Identify, appraise and individualize: clinical practice and prediction models in recurrent pregnancy loss

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CHAPTER 5

EVALUATION OF AN IMPLEMENTATION STRATEGY TO IMPROVE GUIDELINE ADHERENCE IN COUPLES WITH RECURRENT PREGNANCY LOSS

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ABSTRACT

INTRODUCTION

Clinical management of couples with recurrent pregnancy loss (RPL) is often not in accordance with guideline recommendations, resulting in costly and ineffective management of couples with RPL. It is known from guideline implementation research that dissemination of new guidelines alone is not enough to achieve proper guideline adherence and that robust implementation efforts are necessary. Unfortunately, no gold standard exists for successful implementation of new evidence. The objective of this study was therefore to test a multi-faceted implementation strategy on its capability to improve guideline adherence in couples with RPL.

MATERIALS AND METHODS

A cohort study was performed in nine Dutch hospitals within a 12-month period before and a six-month period after the introduction of the strategy. A systematically developed strategy was introduced in the Obstetrics and Gynaecology departments of four hospitals in the Netherlands. Guideline adherence in women with RPL was measured before and after introduction of the implementation strategy. Indicators covered diagnostics, therapy and counselling. Multilevel analyses were performed to compare the change in guideline adherence after the introduction of the strategy. A cost-effectiveness analysis was performed from a health care perspective.

RESULTS

356 women were included before and 243 after introduction of the strategy. Adherence was significantly higher on most indicators on diagnostics and counselling. The highest increase was measured for selective screening for thrombophilia (+37%, Odd Ratio (OR); 5.2, 95% Confidence Interval (CI) 3.6-7.6). The use of the specified medical chart file, patient questionnaire, pocket card and electronic decision program were related to higher adherence. Health care costs in the four participating centres were reduced with 206,916 euros annually.

CONCLUSION

Adherence to the guideline on RPL improved after introduction of the implementation strategy, the strategy was feasible and effective and costs were reduced. This implementation strategy can widely be introduced in clinical practice for RPL, and may serve as an example for future implementation strategies in other areas within obstetrics and gynaecology.

INTRODUCTION

Clinical management of couples with recurrent pregnancy loss (RPL) is often not in accordance with clinical evidence as summarized in guidelines (1-4). Under as well as over diagnostics are observed, resulting in an overall costly and ineffective management of couples with RPL (5). It is known from guideline implementation research that dissemination of new guidelines alone is not enough to achieve proper guideline adherence and that robust implementation efforts are necessary (6, 7).

Although intended to be revised regularly, revision of complete guidelines is a time-consuming process. At the time guideline adherence was measured, the RPL guideline from the Dutch Society of Obstetrics and Gynaecology (NVOG) was just published in the Netherland (3) and adopted by the National Guideline Clearinghouse (2009) (1). A recent study compared guidelines from the European Society of Human Reproduction and Embryology (ESHRE) (8), the British Royal College Obstetrics and Gynaecology (9) and a committee opinion of the American Society for Reproductive Medicine (ASRM 2013) (10, 11), showing both similarities and differences in RPL practice (12). These guidelines were partly in agreement with the Dutch guideline. Currently, an updated version of the ESHRE guideline is being expected, as well as a new RCOG guideline.

Unfortunately, no gold standard exists for successful implementation of new evidence. The most frequently studied interventions include audit and feedback on current quality of care and the dissemination of educational materials, with varying efficacy (13, 14). The effects of patient centred strategies in implementation in reproductive medicine have been explored, and showed varying degrees of success on implementation of guidelines (15-17). In other words, it is not obvious which implementation strategy has to be applied to improve guideline adherence and thereby quality of care in couples with RPL, but strategies tailored to existing barriers and facilitators have the best potential to gain effect in improving guideline adherence (15, 18). The main facilitators for guideline adherence in RPL are lower maternal age, adverse obstetric history, and visiting a doctor knowledgeable in RPL (19). The most important barriers are the guideline being too complicated to be used in the consultancy room, lack of up-to-date patient information and patients' lack of detailed knowledge about

family history. Based on these data, we developed a multi-faceted implementation strategy. The strategy consists of various elements for doctors to tackle complexity and elements for patients to improve information supply and knowledge.

The objective of our study was to test the multi-faceted implementation strategy on its capability to improve guideline adherence in couples with RPL.

MATERIALS AND METHODS

DEVELOPMENT OF MULTI-FACETED IMPLEMENTATION STRATEGY

The implementation strategy was developed systematically and tailored to the determinants of care and the identified barriers for guideline adherence (4, 19). Based on these data, the strategy consisted of 11 elements. For doctors, the elements consisted of a paper and digital version of the revised guideline, a paper and digital short protocol from the guideline, a paper and digital flowchart, an electronic decision program, a pocket card with a point-wise summary of the guideline, and a specified medical chart file for couples with RPL. For patients, we developed a questionnaire about their family history to be filled in prior to their first visit and a patient brochure.

DESIGN

FEASIBILITY

To examine which elements of the strategy are essential in successful implementation, we measured the usage of the elements. We also explored among women and doctors their preferences for the different elements of the strategy.

EFFECTIVENESS

To gain insight into the potential effectiveness of the strategy we performed a study with a before-and-after design. Cohorts consisting of women with RPL were collected both before and after the introduction of the implementation strategy (measurement before strategy: January-December 2006; measurement after strategy: April-September 2009). Nine hospitals participated in the measurement before introduction of the implementation strategy. Results of this measurement have been described

elsewhere in detail (4). The strategy was introduced in four of these nine hospitals in two different regions. Two university hospitals and two non-university teaching hospitals participated. For the purpose of this study, data with regard to before and after measurements of these four hospitals were included. The strategy was introduced in January and February 2009 during a plenary introduction session, where doctors got feedback about their previous guideline adherence. The strategy was explained and all doctors, consultants and registrars, were provided with the 11 elements of the strategy. The measurement of adherence to the quality indicators started three months after the introduction of the strategy.

COST-EFFECTIVENESS

We performed a cost consequence-effectiveness analysis to assess the costs of the development and the actual implementation of the strategy, from a health care perspective. Furthermore, we calculated the direct medical costs for the patients in the situation before and after the introduction of the strategy. Possible effects of the strategy could be a reduction or increase in diagnostic tests, a change in mean consultation time and a change in the mean number of consultations at other specialists.

STUDY POPULATION

For both the before and after measurements regarding effectiveness, all women with a history of two or more miscarriages who had their first visit during the study period were included. They were identified through financial hospitals registries, medical files and clinical genetic registries.

All women included after the introduction of the implementation strategy and their attending doctors were asked for the process evaluation to gain insight into the feasibility of the strategy, that is their preferences for the different elements of the strategy and their usage of the elements.

DATA COLLECTION

FEASIBILITY

To gain insight into the feasibility of the various elements of the implementation strategy from a doctors' perspective, a digital survey was created online (QuestionPro.com). The questionnaire was sent to all doctors who were documented as attending doctor in one or more of the women

included in the study. Use and preferences concerning paper or digital versions of the various elements of the strategy were asked, and possible changes in consultation time. They were asked on a five-point Likert-scale to what extent each element of the strategy was used and to what extent they thought each element was effective for implementation of the guideline. Furthermore, doctors created a top-5 of elements that they consider to be most effective for implementing the guideline, to identify the elements of the strategy with the highest potential for future use. To get insight into the feasibility of the strategy from a patient perspective, the use of the patient questionnaire prior to their visit was documented from the medical files. A paper questionnaire was developed and distributed by mail to the included women. They were asked if they had received a short questionnaire prior to their first visit and if they received an information brochure from their gynaecologist. If so, they were asked how they appreciated both elements and if they had any additional remarks.

Actual use of the short patient questionnaire and prior to the first visit and of the specified medical chart file for RPL were also documented for all patients from their medical files.

EFFECTIVENESS

For the effectiveness evaluation, guideline-based quality indicators were developed just after publication of the Dutch guideline in 2007 (20). The set of quality indicators, covering diagnostics, therapy and counselling for RPL, are an instrument to quantify guideline adherence. Both in the before and after measurement, data needed to establish guideline adherence and patient characteristics, such as obstetric history and family history, was gained from medical records and additional patient questionnaires. Main outcome was the adherence per indicator. The attending doctor was registered for each patient.

COST-EFFECTIVENESS

Throughout the project, all costs associated with the development and the actual implementation of the strategy were assessed using registration forms. All project members (EvdB, MG, JK, FvdV, NL and RH) recorded the travelling hours, travelling costs and number of hours associated with the development of the implementation strategy. The project members also

registered the hours incurred by the specialists to attend focus groups (i.e., part of the development) and introduction meetings (i.e., part of the actual implementation). The costs of medical care before and after introduction of the strategy were assessed by the costs associated with the performed blood tests and consultation time (Payment system DBC).

STATISTICAL ANALYSIS

FEASIBILITY

Descriptive statistics were used to describe usage and preferences of doctors and women with the strategy. To analyse the relationship between indicator adherence and use of the elements, multilevel logistic regression analyses were performed. Corrected for clustering of patients within doctors and the clustering of doctors within hospitals. The first choice of the top five was awarded five points, the second choice four points, the third choice three points, the fourth choice two points and the fifth choice one point. Top 5 score was calculated as the percentage of total point rewarded by all doctors. If all doctors would put the same element on rank 1, this would be a 100% score.

EFFECTIVENESS

Guideline adherence before and after introduction of the strategy was expressed as the percentage of adherence to an indicator, defined as the percentage of women in whom the indicator was followed, divided by the total number of women in whom the indicator should have been followed. The over-all percentage of adherence to the indicators was described as well as the inter hospital range. To test for differences in guideline adherence before and after introduction of the multi-faceted implementation strategy in the four hospitals, both univariable logistic and multilevel logistic regression analysis were performed. The rationale for multilevel regression analysis was the clustering of patients within doctors and the clustering of doctors within hospitals. Multilevel logistic regression analysis per indicator was performed with the percentage of adherence prior to the introduction of the strategy (yes/no) as an independent variable.

COST-EFFECTIVENESS

Time invested by doctors was multiplied by the gross salary (including social premiums and pension contributions) of the persons involved (21). Costs for diagnostics and consultations were reported in 2014 euros with the CPI index obtained from the Statistics Netherlands (CBS). Total costs for diagnostics were calculated for the total group of women before and after the strategy. Average annual saving was extrapolated based on the average number of patients with RPL in the four participating hospitals.

The Statistical Program for the Social Sciences (SPSS for Windows®, SPSS Inc., Chicago, Illinois, USA) and R software (lme4) were used for the analyses. P-values < 0.05 (two-sided) were considered significant.

ETHICS STATEMENT

Subjects did not undergo additional investigations nor treatment. As assessed by the Institutional Review Board (IRB), Academic Medical Centre Amsterdam, the study was not subject to the Dutch 'Medical Research Involving Human Subjects Act' (meaning that no formal IRB approval was needed). Women who lodged an objection to the study were excluded from the study.

RESULTS

We included 599 women in the study, 356 prior to introduction of the implementation strategy and 243 after. From patient questionnaires, which were complementary to the medical files, 300 (50%) were returned fully completed. All 599 women could be included in the analysis with adequate datasets. Baseline characteristics of the patients are presented in Table 1. Baseline characteristics did not differ between women included before and after the strategy, except for the referral pattern. Prior to the strategy more women were already being treated and less women were referred by other specialists compared to population after the introduction of the strategy ($p<0.01$).

Table 1 | Baseline characteristics of the women at time of presentation for recurrent pregnancy loss

	Inclusions prior to implementation n=356	Inclusions after implementation n=243
Maternal age in years[+]	34.5 (5.4)	33.7 (5.1)
Number of preceding miscarriages[√]	2 (1-8)	2 (1-12)
Number of preceding live births[√]	1 (0-4)	1 (0-7)
At least one live birth[∫]	191 (54)	129 (53)
BMI[+]	24.7 (5.0) (n=184)	24.4 (5.0) (n=140)
Referred by[∫*]		
- Self-referral	13 (3.7)	12 (4.9)
- General practitioner	36 (10)	22 (9.1)
- Specialist	37 (10)	50 (21)
- Already being treated[**]	174 (49)	127 (52)
- Other	76 (21)	17 (7.0)
- Unknown	20 (5.6)	15 (6.2)
Nationality[∫]		
- Dutch	180 (51)	126 (52)
- Other	36 (10)	16 (6.6)
- Unknown	140 (39)	101 (42)

+ (mean, SD); √ (median, range); ∫ (n, %); * p< 0.01; ** Patients that were already treated by the attending professional at the time of the diagnosis of recurrent pregnancy loss; BMI: body mass index, SD: standard deviation

MISCARRIAGE

FEASIBILITY

Of the 68 attending professionals, 17 (25%) returned the questionnaire about the strategy. Those professionals together took care of 114 (47%) of the women included after the strategy. Of the 17 professionals, 5 (29%) preferred the elements of the implementation strategy in a paper version, 4 (24%) digital, 5 (29%) a combination of both and 3 (18%) had no specific preference for paper or digital version. The reported use, self-reported effectiveness and top 5 scores are presented in Table 2. The specified medical chart file was used most frequently by the professionals. They chose the "Pocket card" as most useful element for helping to adhere to the guideline. More than 50% of the respondents indicated to intend to use each of the elements in the upcoming year, except for the paper model

protocol and paper flow chart. For the effect of use of the different elements on indicator adherence, the 114 patients treated by the responding professionals could be included. Of the women 100/243 (41%) returned their questionnaire. Fifty-seven (57%) replied they did receive the patient questionnaire prior to their first visit, 30 (30%) that they had not received that questionnaire and 13 women (13%) did not remember whether they received it. Of the 57 women that received the questionnaire, 45 (79%) found the short questionnaire useful, one (2%) found it not useful and 11 (19%) had no opinion. Thirty-eight women (38%) received the patient brochure, 40 (40%) did not receive it and 22 (22%) did not remember. Of the 38 women who received the brochure, 33 (87%) found it useful, four (10%) found it not useful and one (3%) had no opinion on whether it was useful or not.

Table 2 | Use and Top 5 ranking elements from the implementation strategy

	Reported use*#	Reported effectiveness+#	Top 5 score∫
Pocket card	1.5 (1-5)	2.5 (1-4)	19
Guideline digital	2.0 (1-5)	3.0 (1-4)	16
Specified medical chart file	2.5 (1-5)	2.5 (1-4)	14
Flowchart digital	1.0 (1-5)	2.5 (1-4)	11
Patient questionnaire	1.0 (1-5)	3.0 (1-4)	10
Guideline paper	2.0 (1-5)	3.0 (1-4)	8
Electronic decision program	1.0 (1-4)	3.0 (1-4)	7
Patient brochure	1.0 (1-5)	2.0 (1-4)	6
Flowchart paper	1.0 (1-5)	1.5 (1-4)	5
Modelprotocol digital	1.0 (1-5)	1.5 (1-4)	4
Modelprotocol paper	2.0 (1-5)	1.5 (1-4)	0

* Scored on a 5-point Likert scale: 1= Never used, 5= Used in almost all patients; + Scored on a 5-point Likert scale: 1= Not effective, 5= Very effective; # median with range between parentheses;

∫ Top 5 ranking of most effective tools. Rank 1 = 5 points, rank 2 = 4 points, rank 3 = 3 points, rank 4 = 2 points, rank 5 = 1 point. Presented is the percentage of total point rewarded by all professionals. If all professionals put the same tool on rank 1, a 100% score would be rewarded. If none of the professionals mentioned the tool in their top 5, the score would be 0%.

The relationship between the (reported) use of the elements and the adherence per indicator is reported in Table 3. Results are shown for indicators directly related to diagnostic tests, which are related to cost-reduction. The specified medical chart file, patient questionnaire, pocket card and electronic decision program were, in varying combination, related to higher adherence to diagnostic indicators. For the other indicators, no relationship with use of the elements was found, or could not be measured due to low patient numbers.

Table 3 | Multilevel logistic regression analysis for use of elements per indicator related to increase in adherence

	Adjusted OR
*Total number of objectified miscarriages defined**	
Specified medical chart file	4.2 (2.0 – 9.1)
Patient questionnaire	3.5 (1.6 – 7.9)
Selective karyotyping	
Specified medical chart file	2.6 (1.3 – 7.1)
Electronic decision program	1.8 (1.2 – 4.1)
Patient questionnaire	2.3 (1.1 – 5.9)
Antiphospholipid antibodies determined	
Pocket card	4.5 (1.2 – 7.3)
Homocysteine determined	
Pocket card	4.9 (1.8 – 9.1)
Specified medical chart file	5.3 (2.1 – 9.0)
Calculation of pregnancy success in next pregnancy	
Electronic decision program	2.5 (1.1 – 4.8)

* Information available on specified medical chart file and patient questionnaire in all patients. Use of other elements known in n=114 patients; OR: Odds Ratio

EFFECTIVENESS

The adherence per indicator before and after the introduction of the strategy is presented in Table 4. For diagnostic indicators the highest increase in adherence was measured for selective thrombophilia screening (+ 37%, OR 5.2, 95% CI 3.6-7.6). Maternal age at the time of the second miscarriage was reported 32% more often after than before the strategy (OR 8.2, 95% CI 5.3-13). Adherence to selective karyotyping increased significantly from 50% before up to 76% after the strategy (OR 3.3, 95% CI 2.2- 4.6).

Table 4 | Actual care measured per quality indicator for recurrent pregnancy loss

Quality indicator	Before introduction of the strategy		After introfuction of the strategy		Difference in adherence (%)	OR (CI 95%)
	Indicator followed	Adherence (%)	Indicator followed	Adherence (%)		
Medical history[+]						
Lifestyle	282/356	80	195/243	80	-	1.1 (0.7–1.7)
History of thrombophilia	243/356	68	197/243	81	13	1.7 (1.1–2.4)
Number of objectified miscarriages	217/356	61	159/243	65	4	1.3 (0.9–1.8)
Family history of RPL	171/356	48	144/243	59	11	1.6 (1.2–2.3)
Maternal age 2nd miscarriage	32/356	9	108/243	41	32	8.2 (5.3–13.0)
Family history on thrombophilia	9/356	2.5	133/243	55	53	Not available
Diagnostics						
Antiphospholipid antibodies	197/356	55	153/243	63	8	1.4 (1.0–2.0)
Karyotyping (selectively)	177/356	50	185/243	76	26	3.3 (2.2–4.6)
Homocysteine	176/356	49	158/243	65	16	1.9 (1.4–2.7)
Thrombphilia factors (select)	158/356	44	195/243	81	37	5.2 (3.6–7.6)
Length, weight, BMI	47/356	13	75/243	31	18	3.0 (2.0–4.6)

Quality indicator	Before introduction of the strategy		After introduction of the strategy		Difference in adherence (%)	OR (CI 95%)*
	Indicator followed	Adherence (%)	Indicator followed	Adherence (%)		
Therapy						
Supplement vitamins in low levels	2/2	100	0/0	-	-	Not available
Withhold immunological therapy	356/356	100	243/243	100	0	Not available
Prescribe aspirin/LMWH in APS	2/2	100	5/5	100	0	Not available
Refer to geneticist	7/7	100	3/3	100	0	Not available
Withhold aspirin in uRPL	327/331	99	221/224	99	0	Not available
Experimental treatment only in RCT	325/331	98	223/224	99	0	Not available
Counselling/Advice						
Carrier couples on high success rate	4/7	57	3/3	67	10	Not available
Quit smoking	7/61	12	31/50	62	50	Not available
Weight loss	14/66	21	30/51	59	38	5.3 (2.4–12.0)
TLC	Not measurable					
Discuss success rate uRPL	62/331	19	60/224	27	8	1.6 (1.1–2.4)
Folic acid use	Not measurable					

* Multilevel analysis Odds Ratio (OR); + Reporting of indicators of medical history; RPL: recurrent pregnancy loss; BMI: body mass index; LMWH: low molecular weight heparin; APS: antiphospholipid syndrome; uRPL: unexplained recurrent pregnancy loss; RCT: randomized controlled trial;

Significant increase in adherence was also seen for determination of Body Mass Index (BMI) (+18%, OR 3.0, 95% CI 2.0-4.6), homocysteine (+16%, OR 1.9, 95% CI 1.4-2.7) history of thrombophilia (+13%, OR 1.7, 95% CI 1.1-2.4), family history of RPL (+11%, OR 1.6, 95% CI 1.2-2.3) and antiphospholipid antibodies (+8%, OR 1.4, 95% CI 1.03-2.0). For the indicator to report the number of objectified pregnancy losses a trend towards increase of adherence was seen but these indicators did not reach significance. Report on lifestyle remained 80%. None of the indicators showed a decrease in adherence. Report on family history of thrombophilia showed the highest increase in adherence (+53%), but could not be included in multilevel analyses due to a small number of patients (n=9) prior to the introduction of the strategy. For the indicators on therapy, none of the indicators showed a significant increase (before the strategy adherence was almost 100%) or decrease in adherence. Variation in adherence between the different hospitals both before and after the strategy was very small. For the indicators on counselling, for two out of four measurable indicators an increase in adherence was observed after the strategy: Advise weight loss (+38%, OR 5.3, 95% CI 2.4-12), and discuss individual chances on reproductive outcome in unexplained RPL (+8%, OR 1.6, 95% CI 1.1-2.4). The indicator advises patient and partner to quit smoking increased with 62%, and the indicator to inform carrier couples about good reproductive chances showed an increase in adherence of 10%. Multilevel analyses were not possible for these indicators due to the small number of patients.

COST-EFFECTIVENESS

The costs were 69,028 euros for the development of the implementation strategy and 19,325 euros for the actual implementation. So, the over-all costs were 88,353 euros. Costs for the development consisted of personnel costs of the project group (60,254 euros), travelling costs (personnel and travelling budget: 1,562 euros) and costs for focus groups (7,212 euros). Cost for the actual implementation included for six introduction meetings that resulted in 127 personnel hours with a total cost of 7,457 euros (travelling costs included), other travelling costs (personnel and travelling budget: 806 euros), and costs for dissemination of the elements of the strategy (11,063 euros).

In addition, the mean time for a specialist to study the digital and/or the paper version of the implementation package was 14 minutes. One of the changes in costs of medical care before and after introduction of the strategy included the consultation time. Professionals indicated to use on average an estimated 18 minutes per consultation for RPL before the implementation package was introduced (range 10-45 minutes). After the introduction of the implementation strategy, professionals indicated to use on average an estimated 16 minutes per consultation (range 8-30 minutes). The cost of a consultation was fixed at 112 euros. When professionals were asked about changes in the number of consults required for RPL patients since the introduction of the implementation strategy, nine professionals (53%) reported having needed less consultations, while eight (47%) did not recognize a change in the number of consults. Changes in costs of medical care before and after introduction of the strategy were as follows (Table 5). During the 6 months study period after the strategy, a reduction of 91,892 euros was achieved. In the four participating centres, 535 couples with RPL were seen annually, which would have resulted in a saving of 206,916 euros.

DISCUSSION

Guideline adherence in couples with RPL was improved after introducing a tailored multifaceted implementation strategy. Prior to the strategy, 9 out of 21 measurable indicators showed an adherence below 50%. After the implementation strategy, adherence was below 50% for just three out of 21 indicators. Adherence increased significantly in ten indicators, mainly on diagnosis. For two indicators we observed a trend towards increase of adherence, but the confidence intervals for these indicators did not reach significance. For none of the indicators a decrease in adherence was observed.

The "Specified medical chart file" was used most by professionals. Professionals chose the "Pocket card" as most useful element of the strategy to improve guideline adherence. The measured as well as the self-reported use of the various elements were related to a better adherence to the guideline compared to the use of the other elements – the ones used less. Thirty-five percent of the doctors reported that fewer consultations were needed after the introduction of the implementation strategy and over 79%

of the women appreciated the patient related elements of the strategy; The specified medical chart file, patient questionnaire, pocket card and electronic decision support instrument significantly helped to improve the quality of care delivered.

Table 5 | Cost effectiveness of the developed implementation strategy

Diagnostic test	Diagnostic test performed before/after implementation*				Cost change across 4 centres+	
	Before	After	Difference	Cost of test*	6 months	12 months
Karyotyping	74%	52%	-22%	€1.664,-	-€86.987,-	-€193.498,-
APS	55%	63%	+8%	€36,-	+€697,-	+€1.541,-
Homocysteine	49%	65%	+16%	€39,-	+€1.510,-	+€3.338,-
Thrombophilia#	56%	20%	-36%	€95,-	-€8.276,-	-€18.297,-
				Total	-€93.056,-	-€206.916,-

* percentage of couples that received the diagnostic test before and after implementation strategy; + change in costs of diagnostic testing compared to before implementation strategy, calculated by multiplying number of couples that received the tests by the cost per diagnostic test; # antithrombin III, protein C, protein S, factor V Leiden, factor II, factor VIII ; APS: antiphospholipid syndrome (anticardiolipin antibodies IgG and IgM, lupus anticoagulant);

Regarding the costs, a reduction of 206,916 euros per annum for the four participating hospitals together was achieved. If the implementation strategy was applied throughout The Netherlands even higher annual savings would be expected, due to the lack of further developmental costs and expected lower costs of the introduction of the strategy. It is difficult to indicate the exact number of couples with RPL per year in The Netherlands, since it is a condition that is not registered on a national level. In our measurement prior to the strategy, 72% of all new couples were karyotyped. Annually, 1470 couples with RPL are karyotyped in The Netherlands (registries by genetical testing centres in the Netherlands). When extrapolated, an estimated number of 1,900 couples are seen per year with RPL. This indicates a cost reduction of at least 791,367 euros per year in The Netherlands.

The most important strength of our study is the structured development of the strategy. We incorporated the results of the measurement of actual care, the determinants for non-adherence and the results from barriers and facilitators (18). By testing in two different regions in the country, local cultural differences were covered, increasing the potential for wider use of the strategy. Also, this is one of the first studies that actually related the effect of the strategy on guideline adherence to the use of the various elements of that strategy by the professionals involved. This step is necessary to know which elements are actually the effective ones, and useful for future implementation, to make it more effective and less expensive (22-24). The cost-effectiveness analysis includes costs of the development as well as the use and effect of the strategy, which gives a realistic perspective of the actual costs in daily clinical practice.

Some limitations should be discussed while interpreting the results. Due to the method of before and after measurement used in our study, the results only present a potential effect of the strategy on guideline adherence. The exact strategy-related effectiveness should be measured within the setting of a double blind randomized clinical trial (RCT)(25). Such a RCT is difficult, since a complete non-intervention group is hard to accomplish. In other words, the quality of care is the outcome measurement and attention of professionals for the guideline alone is already a first to attempt towards implementation. The response rate for the feasibility study was quite low

among doctors and patients, which might explain and the wide 95% CI, described in Table 1.

Even though the results are promising, caution is needed in interpreting the results in current practice. As the implementation strategies were implemented and carried out between 2006 and 2009, they reflect on a different era, in which protocols with electronical availability were not yet available automatically. Nevertheless, in our view this does not invalidate the results of our study, since the technological developments will lead to easier access to the various elements of the strategy. For example, a digital patient file could be designed with a customized module for couples with RPL. Thereby incorporating the specified medical chart file and electronic decision program in standard patient care.

Revised international guidelines in RPL are about to be published. Within the field of reproductive medicine, implementation strategies to improve guideline adherence were tested with varying success (16, 17). A gold standard for implementation strategies does not exist but our results underscore that a strategy should be tailored to the results of the actual care measurement, the determinants of care and the identified barriers for guideline adherence (14, 26).

Recently, the ESHRE stated that implementation tools are important, although there is little evidence for their efficacy, and that current implementation strategies are lacking (27). This study provides clear evidence for the efficacy of implementation strategies, as portrayed in the high cost -reduction.

The ESHRE guideline on RPL is currently under revision and we encourage that its publication – as well as future revisions- should be accompanied with electronical implementation tools which were effective in our strategy, to optimize a prompt implementation of this revised guideline.

CONCLUSION

Robust implementation strategies are necessary to achieve proper adherence in RPL care. A multi-faceted implementation strategy was tested, showing that implementation strategies are feasible, effective in increasing adherence and could lead to cost-reductions. This implementation strategy can widely be introduced in clinical practice for RPL, and may serve as an example for future implementation strategies in other areas within obstetrics and gynaecology.

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