WHO systematic review of randomised controlled trials of routine antenatal care

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Summary

Background There is a lack of strong evidence on the effectiveness of the content, frequency, and timing of visits in standard antenatal-care programmes. We undertook a systematic review of randomised trials assessing the effectiveness of different models of antenatal care. The main hypothesis was that a model with a lower number of antenatal visits, with or without goal-oriented components, would be as effective as the standard antenatal-care model in terms of clinical outcomes, perceived satisfaction, and costs.

Methods The interventions compared were the provision of a lower number of antenatal visits (new model) and a standard antenatal-visits programme. The selected outcomes were pre-eclampsia, urinary-tract infection, postpartum anaemia, maternal mortality, low birthweight, and perinatal mortality. We also selected measures of women's satisfaction with care and cost-effectiveness. This review drew on the search strategy developed for the Cochrane Pregnancy and Childbirth Group of the Cochrane Collaboration.

Findings Seven eligible randomised controlled trials were identified. 57 418 women participated in these studies: 30 799 in the new-model groups (29 870 with outcome data) and 26 619 in the standard-model groups (25 821 with outcome data). There was no clinically differential effect of the reduced number of antenatal visits when the results were pooled for pre-eclampsia (typical odds ratio 0·91 [95% CI 0·66–1·26]), urinary-tract infection (0·93 [0·79–1·10]). postpartum anaemia (1·01), maternal mortality (0·91 [0·55–1·51]), or low birthweight (1·04 [0·93–1·17]). The rates of perinatal mortality were similar, although the rarity of the outcome did not allow formal statistical equivalence to be attained. Some dissatisfaction with care, particularly among women in more developed countries, was observed with the new model. The cost of the new model was equal to or less than that of the standard model.

Interpretation A model with a reduced number of antenatal visits, with or without goal-oriented components, could be introduced into clinical practice without risk to mother or baby, but some degree of dissatisfaction by the mother could be expected. Lower costs can be achieved.

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See Commentary page

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Introduction

There is a lack of strong evidence that the content, frequency, and timing of visits in currently recommended "western" programmes for routine antenatal care are effective. Observational studies have consistently shown that groups having more antenatal-care visits have lower maternal, fetal, and neonatal morbidity and mortality than those who have fewer antenatal-care visits. Conversely, randomised comparative trials of differing numbers of visits, reported in the past few years, suggest that a model with a lower number of visits is at least as effective as the standard model. We undertook a systematic review to answer the question of whether a model with a lower number of antenatal visits, with or without goal-oriented components, is at least as effective in clinical terms, satisfaction perceived by women, and costs as the standard model.

Methods

We considered for this review any randomised controlled trial that compared a model of a lower number of antenatal visits with the standard model. The participants in these trials were pregnant women attending antenatal care. We classified as "goal oriented" models in which the researchers explicitly gave priority to the implementation of components shown to be effective in improving clinically relevant maternal and perinatal outcomes. We selected a priori for the meta-analyses outcomes for which antenatal care should have an effect: pre-eclampsia, urinary-tract infection, postpartum anaemia, and maternal mortality. Low birthweight and perinatal mortality were chosen as fetal and neonatal outcomes. Also, we selected measures of satisfaction with care perceived by the women and cost-effectiveness measures.

This review drew on the search strategy developed for the Cochrane Pregnancy and Childbirth Group of the Cochrane Collaboration. Briefly, it comprised an electronic search of MEDLINE, handsearching of the major obstetrics and gynaecology journals and relevant unpublished literature, and a search of the Cochrane Controlled Trials Register.[1] The search was complemented by other strategies, such as scanning of the reference lists of original papers and review articles, personal communications, and an independent search of the Cochrane Controlled Trials Register to ensure that all relevant studies were included in the review and to keep selection bias to a minimum. All these searches were done up to June, 2000, and updated in December, 2000. We contacted principal investigators of trials included to obtain additional data on outcomes that were not reported in the original publication.

We selected a list of criteria from a methodological review[2] and from the recommendations in the *Cochrane Collaboration Reviewers' Handbook*[3] to assess the quality of the trials. The criteria used were: randomisation; allocation concealment; masking with respect to outcome assessment, care providers, and treatment recipients; contamination in the control group; attrition bias; cointervention; protocol deviation; and intention-to-treat analysis. Each criterion was rated as met, unmet, or unclear, and final decisions were made by consensus

Ref (year)	Random allocation method	Allocation concealment	Participants	New model	Standard	Outcome measures
4 (2001)	Cluster randomisation (urban clinic). Analysis took account of between-cluster variation.	By facsimile	All women attending antenatal care clinics (12 568 new model, 11 958 standard model)	4 goal-oriented visits based on scientifically evaluated activities for low-risk women. Women requiring any further assessment or special care were referred to a higher level. Visits achieved=5	Standard antenatal care presently offered in the selected sites, which follows the traditional multivisit model. Visits achieved=8	Low birthweight; maternal morbidity index; maternal and perinatal morbidity and mortality: satisfaction of women and providers of care; economic outcomes
11 (1996)	Cluster randomisation (urban clinic)	Sequentially numbered sealed envelopes	Low-risk pregnant women (9674 new model, 6320 standard model)	6 goal-oriented visits which directed the care provider towards a certain purpose Visits achieved=4	14 visits, standard multivisit model Visits achieved=6	Preterm delivery; low birthweight; small for gestational age; maternal morbidity; maternal mortality; and perinatal mortality
20 (1995)	Woman's date of birth	No	Low-risk pregnant women (320 new model, 229 standard model)	8 antenatal visits; one care provider assigned for entire pregnancy in each woman. Visits achieved=8	13 antenatal visits; each visit was potentially with a different care provider. Visits achieved=11	Preterm delivery, low birthweight; caesarean section; Apgar score at 5 min less than 7; women's satisfaction
21 (1996)	Random numbers table	Sealed, opaque envelopes	Low-risk pregnant women (1382 new model, 1382 standard model)	9 visits: at 8, 12, 16, 24, 28, 32, 36, 38, and 40 weeks. Visits achieved=12	14 visits: every 4 weeks from 8 to 28 weeks, every 2 weeks until 36 weeks, and weekly thereafter. Visits achieved=15	Preterm delivery; low birthweight; mild and severe pre-eclampsia; caesarean section
22 (1996)	Random permuted blocks of 8 and 16 women stratified by recruiting offices	Sequentially numbered non-resealable opaque envelopes	Low-risk pregnant women (1446 new model, 1446 standard model)	7 visits for nulliparous at 24, 28, 32, 36, 38, 40 weeks plus booking visit. 6 visits for multiparous at 26, 32, 36, 38, 40 weeks plus booking visit. Visits achieved=9	13 visits at 16, 20, 24, 28, 30, 32, 34, 36, 37, 38, 39, 40 weeks plus booking visit. Visits achieved=11	Caesarean section for pregnancy-related hypertensive disorders; maternal and fetal morbidity; women's satisfaction
23 (1997)	Computer program	Unclear	Low-risk pregnant women (61 new model, 61 standard model)	8 visits: an initial visit then visits at 15–19, 24–28, 32, 36, and 38 weeks until delivery. Visits achieved=8	13 visits: an initial visit then visits every 4 weeks until 28 weeks, every 2 weeks until 36 weeks, and weekly until delivery. Visits achieved=11	Gestational age at birth; birthweight; mode of delivery; neonate's stay in nursery; neonate's stay in intensive care; neonatal morbidity; preterm labour; small for gestational age; recurrent urinary-tract infection; pregnancy-induced hypertension; women's satisfaction
10 (1999)	Cluster randomisation (rural health centre)	Unclear	All women booking for antenatal care (5348 new model, 5224 standard model)	5 goal-oriented prenatal visits with reduced routine procedures. Visits achieved=4	Standard antenatal visits for rural areas. Visits achieved=4	Number and timing of visits; use of rural health centres for delivery; fetal and maternal outcomes

*Pre-eclampsia, severe postpartum anaenua, treated urinary-tract infection.

Table 1: **Characteristics of trials included in the review**

among the researchers. Methodological quality was assessed without knowledge of study outcome except for the trial by Villar and colleagues,[4] in which some of us were involved.

Data were extracted from each publication independently by GC, JV, and DKN without masking of authors' names, study site, intervention, or trial results.[5] These researchers jointly reviewed the extracted data. After the accuracy had been checked, data were entered into the appropriate tables.

Some trials used the clinic as the unit of randomisation (cluster randomisation) rather than the individual woman (individual randomisation). For some outcomes, we did pooled analyses and analyses stratified by unit of randomisation.[6]

Overall and stratified results are presented as typical odds ratio with 95% CI for biomedical outcomes and as rate difference with 95% CI for perception of care

Trial ref	Criterion met, unclear, or unmet								
	Randomisation	Allocation concealment	Masking			Contamination	Cointervention	Protocol deviation	ITT analysis
			Woman	Care provider	Outcome				
4	Met	Met	Unmet	Unmet	Unmet	Met	Met	Met	Met
11	Met	Met	Unmet	Unmet	Unmet	Met	Met	Met	Unclear
20	Unmet	Unmet	Unmet	Unmet	Unmet	Unmet	Unmet	Met	Met
21	Met	Met	Unmet	Unmet	Unmet	Met	Met	Met	Met
22	Met	Met	Unmet	Unmet	Unmet	Met	Met	Met	Met
23	Met	Unclear	Unmet	Unmet	Unmet	Met	Met	Met	Unclear
10	Met	Unclear	Unmet	Unmet	Unmet	Unclear	Unclear	Unclear	Unclear

ITT=intention to treat.

Table 2: **Methodological quality of trials included in the review**

outcomes. We assumed for both a fixed-effect model because we wished to draw inferences about the particular studies assembled and there was no strong heterogeneity between studies for the outcomes considered.[7] Odds ratios were used when the interest by measuring the effectiveness of the intervention and rate differences when assessment of the intervention's impact in terms of an absolute measure was more relevant.

Analysis of cluster-randomisation trials requires special analytical techniques that take into account the between-cluster variation.[8,9] Two of the three cluster-randomisation trials used a stratified design[4,10] and another used a completely randomised design.[11] We used the clustered Woolf method,[12] to obtain the pooled odds ratio and its 95% CI for these two trials. To calculate the variance inflation factors required for this method, we used a common intraclass correlation coefficient for each outcome variable[13] obtained from one of the two trials,[4] and the actual cluster sizes. To obtain the pooled estimates for all trials, we used the same procedure with variance inflation factors equal to one for the individual-randomisation trials.[14]

To obtain rate difference and its 95% CI we used cluster percentages. For the trial that did not take the between-cluster variation into account, we inflated the variance of the difference by the variance inflation factor before pooling. We pooled the differences of the two trials, weighting by the inverse of the variance.[15]

Homogeneity tests across individual randomisation trials were done with χ^2 tests.[3] For cluster-randomisation trials, a homogeneity test described by Fleiss[16] was used, modified to account for cluster design. Publication bias was assessed with the test of Egger and colleagues[17] and funnel plot evaluation.[18]

We chose 1·2 as the maximum value of the odds ratio regarded as consistent with the conclusion that the model with a lower number of antenatal visits is statistically equivalent to the standard model.[19] This value was estimated to be clinically relevant for those outcomes that have a prevalence of about 10%. We therefore expected to have sufficient power to answer reliably the hypothesis on low birthweight.

Results

Seven eligible randomised controlled trials were identified (table 1).[4,10,11,20–23] Four of them took place in more developed countries.[20–23] Two were done in Zimbabwe.[10,11] The largest was a multicentre trial in Argentina, Cuba, Saudi Arabia, and Thailand.[4] Four of the studies were individual-randomisation trials,[20–23] and three cluster-randomisation trials.[4,10,11]

A total of 57 418 women participated in these studies: 30 799 in models with reduced numbers of antenatal visits, of whom 26 619 were followed up through the entire pregnancy, and 26 620 in the standard model, of whom 25 821 had outcome data available. The trial by Walker and Koniak-Griffin[23] had the highest proportion of women lost to follow-up; 30% of women in the new model and 38% of those in the standard model had no data available. There were also high rates of loss to follow-up in the trial by Binstock and Wolde-Tsadik (29% new model, 24% standard model).[20] In the trial by McDuffie and colleagues, about 16% of women in each group were lost to follow-up.[21] For the rest of the trials, the rates of loss to follow-up were low: 5% in the new model and 2% in the standard model in the trial by Sikorski and colleagues;[22] 3% for both groups in the trial by Munjanja and colleagues;[11] and about 2% in both groups for the trial by Villar and colleagues.[4] The trial by Majoko and co-workers was available only in abstract form, and rates of loss to follow-up were not reported.[10]

Overall, the methodological quality of the included trials was acceptable with moderate risk of bias (table 2). One trial[20] was methodologically weak with high probability of bias, because the allocation method was based on mother's date of birth, it had unbalanced group sizes, there was evidence of contamination and cointervention in the trial, and there was a high proportion of loss to follow-up. Given the nature of the intervention, masking of care providers or women was not possible in all trials, although the assessment of primary outcomes was partially masked in most of them.

We did publication bias statistical tests for all trials with low birthweight (p=0·91) or pre-eclampsia (p=0·48) as an endpoint. We also constructed funnel plots for both outcomes and again found no evidence of publication bias.

Two trials done in less developed countries[4,11] showed a clinically relevant proportional reduction in the median number of visits. In the trial of Munjanja and colleagues,[11] the median number of visits was six in the standard model and four in the new model. In the trial by Villar and colleagues,[4] the corresponding median numbers were eight and five. These two trials also included a component of goal-oriented activities in which priority was given to effective interventions over more ritualistic routine activities. In the four trials that took place in more developed countries, the recommended number of visits was not strictly followed in either study group. The median numbers of visits during the trial are given in table 1.

There was no differential effect of the intervention when the results were pooled for low birthweight (typical odds ratio 1·04 [95% CI 0·93–1·17]). The same pattern was observed for individual-randomisation trials and cluster-randomisation trials (table 3). A sensitivity analysis by methodological quality, which excluded the trial of Binstock and Wolde-Tsadik[20] gave similar results for both the overall meta-analysis (1·04 [0·93–1·17]) and that for individual-randomisation trials (0·98 [0·78–1·24]). Walker and Koniak-Griffin[23] did not report rates of pre-eclampsia and low birthweight so their data could not contribute to the meta-analysis. However, related outcomes were measured in that trial. Pregnancy-induced hypertension was detected in two of 43 women in the new-model group and in one of 38 women in the standard-model group. Mean birthweight was 3356 g (SD 401) in the new-model group and 3507 g (429) in the standard-model group (p=0·11). Only one baby who was small for gestational age was reported in that trial (standard-model group).

The new model showed similar odds of pre-eclampsia to the standard model when all trials were pooled (typical odds ratio 0·91 [95% CI 0·66–1·26]). When stratified for individual or cluster randomisation, the pattern of results

Study reference	Number of events/total		Typical odds ratio (95% CI)
	New model	Standard model	
Individual-randomisation trials			
20	12/227	7/174	1·33 (0·51–3·46)
21	64/1175	72/1176	0·88 (0·62–1·25)
22	85/1356	82/1395	1·07 (0·78–1·46)
Subtotal	161/2758	161/2745	1·00 (0·80–1·25)*
Cluster randomisation trials			
4	886/11 534	788/11 040	1·10 (0·95–1·27)
11	723/9394	491/6138	0·96 (0·81–1·13)
Subtotal	1609/20 928	1279/17 178	1·05 (0·92–1·21)†
Total	1770/23 686	1440/19 923	1·04 (0·93–1·17)‡

Tests of homogeneity: *p=0·60; †p=0·34; ‡p=0·51.

Table 3: **Risk of low birthweight (<2500 g) according to antenatal-care model**

Study reference	Number of events/total		Typical odds ratio (95% CI)
	New model	Standard model	
Individual-randomisation trials			
20	9/227	4/174	1·75 (0·53–5·80)
21	59/1165	66/1163	0·89 (0·62–1·27)
22	9/1240	11/1286	0·85 (0·35–2·05)
Subtotal	77/2632	81/2623	0·93 (0·68–1·28)*
Cluster randomisation trials			
4	189/11 672	144/11 121	1·22 (0·88–1·68)
11	441/9394	396/6138	0·71 (0·55–0·92)
Subtotal	630/21 066	540/17 259	0·91 (0·58–1·43)†
Total	707/23 698	621/19 882	0·91 (0·66–1·26)‡

Tests of homogeneity: *p=0·55; †p=0·16; ‡p=0·29.

Table 4: **Risk of pre-eclampsia according to antenatal-care model**

Study reference	Number of events/total		Typical odds ratio (95% CI)
	New model	Standard model	
Individual-randomisation trials			
21	8/1175	7/1176	1·14 (0·41–3·17)
22	7/1361	10/1396	0·72 (0·27–1·89)
Subtotal	15/2536	17/2562	0·89 (0·45–1·79)*
Cluster randomisation trials			
4	234/11 672	190/11 121	1·14 (0·83–1·57)
11	162/9394	88/6138	1·21(0·93–1·57)
10	91/5348	110/5224	0·80 (0·61–1·07)
Subtotal	487/26 414	388/22 483	1·07 (0·83–1·39)†
Total	502/28 950	405/25 055	1·06 (0·82–1·36)‡

Tests of homogeneity: *p=0·51; †p=0·06; ‡p=0·10.

Table 5: **Risk of perinatal mortality according to antenatal-care model**

did not change (table 4). Again, a sensitivity analysis without the trial of Binstock and Wolde-Tsadik[20] gave similar results to the whole dataset in both the overall meta-analysis (0·90 [0·66–1·24] and the individual-randomisation trials meta-analysis (0·88 [0·63–1·23]).

For the outcomes of severe postpartum anaemia (odds ratio 1·01) and urinary-tract infection (0·93 [95% CI 0·79–1·10]) only the trial by Villar and colleagues gave data; the risk was similar in both groups of the trial.[4] The odds ratio for severe postpartum anaemia should be viewed cautiously because there was heterogeneity between study sites and thus 95% CI were not calculated.

The overall meta-analysis for perinatal mortality gave a typical odds ratio of 1·06 (0·82–1·36; table 5).

For maternal mortality, two individual-randomisation trials[21,22] reported this outcome, with one maternal death in 2405 deliveries in the new-model groups, and no maternal deaths in 2449 deliveries in the standard-model groups. Two cluster-randomisation trials[4,11] reported maternal mortality, with 13 maternal deaths in 21 962 deliveries in the new-model groups and 11 in 18 095 deliveries in the standard-model groups (typical odds ratio 0·87 [0·50–1·50]). The overall meta-analysis gave a typical odds ratio for this outcome of 0·91 (0·55–1·51; test of homogeneity p=0·99).

There was statistical heterogeneity in most of the variables used to describe satisfaction with care (quality of prenatal care, p=0·09; frequency of visits, p<0·0001; question answered/felt listened to, p=0·17; amount of visit time, p=0·002; would choose same schedule, p=0·02) and therefore we decided not to combine the results of the two types of trials.

For individual-randomisation trials only, women were less satisfied with the new model in analyses of quality of antenatal care, frequency of visits, questions answered/felt listened to by providers, and amount of visit time. We found clinically and statistically significant heterogeneity (homogeneity test p<0·0001) also among the three trials for the variable satisfaction with the frequency of visits (table 6). We therefore undertook a sensitivity analysis by methodological quality, excluding the trial with high possibility of bias.[20] In that analysis (homogeneity test p=0·47), the direction of the effect was unchanged, but the magnitude was greater (rate difference −16% [95% CI −19 to −12]). No differences in the quality of care perceived by the women were seen between the two models in the trial reporting that variable.[20] More women in the new-model groups than in the standard-model groups would choose the same schedule of visits in future (table 6).

When the cluster-randomisation trials were analysed, the results showed no evidence of significant differences in the degree of satisfaction perceived by the women, although more women in the new-model groups than in the standard-model groups reported some degree of dissatisfaction with regard to the frequency of visits in the only trial reporting that outcome.[4] Conversely, more women were satisfied with the amount of time spent during the visit in the new model (table 6).

Two trials[4,22] reported investigation of the economic implications of the two models of antenatal care. Villar and colleagues[4] did detailed economic analyses in two of the four participating sites in their trial (Cuba and Thailand). The results obtained overall show that costs per pregnancy to women and providers were lower with the new model than with the standard model.

An economic analysis on data from the trial by Sikorski and colleagues has been published.[24] That study looked only at costs to the UK National Health Service. The antenatal costs were lower with the new model than with the standard model (UK £225 *vs* £251) but there were higher costs related to length of stay of babies in the intensive-care unit with the new model than with the standard model (£181 *vs* £126). This higher cost of neonatal care was due to a higher rate of neonatal admissions to special care in the new-model group than in the standard-model group (3·5% *vs* 3·2%; odds ratio 1·07 [95% CI 0·71 –1·63]) as well as longer mean duration of stay in special care among the neonates admitted (22·6 days [47 babies] *vs* 17·2 days [45 babies] mean difference 5·4 days [–5·8 to 16·6]). If the cost analyses were restricted to antenatal-care activities that were significantly reduced in the new model (number of visits, number of maternal "day" admissions, and number of ultrasound scans), the

Type of study outcome	Number of studies	Number satisfied/total		Rate difference in % (95% CI)
		New model	Standard model	
Individual-randomisation trials				
Quality of antenatal care	1	574/589	587/600	–0·4 (–2·1 to 1·3)
Frequency of visits	3	1243/1690	1397/1703	–8·5*
Questions answered/ felt listened to	1	693/881	778/937	–4·4 (–8·0 to –0·8)
Amount of visit time	1	515/916	594/960	–5·7 (–10·1 to –1·2)
Would choose same schedule	1	643/915	593/947	7·7 (3·4 to 11·9)
Cluster randomisation trials				
Quality of prenatal care	2	825/887	773/844	1·0 (–3·2 to 5·2)†
Frequency of visits	1	612/789	649/744	–7·9 (–16 to 0·2)
Questions answered/ felt listened to	1	78/100	70/100	8·0 (–9·4 to 25·4)
Amount of visit time	2	750/889	657/847	6·6 (0·1 to 13·1)‡
Would choose same schedule	1	757/785	703/742	1·4 (–2·2 to 4·9)

Tests of homogeneity: *p=0·001; †p=0·11; ‡p=0·97.

Table 6: **Women's perception of care according to antenatal-care model**

new model would be overall £25 less costly to health services than the standard model.[24]

Long-term follow-up of the women enrolled in Sikorski and colleagues' trial to 2·7 years after delivery has been reported.[25] Only 1117 women (60% of the total) completed the study. No differences were seen between groups in terms of relationship between mother and child, maternal psychological wellbeing, health-service use, health-related behaviour, or health beliefs.

Discussion

In this systematic review, we selected a priori several outcomes thought to be substantial health problems closely linked with antenatal care. However, the outcomes selected for the review were not in all cases the same primary outcomes as identified in the individual trials or the reported outcomes in each of the trials. Antenatal care consists of several activities and intervention procedures aimed at improving various events. Therefore, different researchers selected different variables as primary or secondary outcomes.

We are confident that the possibility of publication bias in our systematic review is very low. Our literature search was systematic and extensive, and we contacted researchers working on this subject. Statistical and graphic assessment did not suggest any such publication bias.

In general, the trials were of acceptable quality with low or moderate risk of bias, except for that by Binstock and Wolde-Tsadik.[20] Sensitivity analysis without that trial gave similar results. We should point out that owing to the unmasked and pragmatic nature of these trials, some degree of protocol deviation, contamination, and cointervention should be expected in all of them.

Our meta-analysis included both trials that used the individual as the unit of randomisation and those that used clinics. We have presented both pooled and stratified meta-analyses by the two types of trials. When we pooled the odds ratios or rate differences, the between-cluster variation was taken into account for the cluster-randomisation trials. Fawzi and colleagues adjusted for the clustering effect by increasing the variance of the pooled odds ratio estimator (in the log scale) by an arbitrary 30%. We went a step further, using an estimate of the intraclass correlation coefficient to calculate variance inflation factors,[14] although our procedure has the limitation that this estimate is based on only one trial.[19]

We stratified the meta-analyses by type of randomisation because in addition to the different unit of randomisation, the model with a lower number of antenatal visits in the cluster-randomisation trials included goal-oriented components, whereas in the individual-randomisation trials the aim was only to decrease the number of visits. Furthermore, the method of implementing the intervention (clinic policy *vs* individual schedule), the site of the trials (less *vs* more developed countries), the proportional reduction in the number of visits (large *vs* small), and the sample size (large *vs* small) clearly differ between the two types of trials.

The objective of equivalence trials, as in this review, is to demonstrate equivalent efficacy of the intervention and control approach, in contrast to superiority trials which aim to establish that a new treatment is better than an existing one or placebo. A problem that should be taken into account in equivalence trials is that when the two groups of a trial are implementing rather similar interventions, the outcome results are expected to be similar. As is evident from the results, the proportional reduction in the number of visits in the trials in more developed countries was very small. An absolute difference of two to three antenatal-care visits, in more developed countries, where the norm is 11 to 14 antenatal-care visits, is unlikely to have any clinical significance. On the other hand, the two largest trials, which took place in less developed countries,[4–11] achieved proportionately larger reductions in the number of visits. This reduction is highly relevant clinically and has public-health implications, especially in countries such as those where resources are scarce and should be allocated in the most efficient way. At the same time, the results of these trials are reassuring in that such a reduction is not associated with an increase in adverse maternal and perinatal outcomes.

Overall, we showed equivalence for low birthweight within the preset margin. When we stratified meta-analyses by unit of randomisation, the results had the same pattern and were similar in clinical terms, although we could not claim statistical equivalence because of the lower power. Although we did not show statistical equivalence for pre-eclampsia within the upper margin established for low birthweight (a 20% increase), the rates were clinically very similar and the upper limit of the 95% CI (a 26% increase) was very close to this margin. Similar considerations applied to the upper limit of the 95% CI for perinatal mortality (1·36, or 36% increase risk). For these outcomes with low prevalence the power is lower. Two approaches can be explored to facilitate their interpretation: the first is to set larger limits of clinical equivalence based on the absolute risk; the second is to decrease the level of confidence (ie, 90% CI).[26] For example, the 90% CI for pre-eclampsia was 0·70 to 1·19, within the 20% margin of equivalence. We have then, of course, an increased risk of falsely concluding that the models are equivalent.

Assessment of women's perception of care in individual-randomisation trials, done in more developed countries, indicated overall dissatisfaction with the model of a lower number of antenatal visits, although more women than in the standard-model groups would choose this model for the next pregnancy. In less developed countries, women assigned the new model were overall as satisfied as those assigned the standard model, but they also were concerned about the frequency of visits.

The model with a lower number of antenatal visits showed slightly lower costs in comparison with the standard model in the trial by Villar and colleagues.[4] The economic evaluation based on Sikorski and colleagues' trial[24] was a secondary analysis to the trial, based on unit cost data taken from various external sources. The most important limitation of that analysis was that it did not include costs to women, such as those associated with hours loss of work, travel, and child care, and marginal costs or overheads, components that are more likely to be influenced by a decrease in the number of antenatal-care visits. Providers are unlikely to realise actual cost savings from a lower number of antenatal visits; however, women's time and energy, staff, and buildings would be freer for other more useful activities.

The objective of routine antenatal care is to deliver effective and appropriate screening, preventive, or treatment interventions. Thus, the number of visits should be the result of how these effective interventions can be delivered in a timely way during pregnancy. The results of this systematic review suggest that these effective interventions can be provided within fewer visits than presently recommended, without any clinically important increase in the risk of adverse outcomes.

Contributors

Guillermo Carroli, José Villar, and Dina Khan-Neelofur were responsible for the idea, conception, and preparation of the review, reviewed the quality of the trials, and extracted the data. Gilda Piaggio, Guillermo

Carroli, and José Villar planned and conducted the analysis. Guillermo Carroli, José Villar, Metin Gülmezoglu, Gilda Piaggio, and Dina Khan-Neelofur wrote the paper with input from Miranda Mugford, Pisake Lumbiganon, Ubaldo Farnot, and Per Bergsjø. All the contributors read the report and made substantive suggestions on its content.

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