Rationale, Study Protocol and the Cluster Randomization Process in a Controlled Trial Including 40 000 Women Investigating the Effects of Mindfetalness

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Abstract

Background. Shortening pre-hospital delay may decrease stillbirth rates and rates of babies born with a compromised health. Stillbirth may be preceded by a decrease in fetal movements. *Mindfetalness* has been developed as a response to the shortcomings of kick-counting for the monitoring of fetal movements by the pregnant woman. We do not know if practicing *Mindfetalness* may diminish pre-hospital delay. Nor do we know if practicing *Mindfetalness* may increase or decrease the percentage of women seeking health care for unfounded, from a medical perspective, worry for her fetus' well-being.

Methods. This article describes the rationale, study protocol and the randomization process for a planned study randomly allocating 40 000 pregnant women to receive, or not receive, proactive information about practicing *Mindfetalness.* The unit of randomization is 63 antenatal clinics in the Stockholm area. Midwifes in the antenatal clinics randomized to *Mindfetalness* will verbally inform about practicing *Mindfetalness*, hand out brochures (printed in seven languages) and inform about a website giving information about *Mindfetalness*. Routine care will continue in the control clinics. All information for the analyses, including the main endpoint of an Apgar score below 7 (e.g., 0-6 with stillbirth giving a score of 0), measured five minutes after birth, will be retrieved from population-based registers.

Results. We have randomized 33 antenatal clinics to *Mindfetalness* and 30 to routine care. In two clinics a pilot study has been performed. One of the clinics randomly allocated to inform about Mindfetalness will not do so (but will be included in the intention-to-treat analysis). In October 2016 we started to recruit women for the main study.

Conclusion. The work up to now follows the outlined time schedule. We expect to present the first results concerning the effects of *Mindfetalness* during 2018.

Background

A shortened prehospital delay after the pregnant woman perceive a decrease in fetal movements may decrease rates of stillbirth and rates of babies born with a compromised health. At the same time the percentage of unwarranted visits, from a medical perspective, to obstetric clinics due to worry for decrease fetal movements is far too high. Empowering women to monitor fetal movements with a new method, *Mindfetalness*, (1) may shorten pre-hospital delay after decreased fetal movements and simultaneously lower the frequency of unwarranted visits from a medical perspective. We here present the rational, study protocol, randomization process and ongoing activities 1 October 2016 in a study allocating women randomly to receive midwife-administered information about *Mindfetalness* or routine care.

The success of modern obstetric care during the last century to bring down stillbirth rates, and rates of babies born with a compromised health, rests on the window of opportunity to turn objective signs of compromised fetal wellbeing to the birth of a healthy child. Inducing a vaginal delivery, or performing a caesarian section in time, results in the vast majority of cases in a healthy live child. However, the stillbirth rate in Sweden has been stable for three decades, 4.0 per 1000 births in 2014, without showing any tendency to decrease. In Sweden in 2014, 464 babies were stillborn after 22 gestational weeks, another 177 babies died within 27 days after birth (2). New approaches are needed to reduce the rates. Pre-hospital delay is the period between the time when fetal movements decrease and the time the pregnant woman seeks health-care. If pre-hospital delay is shortened, a higher percentage of the children than today will be in the window of opportunity to be saved from death or compromised health.

The knowledge that a stillbirth may be preceded by fetal movements gradually becoming

weaker and less frequent probably goes back to before historical times. Thus, as obstetric care gained technology and clinical skill to diagnose compromised fetal wellbeing and induce a delivery, the idea of shortening the pre-hospital delay after the occurrence of decreased fetal movements arose. Authors in the 1970s searched for monitoring instruments and ended up with kick-counting as the preferred method (3-4). In it, the pregnant mother times the period needed to sense, e.g., 10 kick from the fetus or count fetal movement during a specific time. But, a large-scaled study failed to show that kick-counting is efficient (5). The authors randomly allocated 68 000 pregnant woman to kick-counting or standard care and found no difference in stillbirth rates between the groups. The women were asked to seek health care at an alarm count: no kicks during a day or less than 10 kicks during 10 hours on two successive days. The article was published in the Lancet 1989 and after that the interest in shortening the pre-hospital delay fell drastically.

After the turn of the century the literature reflects a revived interest in shortening the pre-hospital delay. But, kick-counting prevail as the method for structured fetal monitoring. Holm-Tveit, and co-workers (6) randomly allocated 1076 pregnant women at nine Norwegian hospitals to either a modified count-to-ten method or to standard care. In the intervention group two babies (0.4%) had Apgar scores below four at one minute, versus 12 (2.3%) in the standard-care group. The frequency of consultations for concerns related to fetal wellbeing was 13.1 percent in the kick-count group and 10.7 percent in the standard-care group. Study design and interpretation of the results have been hotly debated (7). Nevertheless, the study has evoked a growing interest in diminishing pre-hospital delay. In Scotland (8), authors plan to randomize 120 000 pregnant woman to a care package concerning fetal monitoring or to standard care.

No large-scale studies have been done to gain knowledge that can be used to lessen the numbers of visits of obstetrics clinic for concerns about decrease fetal movements that turn out to be unfounded from a medical perspective. Setting alarm cut-offs for kick-counting may rather prolong than shorten the pre-hospital delay; instead of trusting her intuition the pregnant woman feels obliged to follow decision rules given by others. Another explanation for kick-counting's lack of efficiency may be its insensitivity to the combined fetal movements. A fetus stretching, or changing position, certainly moves but the sensation may not be documented as a "kick". Decreased fetal movements induce denial; to shorten pre-hospital delay the pregnant mother must monitor her fetus daily and act directly when the fetus does not move as usually. A third explanation for the inefficiency of kick-counting, possibly the most important one, may be that it does not help the mother to get passed the denial, to understand that the health of the fetus may be compromised and to act promptly. To overcome the problems with kick-counting, we have introduced the concept of *Mindfetalness* (1). We know many women prefer practicing *Mindfetalness* before kick-counting (9), but we do not know if it can decrease the number of unwarranted (from a medical perspective) unscheduled health-care visits or increase the rates of babies born healthy by decreasing pre-hospital delay.

Setting aside 15 minutes per day while the fetus is awake, and by documenting the experience, the pregnant woman gets to know the movement's pattern of her fetus. Practicing *Mindfetalness* may decrease the pre-hospital delay. Moreover, when the woman has learned her fetus' movement pattern, she may be more secure in her diagnosis of fetal wellbeing, preventing unnecessary (from a medical perspective) unscheduled visits to obstetric clinics. In preparatory studies we have found a high compliance for practicing *Mindfetalness*. The planned main study uses logistical and scientific findings from the following studies

performed by us.

Documentation of pre-hospital delay. We collected data by a web-based questionnaire accessible on the homepage of Swedish National Infant Foundation from 27 March 2008 to 1 April 2010 (10). Six hundred and fourteen women provided data and fulfilled the inclusion criteria, including having a stillbirth after the 22nd gestational week. In all, 392 (64%) of the women had had a premonition that their unborn baby might be unwell. Remarkable was that 88 (22%) decided to wait until their next routine check-up to seek health care. Clearly, a significant pre-hospital delay exists (10).

Perception of fetal movements. We asked 40 women in gestational weeks 37 to 41 "Can you describe how your baby has moved this week?"(11). By using content analysis we found six categories "Strong and powerful", "Large", "Slow", "Stretching", "From side to side" and "Startled" movements. Within these categories, women's wording varied considerably. So, we concluded that trying to capture the frequency and strength of movements in each category would require extensive instruments. Moreover, since the wording varies between women, the measurement errors (amount of misclassification) would be large. Also, any reduction, for example to "kicks", implies that a large part of the movements (e.g., stretching and moving from side to side) not would be documented. Just counting kicks implies a huge loss of information and we must find new means for fetal monitoring (11). The results in this qualitative study have been validated in a study with 400 women in full-term pregnancy (12).

Awareness of decreased fetal movements. We asked 26 women who have experienced stillbirth the process of realizing this dreadful truth (13). Several of the women, avoidance (stopping monitoring) and denial (not acting of the monitoring results) was obvious during

the process. Thus, to shorten pre-hospital delay, any monitoring schedule must overcome avoidance and denial.

Acceptance of Mindfetalness. The count-to-ten (kick-counting) method many consider as the standard for fetal monitoring. We recruited 40 healthy women with an uncomplicated full-term pregnancy (9). In a crossover trial, the woman practiced *Mindfetalness* as well as the count-to-ten method. Twenty started with one of the methods, 20 with the other, giving 80 assessments observed by a midwife. Twenty (50%) of the women preferred practicing *Mindfetalness* before the count-to-ten method, five women (12.5%) preferred the count-to-ten method and 14 (35%) had no preference for one method over the other. One woman (2.5 %) did not find any of the two methods suitable for fetal monitoring. Together with the documented insensitivity of kick-counting, we choose *Mindfetalness* for the planned large-scaled study.

Misinterpretation of fetal movements. In further analyses of information from a web-based questionnaire, we found that women in late pregnancy may misinterpret uterine contractions as fetal movements (14). That is, after the fetus had died, the women believed her unborn baby was moving. This observation further strengthened our belief that the woman must learn the unique behavior of her fetus in terms of nature in addition to frequency and strength of movements.

Seeking health care for decrease fetal movements. In a completed data-collection we quantify the percentage of woman seeking health care for decrease fetal movements. All seven obstetric clinics (Södersjukhuset, Karolinska Universitetssjukhuset Solna and Huddinge, Danderyds sjukhus, BB Stockholm, BB Sophia and Södertälje Sjukhus) in Stockholm

participated. We attempted to collect information from all women coming to an obstetric clinic during 2014 declaring a worry for decreased fetal movements. A completed questionnaire has been received from 3555 women, analyzes of data as well as estimating the prevalence of women seeking care for decrease fetal movements are on-going.

Purpose

We do not know if practicing *Mindfetalness* can diminish the pre-hospital delay to such an extent that the well-being of the fetus improves. And, we do not know if practicing *Mindfetalness* can diminish, or may increase, unfounded worry leading to unnecessary consultations from a medical perspective. Therefore we will address the following two hypotheses:

Hypothesis 1:"By taking a proactive approach to get the pregnant woman to practice Mindfetalness the percentage of babies stillborn or born with signs of hypoxia can be reduced". In short, a total of 40 000 women will be randomly allocated either to midwives using a proactive approach to *Mindfetalness* or to midwives practicing standard care. An Apgar score less than seven measured five minutes after birth, as retrieved from the Swedish Medical Birth Register, is the primary endpoint.

Hypothesis 2"By taking a proactive approach leading pregnant women to practice Mindfetalness the percentage of women seeking health care for decreased fetal movements can be reduced." In the data collection described above, the rate of visiting an obstetric clinic because of decrease fetal movements will be retrieved in the medical record system Obstetrix and studied as the secondary endpoint in the data collection addressed above.

Methods

Overview. During the recruitment period 1 October 2016 to 31 January 2018 about 40 000 pregnant women in Stockholm reaching pregnancy week 25 will be randomly allocated to receive, or not receive, guidance in practicing *Mindfetalness* by a proactive midwife. The level of randomization will be 63 antenatal clinics in the Stockholm area. The proactivity will be supervised by the study secretariat. Possible effect-modifying factors, possible confounding factors and outcomes will be retrieved by data linkage to the Swedish Medical Birth Register, the Pregnany Register, the medical record system Obstetrix, the Swedish Educational Register, the Prescribed Drug Register and the National Patient Register. The primary analysis for the primary and secondary end points will be done according to the intention-to-treat (intention-to-receive-midwife-administered-information-about-*Mindfetalness*) principle and will include all pregnant women registered at one of the 63 randomized antenatal clinics during the recruitment period. That is, the primary analyses will not take into account whether or not the pregnant women have practiced *Mindfetalness*, misclassification will be accounted for in the interpretation of the results. We have reported the study to ClinicalTrials.gov (identification number NCTØ2865759) and have received ethical approval (Dnr. 2015/2105.31/1) from the appropriate Swedish state authorities.

Intervention. During one antenatal visit around gestational week 25, the pregnant woman will be informed about the possibility of practicing *Mindfetalness*. The midwives will hand out a brochure (printed in seven languages; Swedish, English, Spanish, Arabic, Farsi, Somali and Sorani) in which the women are asked to spend 15 minutes every day (from gestational week 28) to get to know the fetal-movement pattern. These 15 minutes must take place when the fetus is awake; the recommendation is that the woman is lying on her left side when she observes the movements. Moreover, she is asked to describe something about the nature,

frequency or strength of the fetal movements in a diary in the brochure (for personal use). The woman will be informed about a website with the same information as in the brochure and can use these media to document her observations if she prefers so. If the woman experiences decreased frequency of fetal movements or weaker movements she is instructed to seek health-care without unnecessary delay. The key in practicing *Mindfetalness* is that the pregnant women does it every day in the same way, that she learns to trust her intuition concerning the fetus's wellbeing and that she acts promptly when she feels something may be wrong.

Midwives in each antennal clinic randomized to *Mindfetalness* and accepting to participate will be given a lecture about fetal monitoring and how to inform about *Mindfetalness*. The lecture will be repeated after needs. A midwife from the study secretariat will regularly visit each clinic in the proactivity group and discuss the experiences with being proactive concerning *Mindfetalness*. The midwife will also see to it that all clinics have a sufficient supply of the brochures which will be handed out to the women. A website will open that has all the information. In the clinics randomized to routine care no activities will take place and routine care will continue.

The randomization process. The randomization of the 63 antenatal clinics registered in 2014 in the Stockholm area were done at Sophiahemmet University during a seminar with in total eight researchers and doctoral students witnessing the randomization. The seminar was held 18 April in 2016 after the pilot study had started. We received from the (samordningsbarnmorskan) in the Stockholm area a list of all antenatal clinics in the region (n=73) specified with the number of pregnant women listed in 2014. Excluded from the randomization were four antenatal clinics for special cares were women with pregnancy

complication were listed (in total 228 women). Further, excluded from the randomization were three small clinics with less than 50 women listed in 2014 (in total 85 women). Based on facts on the number of women listed at each antenatal clinic we sorted the clinics in large (more than 1000 women listed), medium (less than 1000 but more than 500 women listed) and small clinics (less than 500 but more than 50 women listed). The randomization was performed in clusters with the same amount of number of women listed in 2014 e.g. large, medium and small clinics. To increase efficacy we further made blocks according to sociodemographic factors; we classified all small and medium-sized clinics due to areas known to be in high income areas and non-high income areas. All four large clinics were classified as being in high-income areas. Half of the antenatal clinics in each block were randomized to be proactive in practicing *Mindfetalness*. The randomization took place before we contact the clinics. Three of the clinics randomized to routine care merged after the randomization to one medium-sized clinic. One medium-sized clinic merged after the randomization to a medium-sized clinic randomized to the intervention; we allocated the collapsed large-sized clinic to *Mindfetalness (*resulting in five clinics*)*. Thus, the randomization resulted in 33 clinics randomized to intervention (with in total 15 551 women listed in 2014) and 30 clinics to controls (with in total 14 960 women listed in 2014). A list of the included antenatal clinics and if they have been allocated to *Mindfetalness* or routine care has been sent to Ethical Review Board Stockholm.

Population and observation period. Strictly speaking, the study population consists of all fetuses in Stockholm reaching 25 gestational weeks during the recruitment period 1 October 2016 to 31 January 2018. To ClicialTrials.Gov we report as the population all of the about 40 000 pregnant women in Stockholm reaching pregnancy week 25 1 October 2016 to 31 January 2018 having a Swedish personal identity number and attending one of 63 specified

antenatal clinics. In practice, we will retrieve from the registers information on all women having reached gestational week 25, as registered in the Swedish Medical Birth Register, sometime between 1 October 2016 and 31 January 2018. For the primary endpoint, we will observe the registered women's babies five minutes after birth. For the secondary endpoint, we will register all visits to an obstetric clinic due to worry about a decrease in fetal movements during the entire pregnancy for all registered women.

Primary endpoint. Our primary endpoint is having an Apgar score below seven (five minutes after birth). In Sweden, Apgar score is assessed by a midwife, at one, five and ten minutes after birth. It comprises five components scored as zero, one or two, giving a score from zero (stillbirth) to 10. A low Apgar score may indicate a previous deficit of nutrients or oxygen. The Swedish Medical Birth Register contains information on the assessed Apgar score.

Secondary endpoint. The secondary will be the number of visits to an obstetric clinic due to worry about a decrease in fetal movements. The information can be retrieved from Obstetrix, covering all obstetric clinics in Stockholm.

Tertiary endpoints. We will have three additional endpoints. One will be an Apgar score below four at five minutes, strongly associated with a compromised health. The other will be stillbirth or a newborn being transferred to a neonatal clinic. A third endpoint will be stillbirth or death within 27 days after birth.

Possible effect-modifying factors. Educational level may modify the effects of *Mindfetalness*, if any. Two different mechanisms may be hypothesized; either the well-educated woman practices *Mindfetalness* more effectively than other. Or, as an information-seeker, and having

a large social network, she has no need for the extra empowerment for fetal monitoring. Other factors that will be investigated are age, body mass index, parity, country of birth and civil status. Since we have no prior knowledge, the search for effect-modifying factors is explorative.

Main statistical analyses. For each endpoint, we will form a ratio of the prevalence of women with the endpoint. We will compare all pregnant women enrolled at antenatal clinics randomly allocated to proactivity with all pregnant women enrolled in antenatal clinics randomly allocated as controls; that is, we use the intention-to-treat principle. This implies that women listed in ante-natal clinics randomized to *Mindfetalness* will be analyzed as "exposed to Mindfetalness" also when the clinic (or specific midwifes in the clinic) choose not to participate. By a log-binomial regression model, the prevalence ratio ("relative risk") will be adjusted for possible confounding factors. The regression models will also provide us with 95 percent confidence intervals. Apart from a complete-case analysis, we will use imputation by means of Multiple Chained Equations. We will select a group of possible confounding factors, and use available data for these to produce 50 imputed data sets. The prevalence ratio, adjusted for possible confounding factors, will be the mean achieved from these imputed data sets. Some possible confounding factors, such as country of birth, will be handled by restriction. If a main effect is detected, we primarily will study possible effect-modification by examining the prevalence ratios (adjusted for possible confounding factors) in sub-groups and secondarily we will test for interaction by means of log-binomial regression. That analysis path follows that in an article of Steineck and coworkers (15).

Discussion

Aspects on validity, overview. The study design allows us to be able to address two clinically

significant hypotheses in a cost-effective way. In the design, we have incorporated as much as possible of the means utilized in a randomized trial. To be able to carry through the study in real life, we cannot blind the midwife or the pregnant woman for the practice of *Mindfetalness*. We will understand the problems arising due to this and other fallacies with the help of modern epidemiological theory (16). We are well aware that the real effects, if present, are captured by much diluted effect measures. The dilution is balanced by the large sample size, a design inspired by Richard Peto's suggestion of "A large simple trial" (17). Also, for practical and cost-effectiveness reasons, we need to organize the level of randomization at the unit of the antenatal care clinics; residual confounding after randomization thus is a crucial validity issue. However, our setting with a plethora of register-based data available at a low cost in differed register that can be linked by the personal identity numbers gives us information on a large part of the possible confounding factors. Each resident in Sweden has a unique personal identity number.

Confounding. Since the unit of randomization will be the antenatal clinics (cluster randomization), residual confounding not taken care of by the randomization (cluster effects) is a major validity issue. Through the Swedish Medical Birth Register, Pregnancy Register, Obstetrix, the Swedish Educational Register, the Prescribed Drug Register and the National Patient Register we have information on, by and large, all important possible confounders. They include educational level, age, parity, Body Mass Index, country of birth, pre-pregnancy diabetes mellitus, certain other intercurrent diseases, previous stillbirth, gestational-induced diabetes mellitus and preeclampsia. Probably the causes of stillbirth have a considerable overlap with causes of a compromised health at birth. Consequently we are dealing with an outcome that is well studied. This in turn implies that we have knowledge about most of the causal factors that may confound the effect measures we calculate for the

primary endpoint. Apart from producing adjusted affect measures by means of log-binomial regression (or if necessary due to lack of convergence, logistic regression giving estimates of the odds ratio) we will also examine the difference between the adjusted and non-adjusted effect measure (estimated prevalence ratio). This difference, together with subject-matter knowledge, gives an indication about the amount of residual confounding.

Attrition (selection-induced problems). We expect few personal identity numbers to be erroneous in such a way that they hinder data linkage between group (proactivity versus no proactivity) and outcome. Attrition is a non-issue for the validity of the effect measures.

Misclassification. Assessment of Apgar score is typically done by the midwife assisting the birth. We have no reason to believe that this assessment will be affected by the woman having practiced, or not having practiced, *Mindfetalness*. Likewise, we consider reporting the Apgar score to the Medical Birth Register as "blinded". Thus, we believe differential misclassification of outcome to be a non-issue for the validity of the effect measures. The trial will resemble a randomized trial with "blinded" assessment of outcome.

The amount of non-differential misclassification, however, will be large. Concerning "randomly allocated to *Mindfetalness*," the amount of non-differential misclassification sums up all origins to the fact that a certain part of the pregnant women randomly allocated to *Mindfetalness* will not practice it (or not do it accurately), as well as the fact that certain women not randomly allocated to *Mindfetalness* will practice it accurately. We thus expect that the effect measures will be deviated considerably towards 1.0. One of the 33 clinics randomized to *Mindfetalness* have chosen not to participate with any midwife. Some midwives in participating antenatal clinics will forget, or deny, being proactive. Some

midwives will not be effective or give erroneous instructions. Some pregnant women will not accept the idea of monitoring fetal movements by practicing *Mindfetalness*. Others will not practice *Mindfetalness* as instructed, for example by not doing it every day. Others will be affected by avoidance or denial and not contact health-care professionals, as instructed, when they sense the fetus does not behave as during the previous week. In addition we will probably have some contamination, an additional source of non-differential misclassification. *Mindfetalness* may be viewed as a new beneficial technology by some midwives or pregnant women assigned to routine care. We cannot hinder information spread but will of course be clear in the message that *Mindfetalness* needs to be examined with scientific rigor before any statements of efficacy in terms of saving babies lives can be made. As stated by the Medical Research Council, as any complex intervention that is investigated proactivity towards *Mindfetalness* may change and be more effective over time. In our case, during the recruitment period the effectiveness may change over time due to a learning curve among the midwives in teaching *Mindfetalness*. What we measure is a mean effect, and time of enrollment can be studied as an effect-modifying factor.

Statistical power. To calculate the study power for the primary analysis of the primary endpoint we can use the fact that in 2013, 28 999 children were born in Stockholm of whom 304 had an Apgar score of 1 to 6 and 102 were stillborn (Apgar score 0). (Another 50 newborn children died within 27 days.) We thus expect 1.4 percent (406 of 28 999) of the newborn in the control arm to have an Apgar score of 0 to 6. Based on these figures we have calculated a need to randomize close to 38 655 pregnant women which in turn is expected to occur within a 16-month period. With a P-value of 0.05 (one-sided test), we have 54 percent power to detect a decrease of at least 0.2 percent (from 1.4% to 1.2%), 84 percent of 0.3 percent and 98 percent for 0.4 percent (from 1.4% to 1.0%). For the secondary endpoint

(visits for worry of fetal wellbeing), with a P-value of 0.05 (two-sided test, we do not know if the percentage of visits will increase or decrease), we have 87 percent power to detect decrease from 12 percent to 11 percent and 84 percent power to detect an increase from 12 percent to 13 percent.

Ethical considerations. Our major ethical concern is if practicing *Mindfetalness*, with the accompanied instruction to react if fetal movements change, induces unnecessary health-care consumption with invasive or non-invasive investigations. Available data from our preparatory studies tell the opposite (as hypothesis 2 states). Nevertheless, the pilot study and the run-in period in the antenatal clinics randomized to proactivity may give signals of such an effect; if so, we have to reconsider the design of the study. We know kick-counting seems to give a slight increase in the number of unnecessary (from a medical perspective) unscheduled visits to an obstetric clinic (5). We need a gain in scientific knowledge to counteract the loss of time for midwives and pregnant woman in communicating and practicing *Mindfetalness*. We believe that such a gain will occur. The key for the ethical balance is the judgement whether or not the large scale of the study will outweigh the dilution of the effect measures. Ethical approval has been achieved (Dnr. 2015/2105.31/1).

Time plan. During the spring 2016 we have performed a pilot study. We have had a run-in period for the randomized study 1 to 30 September. The recruitment period for main data collection will be 1 October 2016 to 31 January 2018. The main publications will thus be submitted during 2018. During the fall of 2016 we plan to submit results from the pilot study.

On-going activities September 2016.

We have randomized 33 antenatal clinics in Stockholm to the intervention (receiving information about Mindfetalness) and 30 to routine care (Table 1). The randomization was performed in blocks according to varying yearly volumes of pregnant women and socio-

economic residential area. Three small clinics, with a total of 85 women registered in 2015, were not randomized. Another four clinics, receiving referrals of women with need for specialized care, were not randomized either. The recruitment (that is, the register-based analysis) is restricted to the 63 randomized clinics. In a pilot study in two antenatal clinics, the intervention has been tested among 105 women. By 30 September 2016 a run-in period has been ongoing in 22 of 33 clinics randomized to *Mindfetalness*. Of the 33 clinics randomly allocated to *Mindfetalness* will not participate. The recruitment period will start, as planned, 1 October 2016.

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520 **Table 1. Antenatal clinics in Stockholm allocated to Mindfetalness or routine care**
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	Number of antenatal Clinics	**Mindfetalness**	**Routine care**
Small-sized clinic, less than 500 pregnant women listed in 2014	41	21	20
Medium-sized clinic, 500 to 1000 pregnant women listed in 2014	17	9	8
Large-sized clinic, more than 1000 pregnant women listed in 2014	5	3	2
Antenatal clinics in high-income area	25	12	13
Antenatal clinics in a non-high income area	38	21	17
Total number of clinics randomized in the study	63	33	30
Women listed in 2014 in the 63, 33 and 30 clinics, respectively	**30 511**	**15 551**	**14 960**

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