is advocated to diagnose and treat these abnormalities in order to optimize the condition of the uterine environment and thereby the outcome of IVF treatment. However, high-quality evidence that defines the influence of screening for intrauterine pathology on reproductive outcome is absent (Demirol and Gurgan, 2004; Doldi et al., 2005; Oliveira et al., 2003; Rama Raju et al., 2006; Shamma et al., 1992).

At present, the basic work up for evaluation of the uterine cavity prior to IVF consists of transvaginal ultrasound (TVS), possibly followed by gel or saline infusion sonography (GIS or SIS), hysterosalpingography (HSG) or hysteroscopy. The accuracy of HSG in assessment of the uterine cavity integrity in infertile patients has been reported to be rather disappointing (Gaglione et al., 1996; Golan et al., 1996). Whereas gel instillation sonography or SIS are increasingly considered to be useful in diagnosing intrauterine abnormalities, hysteroscopy is still known as the gold standard (Bozdag et al., 2008). It is easy to perform in an outpatient clinic without anaesthesia. Advanced evaluation of the uterine cavity besides TVS is not recommended as routine fertility work up (Crosignani and Rubin, 2000; Dutch Society of Gynaecology, 2004; Royal College of Obstetricians and Gynaecologists, 2004). Daily practice shows that hysteroscopy is chosen over SIS/GIS in the case of a normal TVS, as hysteroscopy enables diagnosis and treatment of intrauterine pathology in the same setting.

Due to paucity of high-quality evidence on the impact of unsuspected intrauterine abnormalities on IVF outcome in asymptomatic infertile patients, there is the possible widespread introduction of hysteroscopy and other imaging techniques prior to IVF, without the certainty that this policy is truly (cost-)effective. Therefore, the aim of the current study was to provide the cost-effectiveness analysis of hysteroscopy as a routine procedure for assessment of the uterine cavity prior to IVF treatment.

Materials and methods

Decision analytic model

To determine whether implementation of routine hysteroscopy prior to IVF treatment could be cost-effective, a decision-making model was made. The hypothetical patient population consisted of infertile women, indicated for IVF/intracytoplasmic sperm injection treatment with no symptoms of intrauterine pathology and a normal transvaginal sonography. The decision model contained three strategies, according to the most commonly used scenarios in daily clinical practice. In strategy ''Nohyst'', all patients underwent IVF treatment cycles without hysteroscopy screening. In the case of a normal TVS, a maximum of three IVF treatment cycles were performed. This strategy was considered as the reference strategy. In stategy ''Failedhyst'', patients with two failed IVF treatment cycles underwent screening hysteroscopy. In the case of a normal TVS and if a pregnancy had not been achieved after two subsequent IVF treatment cycles, hysteroscopy screening was performed. Also, intrauterine abnormalities (endometrial polyps, submucous myoma, adhesions, septa) were treated during the same hysteroscopy procedure. In addition, a third IVF treatment cycle was performed. In final strategy; ''Routinehyst'', patients underwent a hysteroscopy prior to the first IVF treatment cycle. All women with a normal TVS underwent a screening hysteroscopy. Intrauterine abnormalities, predefined as endometrial polyps, submucous myoma, adhesions or septa, were treated during the same hysteroscopy procedure. Afterwards, a maximum of three IVF treatment cycles was performed.

Model input

Probabilities

The probability data of the decision model were obtained from the best available evidence concerning hysteroscopy in fertility treatment. The prevalence of minor intrauterine abnormalities has been widely investigated. However, the results of prevalence studies are rather diverse. The prevalence in studies among asymptomatic, infertile patients, with a normal TVS or HSG, is reported to be between 11—40% (Balmaceda and Ciuffardi, 1995; Fatemi et al., 2010; Hinckley and Milki, 2004; Sala la et al., 1998).

The exact effect of detection and treatment of these abnormalities by hysteroscopy prior to IVF has not been clarified yet. The best available evidence consists of only two randomized trials (Bosteels et al., 2010; Bozdag et al., 2008; El-Toukhy et al., 2008). In a population of women with two or more failed IVF cycles, both Demirol and Gurgan (2004) and Rama Raju et al. (2006) assessed the difference in pregnancy rate between a group without hysteroscopy (I) and a group with hysteroscopy and immediate treatment of detected pathology if present (II). In both studies a firm increase was observed in pregnancy rates in group II compared to group I, irrespective of the absence or presence of intrauterine abnormalities. Demirol and Gurgan (2004) found a pregnancy rate of 22% in group I. The patients in group II with abnormalities had a pregnancy rate of 30%, the patients without pathology 33%. Rama Raju et al. (2006) found a pregnancy rate of 26% versus 40% and 44%, respectively. Moreover, Rama Raju et al. (2006) reported an increase in live birth rate of 8.4% (16.6% versus 25% and 30%). This implies that both finding and treating unexpected abnormalities as well as performing the hysteroscopy itself may improve pregnancy chances.

For population-based pregnancy rates, the Dutch IVF results of the yearly report by the Dutch Foundation of Infertility Registration were used. The live birth rate after IVF in 2007/2008 was 23.3% (Kremer, 2012).

Costs

The cost-effectiveness analysis was conducted from a healthcare provider perspective. The costs per IVF treatment cycle in the Netherlands in 2004 were calculated to be €2381 (Bouwmans et al., 2008). These costs were transferred to the costs per IVF cycle in 2008 by taking into account the health-specific increase in expenses of 1.2–2.5% per year (Hakkaart-Roijen van et al., 2010). The costs of one outpatient screening hysteroscopy have not previously been assessed. Therefore, the direct costs in healthcare sector were estimated, making use of standard prices (**Table 1**) (Hakkaart-Roijen van et al., 2010). Also, questionnaires on the costs of a hysteroscopy were obtained from three different non-academic hospitals. The average costs of one hysteroscopy based on the questionnaires were compared with the costs of one hysteroscopy based on the standard prices. The costs related to possible complications were not assessed. As the TVS carried out prior to starting treatment was normal, only minor intrauterine pathology and therefore a futile complication rate was to be expected. Also, the indirect costs were not assessed, as it would surpass the objective of the current study.

Analysis and outcomes

For analysis of the cost-effectiveness of hysteroscopy prior to IVF, two models were used. Model I was exclusively based on the available evidence, which postulates that all infertile patients undergoing hysteroscopy prior to IVF encounter an increase in pregnancy rate, disregarding the presence or absence of intrauterine abnormalities. This increase in pregnancy rate for patients who underwent hysteroscopy was recharged for every subsequent IVF treatment cycle. Model II is a more hypothetical, although potentially more realistic, model. In this model, the assumption was made that the patients with intrauterine abnormalities had a reduced chance to conceive. The pregnancy rate through IVF would convert to the normal pregnancy rate in the case of the patient underwent hysteroscopy. Thus, in model II, the increase in pregnancy rate through hysteroscopy was solely calculated for patients with intrauterine abnormalities. The increase in pregnancy rate for patients who underwent hysteroscopic treatment was recharged for every subsequent IVF treatment cycle. Models I and II were analysed using Microsoft Excel. The primary study outcome parameters for both models were the total costs per live birth and effects, expressed as cumulative live birth rate after three IVF cycles, for each of the three strategies. The base-case analysis was performed making use of the average value of all model variables (**Table 2**). Sensitivity analysis was performed, to analyse the effect of variation of the baseline assumptions of each of the variables in the model separately.

Forthcoming out of the primary study outcomes, the extra costs for achieving an additional live birth in relation to the reference strategy Nohyst, the incremental cost-effectiveness ratios (ICER) were calculated. To test the uncertainty of the estimated costs and effects of Failedhyst and Routinehyst in relation to Nohyst, a Monte Carlo simulation using 1000 combinations of the values randomly drawn from uniform distributions within the preset range of the variables (**Table 2**) was performed and illustrated in a scatter plot in the incremental cost-effectiveness plane. From these results the probability of a strategy being more cost-effective than the reference strategy at a given

Table 1 Costs for hysteroscopy, based on estimated standard costs.

Variable	€
Personnel	
Gynaecologist	34
Assisting personnel	14
Hysteroscopic procedure	
Hysteroscope (and maintenance)	7
Other material used during procedure (infusion fluid, gloves, paper, etc.)	2
Other hospital services used (histopathological examination)	50
Supporting facilities (reception, hospital cleaning, etc.)	19
Total	126

The direct costs in the healthcare sector were estimated making use of standard prices (Hakkaart-Roijen van et al., 2010).

Table 2 Distribution of each of the variables use in the model analysis.

	Lower range	*Upper range*	*Average (Median)*
Increase in live birth rate through hysteroscopy (%)[a]	1	9	4.5
Prevalence of intrauterine abnormalities (%)	11	40	25.5
Population-based live birth rate after IVF (%)	23	24	23.5
Costs of one screening hysteroscopy)[a]	100	150	125
Costs of one IVF treatment cycle (€)	2500	2600	2550
Drop-out rate (%)	2	2	2

[a]Costs for screening hysteroscopy and see-and-treat in case of abnormalities (**Table 1**).

threshold for society's willingness to pay was visualized in a cost-effectiveness acceptability curve. This curve illustrates the proportion of the 'costs and effects pairs' — shown in the incremental cost-effectiveness plane (*y*-axis) — which are cost-effective for a range of monetary values (*x*-axis).

Results

Model input, probabilities and costs

The estimated costs of a screening hysteroscopy, based on standard prices was €126 (**Table 1**). The overall costs were comparable to the average costs of a hysteroscopy in the three reference hospitals, which was on average €124. Calculating the health-specific increase in expenses per year, the costs of IVF in 2008 were estimated to be on average €2550. An overview of the assumed distribution of all variables of the analysed models is shown in **Table 2**.

Model I

In model I, the live birth rate of all patients increased after hysteroscopy. Base-case analysis, making use of the average values of the variables, showed that the cumulative birth rate in three cycles was 46.7%, 48.4% and 50.4% for Nohyst, Failedhyst and Routinehyst, respectively. The accompanying costs were €10,851, €10,570 and €9341 per live birth, making Routinehyst the least expensive and the most effective of the three strategies (**Table 3**). Sensitivity analysis was performed, comparing the analysis of a scenario in which all model variables were in favour of routine hysteroscopy to a scenario in which all model variables were out of favour of routine hysteroscopy (**Table 3**). This illustrated that Routinehyst was always dominant over Nohyst and Failedhyst. In the case where only the increase in live birth rate through hysteroscopy was varied in the base-case analysis, Routinehyst was found to even give a monetary profit over Nohyst from an increase in live birth rate of 2.8% onwards (**Figure 1A**).

The Monte Carlo uncertainty analysis, illustrated in an incremental cost-effectiveness plane, is visualized in **Figure 2A**. The interventions falling in a south-east quadrant are by definition cost-effective, as they combined positive effects with a decrease in costs. Interventions falling in a north-east quadrant are relatively cost-effective: increase in effects and increase in costs. **Figure 2A** illustrates that Routinehyst is mainly positioned in the south-east quadrant, resulting in a monetary profit. Also, Routinehyst is generally positioned south-east in relation to Failedhyst, thereby visualizing that Routinehyst is the most cost-effective strategy.

The probability of Routinehyst and Failedhyst being cost-effective compared with the reference Nohyst in relation to the willingness to pay for one additional live birth was shown in the cost-effectiveness acceptability curve (**Figure 3A**). Routinehyst is shown to have the highest probability of being the strategy with the highest health benefit compared with the other two strategies. From €2000 per

Table 3 Sensitivity analysis, showing the base-case analysis, the analysis of a scenario in which all model variables are in favour of hysteroscopy and the analysis of a scenario in which all model variables are out of favour of hysteroscopy.

	Model I			Model II		
	Out of favour	Baseline	In favour	Out of favour	Baseline	In favour
Population-based LBR (%)	23	23.5	24	23	23.5	24
Intrauterine pathology (%)	—	—	—	11	23.5	40
Increase in LBR through HY (%)	1	4.5	9	1	4.5	9
Cost of one HY (€)	150	125	100	150	125	100
Cost of one IVF cycle (€)	2500	2550	2600	2500	2550	2600
Cumulative LBR (%)						
Nohyst	45.9	46.7	47.4	45.9	46.6	47.1
Failedhyst	46.3	48.4	50.7	46.0	47.1	48.7
Routinehyst	47.5	50.4	60.2	46.1	48.5	52.8
Total costs for one LB (€)						
Nohyst	10,870	10,851	10,833	10,870	10,867	10,913
Failedhyst	10,903	10,570	10,197	10,984	10,859	10,647
Routinehyst	10,733	9341	8045	11,143	10,604	9610
ICER						
Failedhyst	15,000	2778	1111	13,3267	10,004	−1176
Routinehyst	6728	−1127	−2372	82,554	3938	−1176

Out of favour = all variables in the model are out of favour of hysteroscopy; Baseline = base-case analysis, making use of all the average values of the variables in the model (**Table 1**); In favour = all variables in the model are in favour of hysteroscopy.
Failedhyst = hysteroscopy after two failed IVF cycles; Nohyst = reference strategy of no hysteroscopy; HY = hysteroscopy; ICER = incremental cost-effectiveness ratio (additional costs/additional live births) compared with the reference Nohyst; LB = live birth; LBR = live birth rate; Routinehyst = routine hysteroscopy prior to IVF.

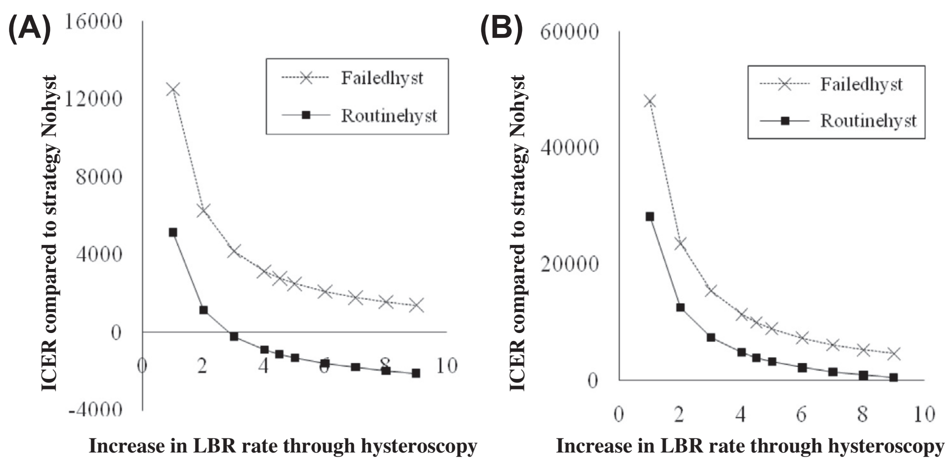

Figure 1 Sensitivity analysis illustrating the effect of the increase in live birth rate (LBR) after hysteroscopy (*x*-axis) on the incremental cost-effectiveness ratio (ICER, the additional costs/additional live birth; *y*-axis) for Failedhyst and Routinehyst in relation to the reference Nohyst. (**A**) Model I: increase in LBR after IVF in all patients who underwent hysteroscopy. (**B**) Model II: increase in LBR after IVF solely in the patients who underwent hysteroscopy and treatment of present, predefined intrauterine abnormalities. Nohyst = reference strategy of no hysteroscopy; Failedhyst = hysteroscopy after two failed IVF cycles; Routinehyst = routine hysteroscopy prior to IVF.

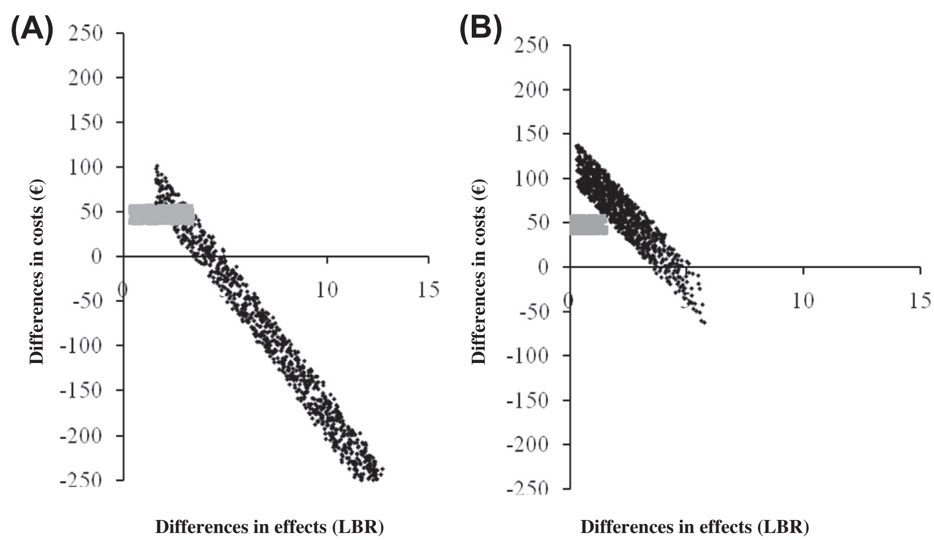

Figure 2 The incremental cost-effectiveness plane, showing the difference in live birth rate (LBR) in relation to the difference in costs for Failedhyst (in grey) and Routinehyst (in black) versus Nohyst (reference strategy). Data built up from 1000 random combinations of the values within the range of the variables that are contained in a model (**Table 2**). (**A**) Model I: increase in LBR after IVF in all patients who underwent hysteroscopy. (**B**) Model II: increase in LBR after IVF solely in the patients who underwent hysteroscopy and treatment of present, predefined intrauterine abnormalities. Nohyst = reference strategy of no hysteroscopy; Failedhyst = hysteroscopy after two failed IVF cycles; Routinehyst = routine hysteroscopy prior to IVF.

added live birth onwards, there is a 90% probability that Routinehyst is cost-effective compared with Nohyst.

Model II

In model II, the live birth rate after IVF was assumed to increase solely in patients with an intrauterine abnormality in case where they underwent screening hysteroscoy. Making use of the average values of the model variables, base-case analysis showed that the cumulative birth rate were 46.6%, 47.1% and 48.5% for Nohyst, Failedhyst and Routinehyst, respectively. The accompanying costs per live birth rate were €10,867, €10,859 and €10,604. Routinehyst was found to dominate Failedhyst; however, hysteroscopy performance was accompanied with extensive costs (**Table 3**). The cost-effectiveness plane shows that the greater part of the Routinehyst did not fall in the south-east quadrant, implying that this strategy will probably not provide monetary profit in relation to Nohyst (**Figure 2B**). The cost-effectiveness acceptability curve showed that the probability of Routinehyst having the highest health benefit was always dominating the probability of Failedhyst having the highest health benefit. From €15,800 per added live birth onwards, there is a 90% probability that Routinehyst is cost-effective compared with Nohyst (**Figure 3B**).

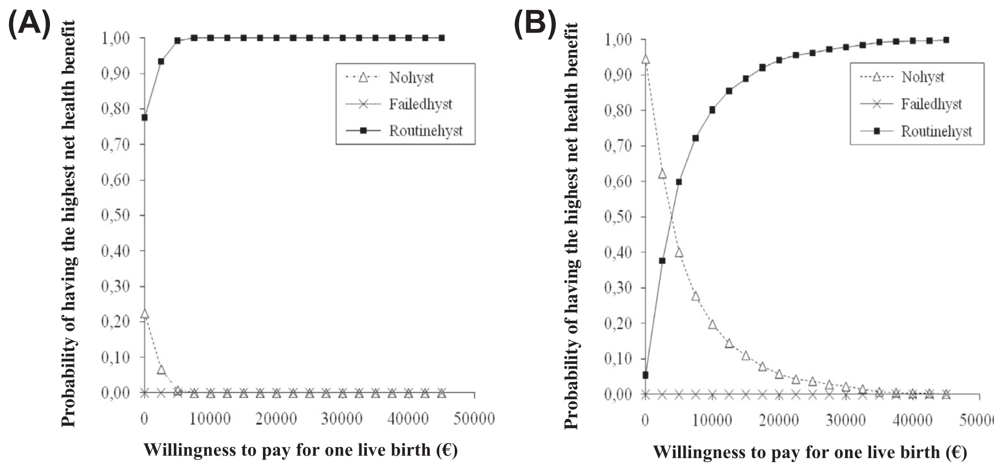

Figure 3 Acceptability curve showing the probability of having the highest net health benefit in relation to the willingness to pay for one additional live birth for the three strategies Nohyst, Failedhyst and Routinehyst. (**A**) Model I: increase in live birth rate (LBR) after IVF in all patients who underwent hysteroscopy. (**B**) Model II: increase in LBR after IVF solely in the patients who underwent hysteroscopy and treatment of present, predefined intrauterine abnormalities. Nohyst = reference strategy of no hysteroscopy; Failedhyst = hysteroscopy after two failed IVF cycles; Routinehyst = routine hysteroscopy prior to IVF.

Discussion

Increasingly, it is recommended to perform a routine office hysteroscopy prior to an IVF treatment cycle (Bozdag et al., 2008; El-Toukhy et al., 2008). The rationale behind this suggestion is however based on limited research and mostly concerns a very specific patient population. Clinical investigation into the significance of hysteroscopy in the fertility work up is time consuming. Model analysis can be useful by giving insight into the relationship between different parameters that influence the outcome after fertility treatment. The current study showed that the cost-effectiveness of a hysteroscopy in the fertility work up mainly depends on its specific impact on the live birth rate and whether the model variable 'abnormality prevalence' was taken into account.

In model I, the abnormality prevalence was not involved in the decision model. All patients who underwent hysteroscopy prior to IVF were considered to benefit from an increase in live birth rate. In such a model, Routinehyst seemed to generally dominate the other strategies. Routinehyst was, with a probability of 90%, cost-effective over the reference strategy in the case of willingness to pay for one added live birth $\geq$€2000. This means that, according to the acceptability curve originating from the Monte Carlo simulation, performance of screening hysteroscopy is most probably cost-effective in the case where society is willing to pay at least €2000 per live birth on top of the costs of a live birth after IVF without screening hysteroscopy. As most Western societies would be willing to pay such a sum of money, routine hysteroscopy would be the preferred final step before starting IVF treatment.

If the abnormality prevalence is taken into account in the decision analysis and solely patients with intrauterine abnormalities gained increase in pregnancy rate after hysteroscopic treatment, as was applied in model II, the cost per live birth were considerably higher for all three strategies. This would necessitate the willingness to pay for one additional live birth to rise to the amount of $>$€15,800 to make routine hysteroscopy cost-effective compared with no hysteroscopy prior to IVF, with a probability of 90%. Such a sum of money would possibly be too high, depending on whether a reimbursement system is present or costs are fully compensated by the patient herself.

In model I, the degree of increase in live birth rate after hysteroscopy was the only model variable which had an exponential effect on the incremental cost-effectiveness ratio of the strategies. This occurred due to the fact that the impact of this variable was accounted for in all subsequent IVF cycles. Unfortunately, the data on the increase in live birth rate after IVF treatment by hysteroscopy is based on sparse research, performed amongst women with two or more failed IVF cycles.

As the cost-effectiveness of a strategy was most sensitive to the variation in the model assumptions concerning the increase in live birth rate, which was based on questionable data, model II was designed. By analysing model II, the aim was to put the possible excessive effect of a routine hysteroscopy in perspective by taking into account the abnormality prevalence. Thereby it was found that variation in the abnormality prevalence also had an exponential effect on the incremental cost-effectiveness ratio of a strategy; however, it was still not as excessive as the degree of improvement in live birth rate after hysteroscopy performance.

Neither decision model contained a scenario including SIS/GIS. In daily practice, SIS/GIS is performed in the case of abnormal findings at TVS, and the diagnostic value in women with normal TVS is currently not known. Also, whereas SIS/GIS are of diagnostic value, hysteroscopy can provide instant treatment. Finally, it is postulated that the hysteroscopy procedure itself might increase the chance to conceive. Embryo implantation comprises a process of physiological inflammation, with several inflammatory mediators such as leukocytes, cytokines and chemokines and other endometrial factors involved (Romero et al., 2004). It has been suggested that the hysteroscopy procedure itself facilitates activation of these factors. Moreover, it has been postulated that pressure dilatation of the uterine cavity and tubes may be effective in improving fertility (Mooney and Milki, 2003). To closely simulate daily practice and make the models least complex, SIS/GIS were not included. In order to include SIS/GIS as a screening tool for cavity assessment direct comparison studies are clearly needed, and currently such a comparison is part of the inSIGHT trial (Smit et al., 2012, trial number NCT01242852).

Another weakness is the lack of research into the costs of outpatient hysteroscopy. The costs of an outpatient hysteroscopy versus a day-case hysteroscopy have been assessed. However, the standard costs (e.g. travel expenses, overheads) have not been analysed (Marsh et al., 2004). Therefore, questionnaires on the costs accompanying hysteroscopy in combination with standard costs had to be used. It appeared from the sensitivity analysis that the influence of the costs of one hysteroscopy on the study outcome was rather small.

Also less distinct endometrial pathology is thought to cause impaired endometrial receptivity resulting in infertility (Kamiyama et al., 2004). Next to treatment of visible intrauterine abnormalities, hysteroscopy offers the major benefit of direct biopsies and histological investigation from suspected endometrial areas. This was not implemented in the decision model because the prevalence of endometrial inflammation varies considerably and the impact of neither the endometritis itself nor the antibiotic treatment of the entity is currently very clear. (Cicinelli et al., 2005; Feghali et al., 2003; Haggerty et al., 2003; Johnston-Macananny et al., 2010; Kasius et al., 2011; Polisseni et al. 2003).

A final limitation could be the restriction to three IVF cycles analysed. Thereby, the performance of hysteroscopy after two failed IVF cycles in Failedhyst led to a significant increase in total costs per live birth, whereas the effect was only accounted for in one IVF cycle. For Routinehyst, relatively more hysteroscopies were carried out, resulting in slightly higher costs, but also in an increase in live birth rate for a total of three following IVF cycles. Nevertheless, analysis of three IVF cycles was thought to be closest to reality. Moreover, the considerable difference in cost-effectiveness between Routinehyst and Failedhyst would probably also remain by analysing an extra IVF cycle and not have changed the study recommendations.

The Dutch Society of Gynaecology as well as the European Society for Human Reproduction and Embryology and Royal College of Obstetricians and Gynaecologists do not recommend hysteroscopy or SIS/GIS as initial investigation prior to starting IVF (Crosignani and Rubin, 2000; Dutch Society of Gynaecology, 2004; Royal College of Obstetricians and Gynaecologists, 2004). It has been argued that the significance of treating unsuspected intrauterine abnormalities has not yet been fully proven. The cost-effectiveness of the three strategies in both models was indeed mainly influenced by the impact of hysteroscopy on the chance to conceive. However, assuming that the impact of hysteroscopy passes through three IVF cycles, performance of hysteroscopy could be promising for improving the cost-effectiveness of IVF treatment. It was shown that the costs per live birth mainly increased if the effect of hysteroscopy on the chance to conceive declined. Therefore, the question rises as to how much society is willing to pay for one additional live birth. In 2004, the costs per ongoing pregnancy resulting from IVF treatment (including the pre-IVF diagnostic work up) was calculated to be €10,768 (Bouwmans et al., 2008). Taking into account the health-specific increase in expenses per year, the costs for an ongoing pregnancy in 2008 would be €11,532. According to model I, these costs most probably increase by a maximum of €2000 in cases where hysteroscopy screening is performed. As stated in model II, the costs per ongoing pregnancy resulting from IVF could raise by €15,800 – and therefore double – making Routinehyst not preferable. The general accepted amount to be paid for one additional QALY (quality-adjusted life year) was found to be >€20,000 (Hirth et al., 2000). Therefore, it is up to the healthcare physicians to decide whether the extra amount of €15,800 per live birth would justify the implementation of routine hysteroscopy prior to IVF treatment.

While interpreting data from a model analysis, one should keep in mind that it concerns a hypothetical analysis, based on the available literature. The results of model analysis are as reliable as the reliability of the literature it is extrapolated from. This study's results should therefore not be interpreted as the evidence that hysteroscopy prior to IVF improves the IVF outcome. It only shows that implementation of a screening hysteroscopy may turn out to be cost-effective, under the assumption of increased live births with hysteroscopy. Consequently, further study on this subject is warranted. Currently, the inSIGHT trial is being conducted, which will investigate the significance of routine hysteroscopy prior to a first IVF/intracytoplasmic sperm injection treatment cycle in asymptomatic patients with a normal transvaginal ultrasound. With the outcomes of this trial, it will be possible to further define the cost-effectiveness of that strategy (Smit et al., 2012, trial number NCT01242852).

Thus, according to the published literature, the application of a routine hysteroscopy prior to IVF may to be cost-effective. However, sensitivity analysis has shown that the cost-effectiveness of a scenario is most influenced by the variance in increase in ongoing pregnancy rate by performing a hysteroscopy, on which the evidence is sparse. Moreover, in the case solely of patients with intrauterine abnormalities who experience the positive effect of hysteroscopy on fertility, hysteroscopy is accompanied with significant extra costs for an additional live birth. Therefore, additional data on this subject is crucial to recommend the most cost-effective strategy for daily practice.

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