Caesarean section surgical techniques (CORONIS): a fractional, factorial, unmasked, randomised controlled trial

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Summary

Background Variations exist in the surgical techniques used for caesarean section and many have not been rigorously assessed in randomised controlled trials. We aimed to assess whether any surgical techniques were associated with improved outcomes for women and babies.

Methods CORONIS was a pragmatic international 2×2×2×2×2 non-regular fractional, factorial, unmasked, randomised controlled trial that examined five elements of the caesarean section technique in intervention pairs. CORONIS was undertaken at 19 sites in Argentina, Chile, Ghana, India, Kenya, Pakistan, and Sudan. Each site was assigned to three of the five intervention pairs: blunt versus sharp abdominal entry; exteriorisation of the uterus for repair versus intra-abdominal repair; single-layer versus double-layer closure of the uterus; closure versus non-closure of the peritoneum (pelvic and parietal); and chromic catgut versus polyglactin-910 for uterine repair. Pregnant women were eligible if they were to undergo their first or second caesarean section through a planned transverse abdominal incision. Women were randomly assigned by a secure web-based number allocation system to one intervention from each of the three assigned pairs. All investigators, surgeons, and participants were unmasked to treatment allocation. The primary outcome was the composite of death, maternal infectious morbidity, further operative procedures, or blood transfusion (>1 unit) up to the 6-week follow-up visit. Women were analysed in the groups into which they were allocated. The CORONIS Trial is registered with Current Controlled Trials: ISRCTN31089967.

Findings Between May 20, 2007, and Dec 31, 2010, 15 935 women were recruited. There were no statistically significant differences within any of the intervention pairs for the primary outcome: blunt versus sharp entry risk ratio 1·03 (95% CI 0·91–1·17), exterior versus intra-abdominal repair 0·96 (0·84–1·08), single-layer versus double-layer closure 0·96 (0·85–1·08), closure versus non-closure 1·06 (0·94–1·20), and chromic catgut versus polyglactin-910 0·90 (0·78–1·04). 144 serious adverse events were reported, of which 26 were possibly related to the intervention. Most of the reported serious adverse events were known complications of surgery or complications of the reasons for the caesarean section.

Interpretation These findings suggest that any of these surgical techniques is acceptable. However, longer-term follow-up is needed to assess whether the absence of evidence of short-term effects will translate into an absence of long-term effects.

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Introduction

Caesarean section is one of the most commonly undertaken operations worldwide and accounts for up to 60% of deliveries in some countries.[1–3] Caesarean section carries a risk of short-term postoperative morbidity, for example, fever, pain, post-partum haemorrhage, damage to the bladder or ureters, and thromboembolic disease. Long-term clinical and obstetric problems include chronic pain, infertility, bowel obstruction, abnormal placentation and its consequences, and uterine rupture.[4–6]

Caesarean section is not done in a standardised way, and there are variations in the surgical techniques used.[7,8] Many of the surgical techniques have not been rigorously assessed in randomised controlled trials and so whether any of them are associated with better outcomes for women and babies is not known.[7] Because large numbers of women undergo caesarean section, even small differences in postoperative morbidity between techniques could mean improved health for a large number of women and substantial savings for health services. Rigorous randomised controlled trials are needed to establish the effectiveness of different surgical techniques. We therefore undertook the present trial to assess whether five specific approaches to the surgical techniques were associated with improved outcomes for women and babies.

Methods

Study design and participants

After widespread interest from many countries to participate in the UK trial of caesarean section surgical techniques (CAESAR),[9] WHO funded a workshop in Oxford, UK, to develop a proposal for a new trial to be undertaken in these countries. At this workshop, investigators reviewed all the available evidence for each element of the caesarean section operation and produced, through a formal consensus process, a ranked list of candidate intervention pairs to include in the trial. Eligibility for inclusion as a trial intervention was based on a range of criteria including the clinical importance of resolving the uncertainty for short-term and long-term

outcomes, the quality and quantity of available evidence, and the feasibility of undertaking the interventions in the participating countries.

Based on the findings from the workshop, we undertook a multicentre, unmasked, randomised controlled trial at 19 sites in Argentina, Chile, Ghana, India, Kenya, Pakistan, and Sudan to assess two surgical techniques (intervention pairs) for five elements of the caesarean section operation. The five intervention pairs were as follows: (1) blunt versus sharp abdominal entry; (2) exteriorisation of the uterus for repair versus intra-abdominal repair; (3) single-layer versus double-layer closure of the uterus; (4) closure versus non-closure of the peritoneum (pelvic and parietal); and (5) chromic catgut versus polyglactin-910 for uterine repair. The methods have been summarised previously.[10]

Pregnant women were eligible if they were to undergo delivery by lower segment caesarean section through a transverse abdominal incision, irrespective of fever in labour, gestational age, or multiple pregnancies. Women were not eligible if there was a clear indication for a particular surgical technique or material to be used that prevented any of the allocated interventions being used, if they had more than one previous caesarean section, or if they had already been recruited into the trial.

The National Perinatal Epidemiology Unit Clinical Trials Unit (Oxford, UK) and each participating site secured approval from their research ethics committee or equivalent body. The trial was overseen by an independent trial steering committee. An independent data monitoring committee monitored effectiveness and safety annually. The data monitoring committee used the Haybittle–Peto[11,12] approach for interim analyses using three standard errors as the cutoff for consideration of early cessation, preserving the type-one error rate across the trial.

Each participating site, advised by their research ethics committee, decided how to provide trial information to women and seek informed consent. Information leaflets were made available, in appropriate languages, which explained the trial objectives, the process of trial entry, and follow-up. The trial was discussed with all eligible women and their partners and relatives as appropriate. If the woman agreed to participate, she signed a formal consent form or used the method of recording consent permitted in that setting (eg, a thumb print).

Randomisation and masking

Although there were five intervention pairs, each site was assigned only three to maximise compliance (appendix), thereby making this a 2×2×2×2×2 fractional, factorial trial (more correctly termed a non-regular fractional, factorial trial).[13] Women were randomly allocated to one intervention from each of the three assigned pairs. Randomisation was done using a bespoke secure web-based system, with a 24-h automated telephone back-up. The system allocated a number corresponding to a unique allocation envelope held at participating sites. The allocation numbers were generated by computer implementation of a pseudo-random generating algorithm. Each envelope contained an allocation sheet detailing the three allocated interventions for a woman, as a reminder to the surgeon. In instances where there was no internet or telephone connectivity, the recruiting clinician selected the lowest sequentially numbered allocation envelope. All randomisation data were held centrally at the international coordinating centre (National Perinatal Epidemiology Unit Clinical Trials Unit).

We used minimisation to ensure balance within sites, within and between intervention pairs, and with respect to in-labour and not in-labour caesarean section and first or second caesarean section. For sites where chromic catgut versus polyglactin-910 was one of the assigned intervention pairs, supplies of both suture materials were provided by the international coordinating centre and were contained in a specific trial box stored in the operating theatre.

All investigators, surgeons, and participants were unmasked to treatment allocation.

Procedures

Each regional coordinator (one per country, except India, which was split into two regions) started and documented a training programme that ensured that surgeons operating within the trial were familiar with the techniques being compared before participating. To facilitate this, the international coordinating centre gave a DVD of the interventions tested to all study sites.

The procedures for blunt versus sharp abdominal entry were as follows. For sharp entry, the abdomen was entered using a scalpel to divide the abdominal skin. Each subsequent layer of the abdomen was then separately identified and divided using either a scalpel or scissors. In blunt entry, the abdomen was entered using a scalpel to divide the abdominal skin. The scalpel was then used to divide the fat and rectus sheath in the midline and the rectus sheath incision extended manually. The parietal peritoneum was then entered digitally and the defect enlarged manually.

For exteriorisation of the uterus for repair versus intra-abdominal repair, once the placenta had been delivered, either the uterus was drawn from the pelvis to rest on the anterior abdominal wall so that the uterine incision could clearly be visualised or the uterus was repaired while in the pelvis.

For the comparison of single-layer versus double-layer closure of the uterus, the uterine incision was closed with either one or two layers of sutures. Each layer could be closed using any accepted technique. Haemostasis of the incision could be done with additional sutures as judged necessary by the surgeon regardless of the method of closure undertaken.

See Online for appendix

For closure versus non-closure, the pelvic and parietal peritoneum was either closed or not closed. For either

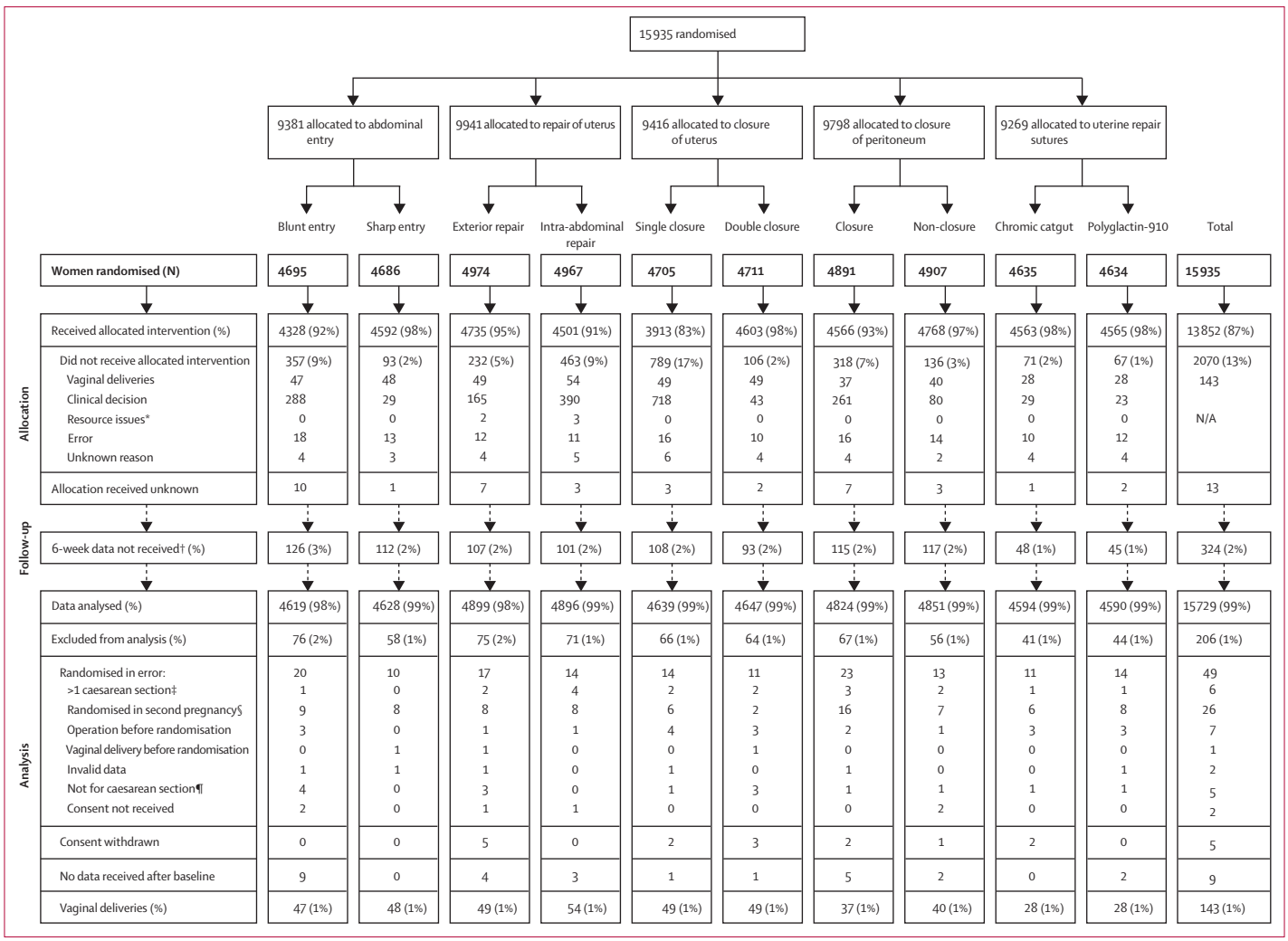

Figure 1: **Trial profile**

N/A=not applicable. *Consisted of power outages and shortage of equipment. †Included in the primary analysis. ‡Ascertained after randomisation. §Randomised twice because the woman had a previous caesarean section in the CORONIS trial. ¶Two were going to have a hysterotomy, one a colpotomy, one was a uterine rupture known before trial entry, and one had a rudimentary horn pregnancy.

technique, haemostasis was achieved as usual, including, where necessary, the use of haemostatic sutures.

Finally, for chromic catgut versus polyglactin-910 for uterine repair, the uterus was repaired using either number 1 chromic catgut (Medsurge, Philadelphia, PA, USA) or number 1 polyglactin-910 (Ethicon, Livingston, NJ, UK). This could be a continuous, continuous locking, or an interrupted layer of sutures. For sites where chromic catgut versus polyglactin-910 was one of the assigned intervention pairs, surgeons were asked to restrict their use of the allocated suture material to repair of the uterine incision and to use their usual suture material for all other layers.

All non-allocated surgical elements and all other aspects of the caesarean section procedure were undertaken at the discretion of the surgeon. In particular, there were no restrictions on the type of suture material that could be used, and standard measures to achieve haemostasis were employed regardless of the allocated intervention.

The primary outcome was a composite of death, maternal infectious morbidity, further operative procedures, or blood transfusion of more than 1 unit of whole blood or packed cells up to the 6-week follow-up visit. Maternal infectious morbidity was defined as one or more of the following: antibiotic use for maternal febrile morbidity during postnatal hospital stay or for endometritis, wound infection, or peritonitis up to the 6-week follow-up visit. Blood transfusion as part of the composite primary outcome was changed on June 14, 2010, from any blood transfusion to transfusion of more than 1 unit of blood when the data monitoring committee and international coordinating centre became aware that one site was transfusing 1 unit of blood routinely.

Secondary outcomes consisted of the individual components of the primary outcome as well as pain,

interventions used for severe primary post-partum haemorrhage, stillbirth after trial entry, other severe maternal morbidity, Apgar score less than 3 at 5 min, laceration of baby at time of caesarean section, and death of the baby by 6 weeks of age. Secondary health service utilisation outcomes consisted of the duration of the operation, duration of hospital stay, admission to intensive care and duration of stay, and readmission to hospital within 6 weeks and duration of stay.

Data were collected at trial entry, immediately after surgery, at hospital discharge (including hospital transfer or death), and at about 6 weeks after delivery. Women who did not return at 6 weeks were located and interviewed by telephone or during a home visit. Serious adverse events were assessed by the chief investigator and data monitoring committee as soon as they were reported to the international coordinating centre.

	Abdominal entry		Repair of uterus		Closure of uterus		Closure of peritoneum		Uterine repair sutures		Total (n=15729)
	Blunt (n=4619)	Sharp (n=4628)	Exterior (n=4899)	Intra-abdominal (n=4896)	Single (n=4639)	Double (n=4647)	Closure (n=4824)	Non-closure (n=4851)	Catgut (n=4594)	PG-910 (n=4590)	
Region											
Argentina	809 (17%)	808 (17%)	807 (16%)	810 (16%)	N/A*	N/A*	808 (17%)	809 (17%)	N/A*	N/A*	1617 (10%)
Chile	N/A*	N/A*	607 (12%)	598 (12%)	353 (8%)	347 (8%)	597 (12%)	608 (13%)	254 (6%)	251 (5%)	1205 (8%)
Ghana	631 (14%)	639 (14%)	N/A*	N/A*	634 (14%)	636 (14%)	N/A*	N/A*	637 (14%)	633 (14%)	1270 (8%)
India: Delhi	1327 (29%)	1330 (29%)	1082 (22%)	1081 (22%)	1875 (41%)	1882 (41%)	1347 (28%)	1347 (28%)	N/A*	N/A*	3757 (24%)
India: Vellore†	790 (17%)	785 (17%)	263 (5%)	263 (5%)	N/A*	N/A*	1047 (22%)	1054 (22%)	1050 (23%)	1051 (23%)	2101 (13%)
Kenya	829 (18%)	828 (18%)	831 (17%)	826 (17%)	N/A*	N/A*	N/A*	N/A*	830 (18%)	827 (18%)	1657 (11%)
Pakistan†	233 (5%)	238 (5%)	514 (10%)	520 (11%)	981 (21%)	985 (21%)	1025 (21%)	1033 (21%)	1029 (22%)	1029 (22%)	2529 (16%)
Sudan	N/A*	N/A*	795 (16%)	798 (16%)	796 (17%)	797 (17%)	N/A*	N/A*	794 (17%)	799 (17%)	1593 (10%)
Maternal characteristics at trial entry											
Mother's age (years)	26·5 (5·3)	26·7 (5·3)	27·1 (5·7)	27·1 (5·7)	26·9 (5·4)	26·8 (5·4)	26·4 (5·2)	26·5 (5·3)	28·0 (5·4)	28·0 (5·4)	27·0 (5·4)
Nulliparous‡	2385 (52%)	2352 (51%)	2186 (45%)	2249 (46%)	2160 (47%)	2248 (48%)	2282 (47%)	2332 (48%)	1976 (43%)	1985 (43%)	7385 (47%)
Previous caesarean section											
None	3351 (73%)	3361 (73%)	3265 (67%)	3266 (67%)	3182 (69%)	3183 (69%)	3113 (65%)	3119 (64%)	2919 (64%)	2927 (64%)	10562 (67%)
One	1268 (27%)	1267 (27%)	1634 (33%)	1630 (33%)	1457 (31%)	1464 (31%)	1711 (35%)	1732 (36%)	1675 (36%)	1663 (36%)	5167 (33%)
Previous caesarean section incision											
Abdominal transverse	1213 (96%)	1214 (96%)	1591 (97%)	1595 (98%)	1421 (98%)	1426 (97%)	1652 (97%)	1672 (97%)	1612 (96%)	1601 (96%)	4999 (97%)
Uterine transverse	1180 (93%)	1189 (94%)	1443 (88%)	1430 (88%)	1273 (87%)	1288 (88%)	1560 (91%)	1577 (91%)	1585 (95%)	1584 (95%)	4703 (91%)
Uterine unknown	83 (7%)	75 (6%)	185 (11%)	192 (12%)	178 (12%)	171 (12%)	146 (9%)	148 (9%)	86 (5%)	74 (4%)	446 (9%)
Operation and delivery details											
Caesarean section undertaken											
Before start of labour	2227 (48%)	2238 (48%)	2848 (58%)	2846 (58%)	2543 (55%)	2570 (55%)	2677 (55%)	2694 (56%)	2797 (61%)	2789 (61%)	8743 (56%)
After start of labour	2392 (52%)	2390 (52%)	2051 (42%)	2050 (42%)	2096 (45%)	2077 (45%)	2147 (45%)	2157 (44%)	1797 (39%)	1801 (39%)	6986 (44%)
Main indication for caesarean section											
Fetal compromise	1167 (25%)	1160 (25%)	966 (20%)	988 (20%)	1033 (22%)	1053 (23%)	1099 (23%)	1110 (23%)	872 (19%)	833 (18%)	3427 (22%)
Failure to progress	988 (21%)	981 (21%)	995 (20%)	944 (19%)	1096 (24%)	1074 (23%)	1089 (23%)	1082 (22%)	1041 (23%)	1042 (23%)	3444 (22%)
Obstetric complications	1572 (34%)	1573 (34%)	1614 (33%)	1662 (34%)	1653 (36%)	1647 (35%)	1460 (30%)	1497 (31%)	1431 (31%)	1470 (32%)	5193 (33%)
Maternal request	201 (4%)	178 (4%)	241 (5%)	201 (4%)	98 (2%)	103 (2%)	265 (6%)	273 (6%)	302 (7%)	310 (7%)	724 (5%)
Previous caesarean section	306 (7%)	331 (7%)	477 (10%)	479 (10%)	250 (5%)	259 (6%)	546 (11%)	517 (11%)	290 (6%)	286 (6%)	1247 (8%)
Other	385 (8%)	405 (8%)	606 (12%)	622 (13%)	509 (11%)	511 (11%)	365 (8%)	372 (8%)	658 (14%)	649 (14%)	1694 (11%)

Data are number (%) or mean (SD), unless otherwise stated. Missing data are <1% unless otherwise presented. Some percentages do not total 100 because of rounding. Excludes women randomised in error, women who withdrew consent, data not received, and vaginal deliveries (n=206 [1%]). Additional baseline characteristics are detailed in the appendix. N/A=not applicable. PG-910=polyglactin-910. *Intervention pairs not assigned in these regions. †Some sites within these regions switched intervention pairs. ‡Women with no previous births. A previous birth is defined as a live or stillbirth of estimated gestational age >24 weeks (or >28 weeks depending on country-specific definitions), regardless of previous mode of delivery or multiple pregnancy (multiple pregnancy counts as one birth).

Table 1: **Demographics and key baseline characteristics**

Statistical analysis

A sample size of 15 000 women was needed, with at least 9000 women in each intervention pair, to have at least 80% power to detect a 15% relative risk reduction in the primary outcome from a baseline incidence of 15% (estimated from a pilot study of 855 consecutive women who were to undergo a caesarean section [Brocklehurst P, unpublished]), assuming 15% loss to follow-up.

A detailed statistical analysis plan was developed and approved by the trial steering committee (appendix). For the analysis of maternal outcomes, women were analysed in the groups into which they were allocated; for example, comparing women allocated to blunt abdominal entry with those allocated to sharp abdominal entry, regardless of what interventions they actually received. For the analysis of neonatal outcomes, neonates were analysed according to the groups allocated to the women. Neonatal outcomes were only analysed in the intervention pair blunt versus sharp abdominal entry because these were the only interventions that could have an effect on neonatal outcomes. In the analysis of neonatal outcomes, neonates from multiple births were treated as independent, but the effect of adjusting for potential clustering was also assessed.[14]

The focus of the primary analysis was the main effects of the five intervention pairs analysed separately. Pairwise interactions were planned if the analyses showed any statistically significant main effects for the primary outcome only. Subgroup analyses according to caesarean

	Abdominal entry			Repair of uterus			Closure of uterus			Closure of peritoneum			Uterine repair sutures			Total (n=15729)
	Blunt (n=4619)	Sharp (n=4628)	RR (CI)	Exterior (n=4899)	Intra-abdominal (n=4896)	RR (CI)	Single (n=4639)	Double (n=4647)	RR (CI)	Closure (n=4824)	Non-closure (n=4851)	RR (CI)	Catgut (n=4594)	PG-910 (n=4590)	RR (CI)	
Primary outcome*																
Number (%)	439 (10%)	428 (9%)	1·03 (0·91–1·17)	434 (9%)	454 (9%)	0·96 (0·84–1·08)	479 (10%)	499 (11%)	0·96 (0·85–1·08)	496 (10%)	469 (10%)	1·06 (0·94–1·20)	334 (7%)	369 (8%)	0·90 (0·78–1·04)	1467 (9%)
Death																
Number (%)	6 (0·1%)	8 (0·2%)	0·75 (0·19–3·02)	1 (<0·1%)	4 (0·1%)	0·25 (0·01–4·45)	8 (0·2%)	5 (0·1%)	1·60 (0·37–6·95)	2 (<0·1%)	3 (0·1%)	0·67 (0·06–7·04)	5 (0·1%)	6 (0·1%)	0·83 (0·18–3·96)	16 (0·1%)
Antibiotics for febrile morbidity†																
Number (%)	91 (2%)	81 (2%)	1·13 (0·76–1·66)	52 (1%)	49 (1%)	1·06 (0·64–1·77)	47 (1%)	47 (1%)	1·00 (0·59–1·70)	100 (2%)	84 (2%)	1·20 (0·82–1·75)	52 (1%)	69 (2%)	0·75 (0·47–1·20)	224 (1%)
Antibiotics for endometritis																
Number (%)	46 (1%)	36 (1%)	1·28 (0·72–2·27)	43 (1%)	43 (1%)	1·00 (0·57–1·74)	38 (1%)	34 (1%)	1·12 (0·61–2·05)	53 (1%)	56 (1%)	0·95 (0·58–1·56)	43 (1%)	52 (1%)	0·83 (0·49–1·40)	148 (1%)
Antibiotics for wound infection																
Number (%)	313 (7%)	276 (6%)	1·14 (0·93–1·40)	302 (6%)	324 (7%)	0·93 (0·76–1·14)	353 (8%)	379 (8%)	0·93 (0·78–1·12)	330 (7%)	310 (6%)	1·07 (0·88–1·30)	218 (5%)	204 (5%)	1·07 (0·84–1·36)	1003 (6%)
Antibiotics for peritonitis																
Number (%)	1 (<0·1%)	3 (0·1%)	0·33 (0·02–6·54)	1 (<0·1%)	0 (0%)	..	0 (0%)	1 (<0·1%)	..	4 (0·1%)	1 (<0·1%)	4·02 (0·23–71·6)	1 (<0·1%)	3 (0·1%)	0·33 (0·02–6·52)	5 (<0·1%)
Any further operative procedures‡																
Number (%)	95 (2%)	91 (2%)	1·05 (0·72–1·52)	82 (2%)	79 (2%)	1·04 (0·69–1·55)	74 (2%)	87 (2%)	0·85 (0·57–1·28)	80 (2%)	67 (1%)	1·20 (0·79–1·83)	33 (1%)	53 (1%)	0·62 (0·35–1·10)	247 (2%)
Blood transfusion§																
Number (%)	40 (1·0%)	56 (1·2%)	0·72 (0·42–1·22)	75 (1·5%)	72 (1·5%)	1·04 (0·68–1·59)	76 (1·6%)	79 (1·7%)	0·96 (0·64–1·45)	63 (1·3%)	62 (1·3%)	1·02 (0·65–1·62)	32 (0·7%)	60 (1·3%)	0·53 (0·30–0·93)	205 (1·3%)

Missing data are <1% unless otherwise presented. Excludes women randomised in error, women who withdrew consent, data not received, and vaginal deliveries (n=206 [1%]). CI values are 95% for primary outcome and 99% for all others. PG-910=polyglactin-910. RR=risk ratio. *A woman may have more than one component but is included only once in the primary outcome. Primary outcome defined as death or maternal infectious morbidity or further operative procedures or blood transfusion (>1 unit of whole blood and packed cells only). †Maternal infectious morbidity defined as one or more of the following: antibiotic use for maternal febrile morbidity during post-partum stay (fever on at least two occasions); antibiotic use for endometritis, wound infection, or peritonitis up to 6 weeks post partum. ‡Includes any operative procedures on caesarean wound, curettage, laparotomy, artery ligation, brace suture, and hysterectomy. §>1 unit of whole blood and packed cells only.

Table 2: **Primary outcome and its components**

	Abdominal entry			Repair of uterus			Closure of uterus			Closure of peritoneum			Uterine repair sutures			Total (n=15729)
	Blunt (n=4619)	Sharp (n=4628)	RR or MD (99%CI)	Exterior (n=4899)	Intra-abdominal (n=4896)	RR or MD (99% CI)	Single (n=4639)	Double (n=4647)	RR or MD (99% CI)	Closure (n=4824)	Non-closure (n=4851)	RR or MD (99% CI)	Catgut (n=4594)	PG-910 (n=4590)	RR or MD (99% CI)	
Further operative procedures on wound*																
Number (%)	60 (1%)	38 (1%)	RR 1·58 (0·93 to 2·69)	35 (1%)	36 (1%)	RR 0·97 (0·53 to 1·79)	30 (1%)	38 (1%)	RR 0·79 (0·42 to 1·48)	48 (1%)	44 (1%)	RR 1·10 (0·64 to 1·87)	20 (<1%)	29 (1%)	RR 0·69 (0·33 to 1·45)	126 (1%)
Additional analgesia given 24–48 h after caesarean section																
Number (%)	316 (7%)	311 (7%)	RR 1·02 (0·83 to 1·24)	204 (4%)	188 (4%)	RR 1·08 (0·84 to 1·40)	203 (4%)	185 (4%)	RR 1·10 (0·85 to 1·42)	250 (5%)	236 (5%)	RR 1·06 (0·85 to 1·34)	159 (4%)	171 (4%)	RR 0·93 (0·70 to 1·23)	741 (5%)
Pain at 6 weeks' follow-up																
Continual (number [%])	62 (1%)	53 (1%)	RR 1·17 (0·73 to 1·89)	97 (2%)	99 (2%)	RR 0·98 (0·68 to 1·41)	85 (2%)	83 (2%)	RR 1·03 (0·69 to 1·53)	103 (2%)	108 (2%)	RR 0·96 (0·67 to 1·36)	81 (2%)	63 (1%)	..	278 (2%)
Data missing (number [%])	109 (2%)	107 (2%)	..	86 (2%)	93 (2%)	..	98 (2%)	81 (2%)	..	103 (2%)	107 (2%)	..	43 (1%)	40 (1%)	RR 1·29 (0·84 to 1·97)	289 (2%)
Interventions used for post-partum haemorrhage†																
Number (%)	48 (1%)	58 (1%)	RR 0·83 (0·50 to 1·37)	76 (2%)	76 (2%)	RR 1·00 (0·66 to 1·51)	49 (1%)	52 (1%)	RR 0·94 (0·57 to 1·57)	71 (2%)	71 (2%)	RR 1·01 (0·65 to 1·54)	15 (<1%)	30 (1%)	RR 0·50 (0·22 to 1·13)	182 (1%)
Any other severe maternal morbidity‡																
Number (%)	11 (<1%)	8 (<1%)	RR 1·38 (0·42 to 4·56)	8 (<1%)	12 (<1%)	RR 0·67 (0·21 to 2·16)	12 (<1%)	16 (<1%)	RR 0·75 (0·28 to 2·01)	24 (<1%)	12 (<1%)	RR 2·01 (0·81 to 4·99)	18 (<1%)	20 (<1%)	RR 0·90 (0·39 to 2·07)	47 (<1%)
Duration of operation (min from incision to closure)																
Median (IQR)	40 (30–48)	40 (30–50)	MD 0 (0 to 0)	40 (30–50)	40 (30–50)	MD 0 (0 to 0)	40 (30–47)	40 (30–50)	MD 0 (0 to 0)	40 (30–50)	40 (30–50)	MD 0 (0 to 0)	35 (30–45)	35 (30–45)	MD 0 (0 to 0)	40 (30–46)
Duration of hospital stay after caesarean section (days)§																
Median (IQR)	4 (4–6)	4 (4–6)	MD 0 (0 to 0)	4 (4–5)	4 (3–5)	MD 0 (0 to 0)	4 (4–6)	4 (4–6)	MD 0 (0 to 0)	4 (4–5)	4 (4–5)	MD 0 (0 to 0)	4 (4–5)	4 (4–5)	MD 0 (0 to 0)	4 (4–5)
ICU stay																
Women admitted to ICU¶																
Number (%)	19 (<1%)	15 (<1%)	..	30 (1%)	14 (<1%)	..	23 (1%)	17 (<1%)	..	18 (<1%)	28 (1%)	..	11 (<1%)	20 (<1%)	..	65 (<1%)
Duration of stay in ICU after caesarean section (days)¶																
Median (IQR)	3·5 (2–8)	2 (2–4)	MD 1 (0 to 3)	3 (2–4)	2·5 (2–4)	MD 0 (–1 to 1)	3 (2–4)	3 (2–4)	MD 0 (–1 to 1)	2 (2–4)	3 (2–4)	MD 0 (–1 to 1)	3 (3–4)	2 (2–5)	MD 1 (0 to 2)	3 (2–4)
Readmission to hospital within 6 weeks of caesarean section																
Number readmitted (%)	43 (1%)	36 (1%)	RR 1·20 (0·67 to 2·14)	37 (1%)	43 (1%)	RR 0·86 (0·48 to 1·53)	37 (1%)	33 (1%)	RR 1·13 (0·61 to 2·08)	47 (1%)	47 (1%)	RR 1·00 (0·59 to 1·71)	27 (1%)	25 (1%)	RR 1·08 (0·53 to 2·20)	125 (1%)
Data missing (%)	109 (2%)	107 (2%)	..	86 (2%)	93 (2%)	..	98 (2%)	81 (2%)	..	103 (2%)	107 (2%)	..	43 (1%)	40 (1%)	..	289 (2%)
Duration of stay for readmissions (days)‖																
Median (IQR)	7 (4–11)	5 (4–9)	MD 1 (–1 to 3)	6 (3–9)	7 (4–10)	MD –1 (–3 to 1)	6 (3–9)	6 (4–9)	MD –1 (–3 to 1)	6 (4–9)	5 (3–9)	MD –1 (–1 to 2)	6 (4–10)	5 (3–6)	MD 1 (0 to 4)	6 (4–9)

Missing data are <1% unless otherwise presented. Excludes women randomised in error, women who withdrew consent, data not received, and vaginal deliveries (n=206 [1%]). ICU=intensive care unit. MD=median difference. PG-910=polyglactin-910. RR=risk ratio. *Includes any procedures on the wound because of infection, dehiscence, or haematoma. †Includes additional uterotonics, balloon tamponade, brace suture, artery ligation, and hysterectomy. ‡Includes at least one of the following: antibiotics for peritonitis (n=5), antibiotics for sepsis (n=8), antibiotics for infection (n=3), post-partum haemorrhage (n=24), deep-vein thrombosis (n=7), pulmonary embolism (n=0), or septic shock (n=2). §Women in some centres were kept in for rest or to wait for the baby to be discharged. ¶In some sites, women were admitted to the ICU routinely; these women have been excluded from this analysis. ‖If admission date and discharge date were the same, the length of stay was regarded as 1 day. Six women had two re-admissions; their lengths of stay have been summed.

Table 3: **Secondary outcomes**

section in or not in labour, multiple or singleton birth, number of previous caesarean sections, type of anaesthetic, experience of surgeon, and country were prespecified in the protocol.[10]

The risk ratio for every outcome was calculated for each intervention pair. For the primary outcome, 95% CIs are presented for each comparison. For secondary outcomes, 99% CIs are presented to take account of the number of comparisons. Subgroup analyses are presented as forest plots along with results of Mantel–Haenszel χ^2 tests for interaction. A p value of less than 0·05 was deemed statistically significant for

	Abdominal entry		Risk ratio (99% CI)	OR (99% CI)*	Accounting for multiple births, OR (99% CI)†	Total neonates (n=9638)
	Blunt	Sharp				
Stillbirth‡	54/4801 (1·1%)	43/4837 (0·9%)	1·27 (0·75–2·14%)	1·27 (0·75–2·15%)	1·27 (0·74–2·18%)	97/9638 (1·0%)
Apgar score ≤3 at 5 min	19/4737 (0·4%)	17/4792 (0·4%)	1·13 (0·48–2·67%)	1·13 (0·48–2·68%)	1·13 (0·48–2·68%)	36/9541 (0·4%)
Laceration of baby at time of caesarean section	3/4747 (0·1%)	2/4794 (<0·1%)	1·51 (0·14–15·9%)	1·26 (0·22–7·10%)	1·26 (0·22–7·10%)	5/9541 (0·1%)
Death of baby by 6 weeks of age§	104/4638 (2·2%)	88/4685 (1·9%)	1·19 (0·83–1·73%)	1·20 (0·82–1·75%)	1·20 (0·82–1·75%)	192/9323 (2·1%)
Stillbirth or death of baby by 6 weeks of age	158/4692 (3·4%)	131/4728 (2·8%)	1·22 (0·90–1·64%)	1·22 (0·90–1·67%)	1·22 (0·90–1·67%)	289/9323 (3·1%)
Data missing at 6 weeks	109/4692 (2·4%)	109/4728 (2·3%)	..	..	..	218/9323 (2·3%)

Data are number (%) unless otherwise stated. Excludes babies born to women randomised in error, women who withdrew consent, data not received, and vaginal deliveries (n=206 [1%]). OR=odds ratio. *ORs are presented because the adjustment to account for multiple births cannot be calculated for risk ratios. †17 stillbirths were from a multiple pregnancy (16 twins [ten blunt, six sharp] and one triplet [blunt]). Twins from two women (one blunt, one sharp) were recorded as both sets stillborn. ‡Because of the correlation of outcomes within babies from multiple births, standard errors were estimated using a clustered sandwich estimator. §Excludes stillbirths.

Table 4: **Neonatal outcomes**

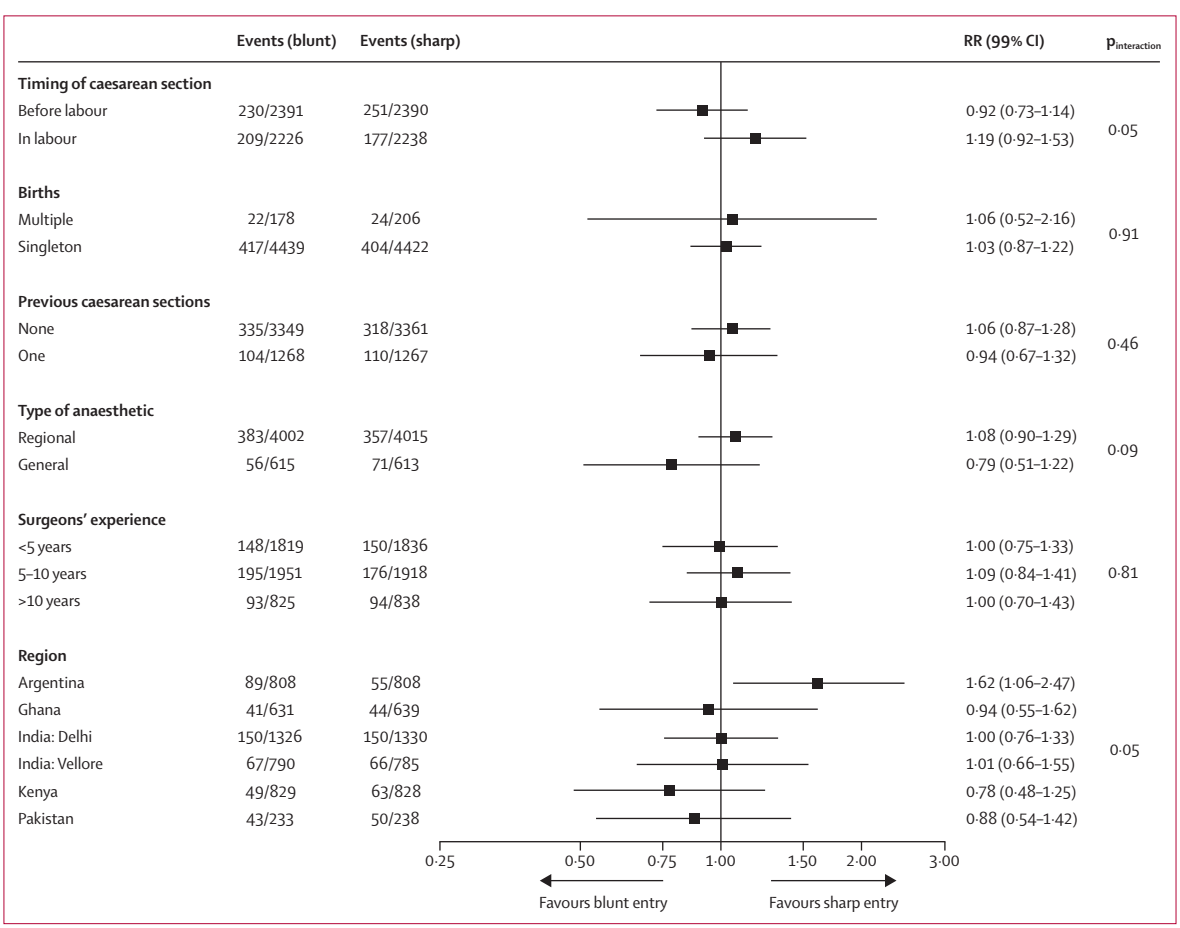

Figure 2: **Abdominal entry subgroup analyses**
RR=risk ratio.

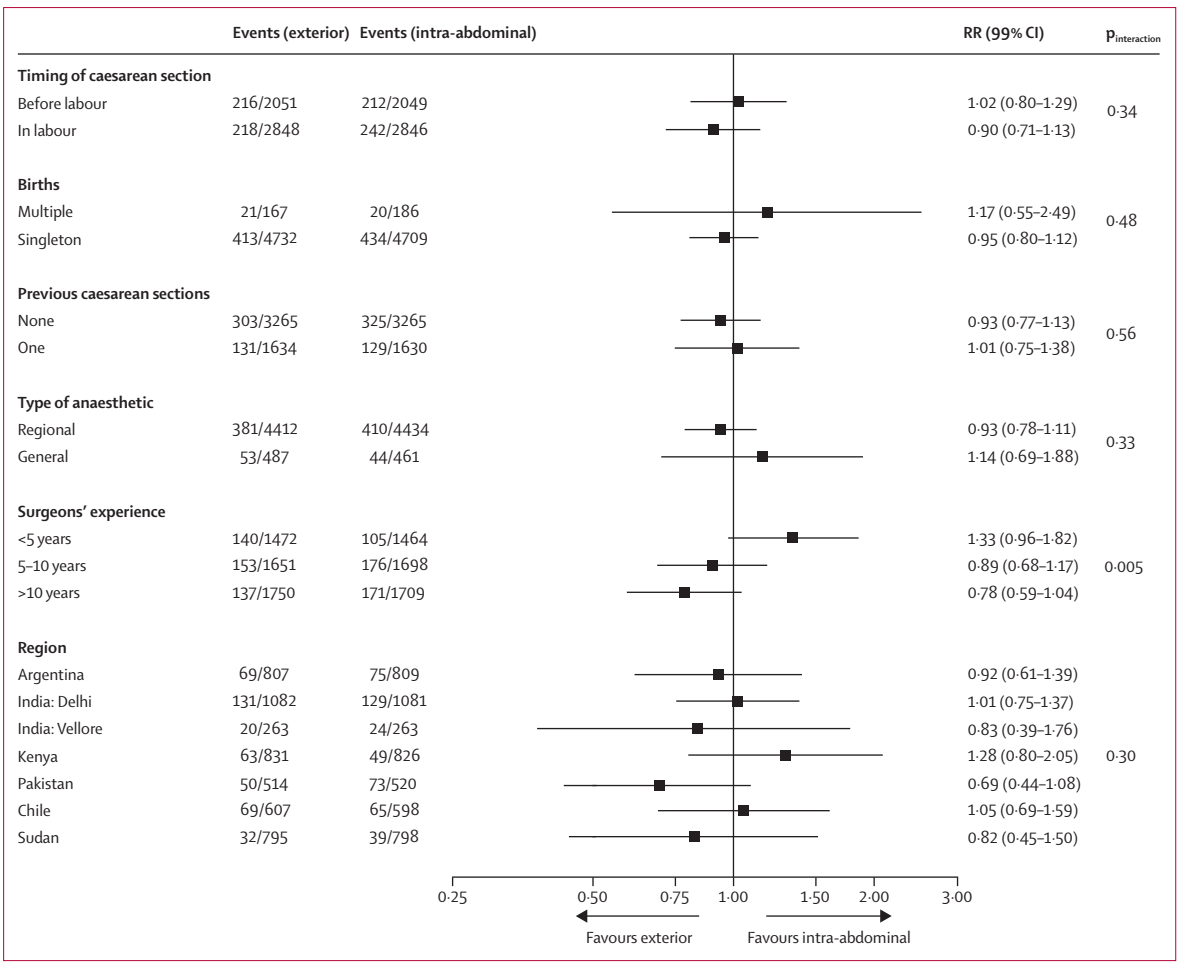

Figure 3: **Repair of uterus subgroup analyses**
RR=risk ratio.

the primary outcome and less than 0·01 for all secondary outcomes and subgroup analyses.

An adjusted analysis was prespecified for the primary outcome to investigate the effect of minimisation factors: in-labour versus not in-labour caesarean section and number of previous caesarean sections. Several sensitivity analyses of the primary outcome were also prespecified in the analysis plan. All analyses were undertaken using Stata/SE (version 11.2).

The CORONIS trial is registered with Current Controlled Trials, ISRCTN31089967.

Role of the funding source

The trial was funded by the UK Medical Research Council. WHO contributed to the cost of the initial protocol development meeting and site set-up costs in the first year. The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between May 20, 2007, and Dec 31, 2010, 15 935 women were recruited at 19 sites in Argentina, Chile, Ghana, India, Kenya, Pakistan, and Sudan (appendix). The appendix describes the characteristics of the participating countries and sites.

After the second meeting of the data monitoring committee on July 22, 2009, when data from 7972 women were reviewed, the data monitoring committee informed the trial steering committee that, instead of an expected primary outcome incidence of around 15%, the incidence was 4·7%. The investigators assessed this discrepancy, masked to treatment allocation, and found that the overall incidence of the primary outcome varied substantially between sites and consequently an extensive validation exercise was undertaken between Aug 13, 2009, and March 3, 2011 (appendix). Validation was done by independent observers and included reviewing source records and interviewing participating women. This exercise resulted in an overall primary outcome incidence of 9·3%. After considering many scenarios,

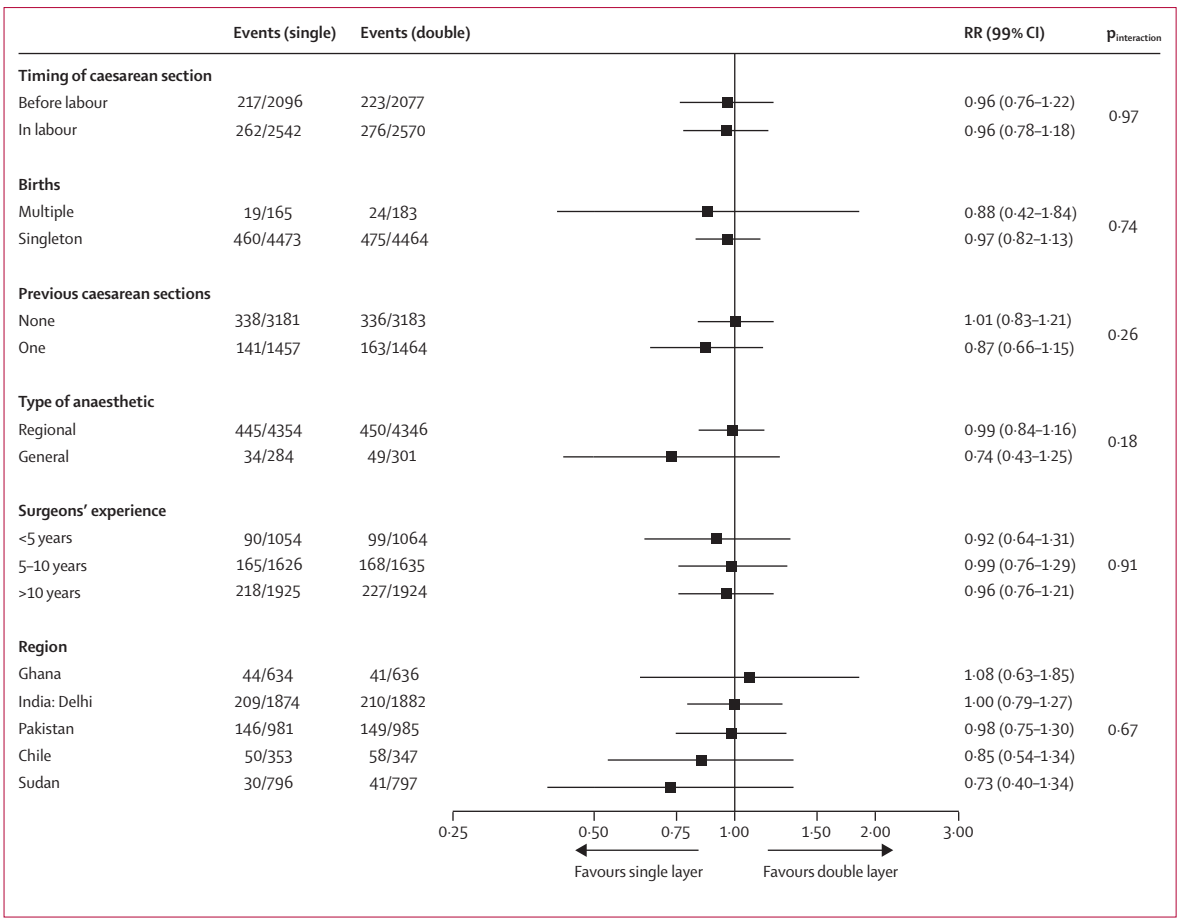

***Figure 4*: Closure of uterus subgroup analyses**
RR=risk ratio.

the trial steering committee recommended continuation of recruitment until the end of 2010 (4 months later than planned), when about 16 000 women would have been enrolled. This would still give 80% power to detect a relative risk reduction of 0·825 if the overall primary outcome incidence was at least 9·0%. To ensure at least 9000 women were included in each intervention pair, close monitoring of recruitment was done weekly by the international coordinating centre. This led to three sites switching intervention pairs in 2010 (appendix).

In accordance with the prespecified analysis plan, 206 (1·3%) of the 15 935 women were excluded from the analysis, of whom 143 (0·9%) had a vaginal delivery (figure 1). These women were evenly distributed among the intervention pairs and were excluded from the analysis because they were not at risk of wound-related problems. Trial entry and discharge data were available for 15 913 (99·9%) of 15 935 women and 6-week data for 15 611 (98·0%) women (figure 1). Compliance with all the allocated interventions was high, 87% overall (figure 1). The difference in compliance between single and double layer closure of the uterus (83% *vs* 98%, respectively) was mostly explained by clinical decisions during surgery.

Baseline characteristics were similar within and across intervention pairs (table 1; appendix). The mean age was 27·0 years (SD 5·4), almost half were nulliparous, about a third were undergoing a second caesarean section, just over half underwent caesarean section before the start of labour, and 15% were less than 37 weeks gestation. 99% of women received prophylactic antibiotics and prophylactic uterotonics and 7% received prophylactic heparin (appendix).

The incidence of the primary outcome was 9·3% overall and varied from 7·3% to 10·7% by intervention pair (table 2). There were no statistically significant differences within any of the intervention pairs for the primary outcome (table 2). As prespecified in the analysis plan, no tests for interaction were done because there was no evidence of main effects for the primary outcome. There was only one statistically significant difference in one component of the primary outcome, which was for the intervention pair chromic catgut versus polyglactin-910 for uterine repair and the outcome of

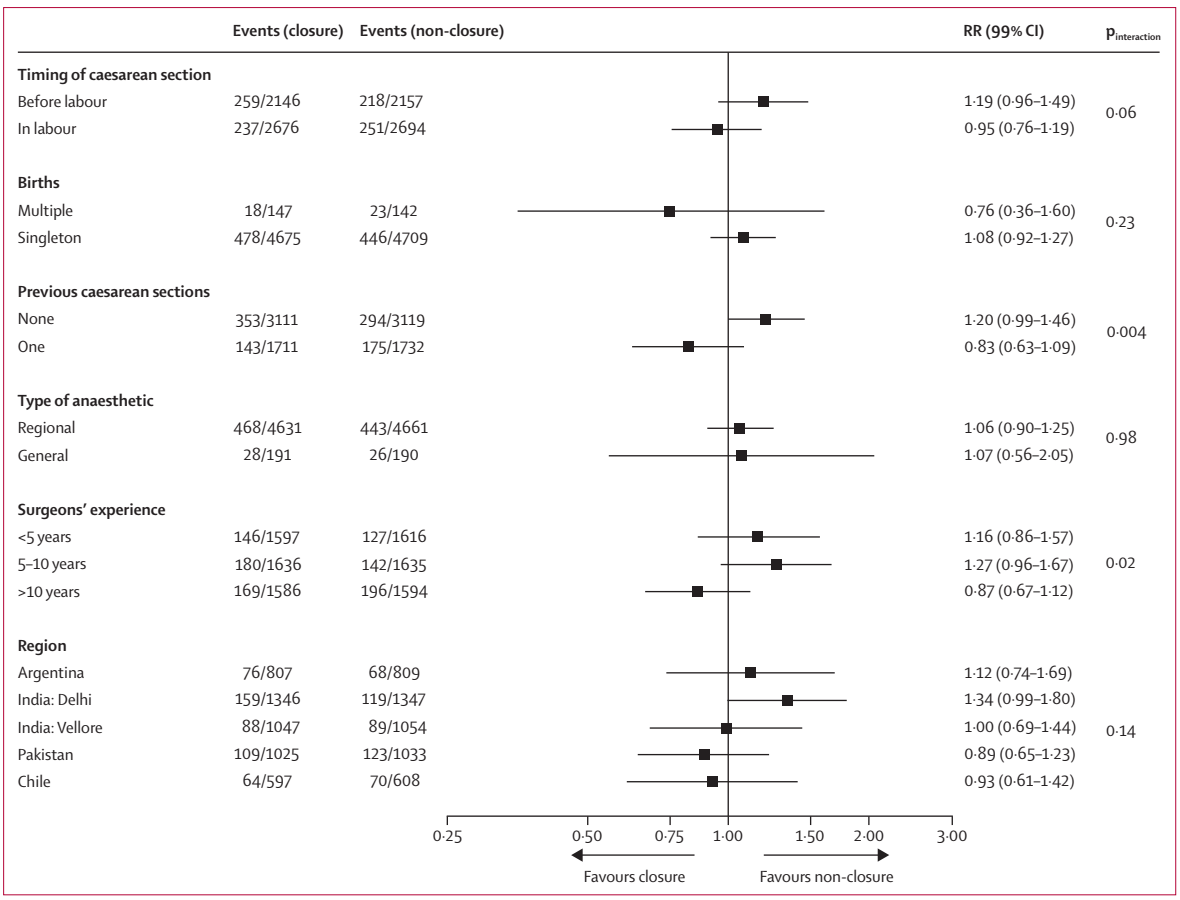

***Figure 5*: Closure of peritoneum subgroup analyses**
RR=risk ratio.

blood transfusion greater than 1 unit (risk ratio 0·53, 99% CI 0·30–0·93; table 2). On further assessment, this result was robust when adjusted for in-labour versus not in-labour caesarean section and suture material used as standard in each site (data not shown).

There was no evidence of a difference within intervention pairs for any of the other secondary outcomes (table 3). For the intervention of blunt versus sharp abdominal entry, where the potential difference in the time taken to enter the abdominal cavity might lead to worse neonatal outcomes, there was no evidence of a difference in the risk of stillbirth or low Apgar score (table 4). These findings did not change after allowing for clustering for multiple births (table 4).

There was limited consistent and corroborated evidence of a differential treatment effect between the subgroups in the effect of the interventions on the primary outcome (figures 2–6). We cannot explain the differences for Argentina in the comparison of blunt versus sharp abdominal entry and for Chile in the comparison of chromic catgut versus polyglactin-910 and assume that they are spurious associations because of the large number of comparisons made. Not all the prespecified subgroup analyses were undertaken because the size of some of the subgroups was too small. HIV infection was present in only 2% of women and intrapartum fever in only 2% (table 1). The adjusted analyses (appendix) and the sensitivity analyses (table 5) resulted in no effect on the findings for the primary outcome.

144 serious adverse events were reported, of which 26 were possibly related to the intervention (appendix). Most of the reported serious adverse events were known complications of surgery or complications of the reasons for the caesarean section; for example, obstructed labour is a risk factor for post-partum haemorrhage. The intra-abdominal bleeding and uterine atony that occurred might have been because of the surgical techniques being used. For example, uterine atony might be caused or exacerbated by the method of closure of the uterine incision (exteriorisation or intra-abdominal repair), single-layer or double-layer closure of the uterus, or the use of chromic catgut or polyglactin-910 sutures. The appendix shows the distribution of all the serious adverse events and those thought to be possibly related to the allocated intervention, by randomised intervention pairs. There were no statistically significant differences in the

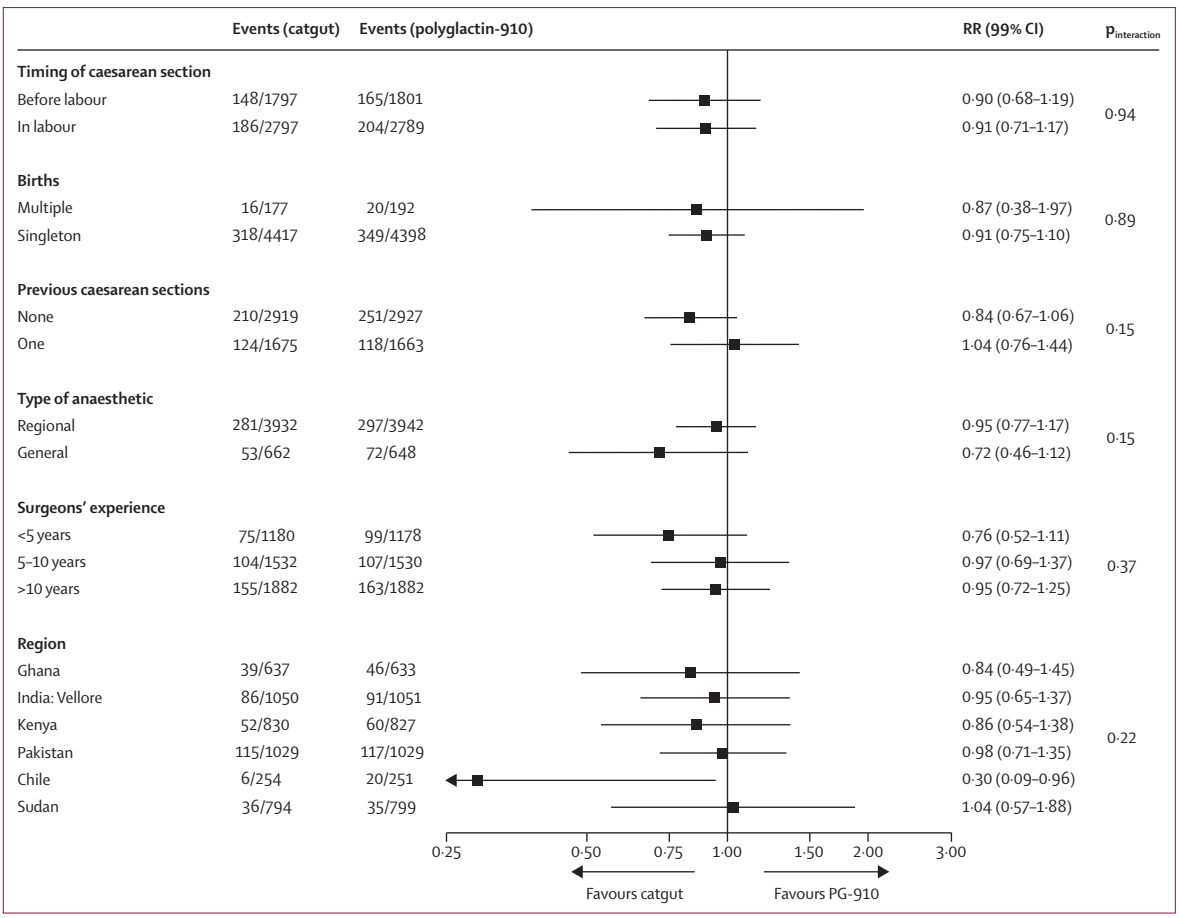

***Figure 6*: Uterine repair subgroup analyses**
RR=risk ratio.

incidence of serious adverse events. The serious adverse events that were possibly related to the allocated intervention were 18 haemorrhage (uterine atony or intra-abdominal bleeding) and six serious infections. The serious adverse events included 16 deaths, of which one was possibly related to the intervention. This was a death due to septicaemia secondary to peritonitis after presumed intestinal perforation. Four deaths were due to hypertensive disease; two to aspiration pneumonitis; two to obstetric haemorrhage; two to thromboembolic disease; one each to renal failure, stroke, brain tumour, and H1N1 variant influenza; and one unknown cause in a woman with hepatitis C.

Discussion

CORONIS was a large randomised trial of caesarean section surgical techniques and provides important evidence to guide clinical practice (panel). There were no statistically significant differences within any of the intervention pairs for the primary outcome. However, there was a statistically significant difference in one component of the primary outcome: chromic catgut versus polyglactin-910 for uterine repair.

This study has limitations. We were unable, for practical reasons, to assess all aspects of the caesarean section operation that could affect maternal morbidity. Our choice was based on a consensus meeting of investigators who prioritised aspects of the operation as being those for which there was little evidence to support either approach, or for which there was the potential for important short-term or long-term implications, such as single-layer versus double-layer uterine closure and uterine rupture during a subsequent pregnancy. Compliance was generally very good; however, for mostly clinical reasons, surgeons could not always comply with the allocated intervention. This might weaken the differences between randomised groups, but represents the pragmatic nature of the trial, thus the findings are generalisable. For sites where chromic catgut versus polyglactin-910 for uterine repair was one of the assigned intervention pairs, surgeons did not always follow the trial protocol and used the suture material allocated for closing the uterine incision to close other layers (appendix). However, adjusting for this non-compliance made no difference to the risk ratio for the primary outcome (appendix).

	Abdominal entry			Repair of uterus			Closure of uterus			Closure of peritoneum			Uterine repair sutures			Total (n=15729)
	Blunt (n=4619)	Sharp (n=4628)	RR (95% CI)	Exterior (n=4899)	Intra-abdominal (n=4896)	RR (95% CI)	Single (n=4639)	Double (n=4647)	RR (95% CI)	Closure (n=4824)	Non-closure (n=4851)	RR (95% CI)	Catgut (n=4594)	PG-910 (n=4590)	RR (95% CI)	
Primary analysis																
Primary outcome (%)	439 (10%)	428 (9%)	1·03 (0·91–1·17)	434 (9%)	454 (9%)	0·96 (0·84–1·08)	479 (10%)	499 (11%)	0·96 (0·85–1·08)	496 (10%)	469 (10%)	1·06 (0·94–1·20)	334 (7%)	369 (8%)	0·90 (0·78–1·04)	1467 (9%)
Excluding missing 6-week primary outcome data																
Primary outcome (%)	439/4520 (10%)	428/4531 (10%)	1·03 (0·91–1·17)	434/4818 (9%)	454/4808 (9%)	0·95 (0·84–1·08)	479/4550 (11%)	499/4575 (11%)	0·97 (0·86–1·09)	496/4726 (11%)	469/4747 (10%)	1·06 (0·94–1·20)	334/4556 (7%)	369/4555 (8%)	0·90 (0·78–1·04)	1467/15462* (10%)
Excluding women assessed after 12 weeks																
Primary outcome (%)	392/4227 (9%)	380/4224 (9%)	1·03 (0·90–1·18)	380/4388 (9%)	404/4354 (9%)	0·93 (0·82–1·07)	443/4270 (10%)	457/4280 (11%)	0·97 (0·86–1·10)	444/4391 (10%)	430/4388 (10%)	1·03 (0·91–1·17)	316/4364 (7%)	353/4371 (8%)	0·90 (0·77–1·04)	1333/14419 (9%)
Subgroup analysis by time to 6-week assessment																
Assessment done at ≤6 weeks																
Primary outcome (%)	42/446 (9%)	37/393 (9%)	1·00 (0·66–1·52)	38/441 (9%)	53/418 (13%)	0·68 (0·46–1·01)	50/422 (12%)	42/419 (10%)	1·18 (0·80–1·74)	33/414 (8%)	51/480 (11%)	0·75 (0·49–1·14)	19/200 (10%)	16/225 (7%)	1·34 (0·71–2·53)	127/1286 (10%)
Assessment done at >6 weeks																
Primary outcome (%)	384/4056 (10%)	380/4115 (9%)	1·03 (0·90–1·17)	388/4359 (9%)	393/4370 (9%)	0·99 (0·87–1·13)	421/4115 (10%)	449/4142 (11%)	0·94 (0·83–1·07)	461/4310 (11%)	416/4266 (10%)	1·10 (0·97–1·24)	308/4335 (7%)	345/4310 (8%)	0·89 (0·77–1·03)	1315/14126 (9%)

The primary outcome of death or maternal infectious morbidity or further operative procedures or blood transfusion (>1 unit of whole blood and packed cells only) was analysed by time to follow-up after delivery. Maternal infectious morbidity defined as one or more of the following: antibiotic use for maternal febrile morbidity during post-partum stay (fever on at least two occasions); antibiotic use for endometritis, wound infection, or peritonitis up to 6 weeks post partum. Includes any operative procedures on caesarean wound, curettage, laparotomy, artery ligation, brace suture, and hysterectomy. Excludes women randomised in error, women who withdrew consent, data not received, and vaginal deliveries (n=206 [1%]). A woman can have more than one component but is included only once in the primary outcome. p values were 0·91 for abdominal entry, 0·08 for repair of uterus, 0·28 for closure of uterus, 0·09 for closure of peritoneum, and 0·22 for uterine repair sutures. RR=risk ratio. PG-910=polyglactin-910. *Number presented in figure 1 does not exclude women randomised in error, women who withdrew consent, data not received, and vaginal deliveries. Primary outcome data are not treated as missing if a primary outcome event is recorded on the post-partum form (ie, before the 6 weeks after delivery form).

***Table 5*: Sensitivity analyses of the primary outcome**

The incidence of the primary outcome was lower than anticipated, as was maternal mortality. This finding is a result of the nature of recruitment of participants to randomised controlled trials who are potentially healthier than the represented patient population. The pilot study (Brocklehurst P, unpublished) assessed outcomes for consecutive caesarean sections taking place in several of the CORONIS participating sites. By introducing a process of enrolment into a trial, women with the greatest risk of an adverse outcome are less likely to be recruited; this includes women who were to undergo a caesarean section in labour but were judged to be unable to provide informed consent. This factor might also explain the low maternal mortality in this sample of women. Because of the lower than expected frequency of the primary outcome, we undertook an extensive validation exercise. Validation revealed that follow-up personnel were sometimes missing important outcomes, such as wound infections. Review of source documents and re-interviewing women (by independent staff) identified several unreported outcomes; extensive additional training was initiated to ensure accurate data capture of these outcomes at the postnatal interview for the remainder of the trial.

Despite these potential limitations and the lower than anticipated incidence of the primary outcome, this trial had sufficient power to identify modest differences in short-term outcomes. The only intervention–outcome combination for which there was statistical evidence of an effect was blood transfusion of greater than 1 unit for the chromic catgut versus polyglactin-910 comparison. When we explored the reasons for the blood transfusion, there was an increase in the number of women having a blood transfusion for post-partum haemorrhage in the polyglactin-910 arm compared with the chromic catgut arm. The number of cases was small (36 *vs* 20), so the findings could have arisen by chance. However, there is no suggestion, as was widely anticipated, that polyglactin-910 was superior to chromic catgut.

CORONIS provides evidence, on the basis of short-term outcomes, that clinicians can remain free to use whichever surgical technique they prefer. Although undertaken in low-income and middle-income countries, these findings are probably generalisable to other settings. The complications of caesarean section are the same in all settings, albeit with different frequencies. The absence of evidence of a difference among any of the

Panel: Research in context

Systematic review

There are systematic reviews (including Cochrane reviews) for all the intervention pairs included in the CORONIS trial. For the comparison of sharp versus blunt abdominal entry at caesarean section, a Cochrane review was published in 2008.[6] This review included 11 randomised controlled trials (with a total of 1740 women) that compared different approaches to abdominal entry, which are comparable to the comparison blunt versus sharp abdominal entry in the CORONIS trial (described as Joel-Cohen based versus Pfannenstiel). The findings from this review suggested that the blunt approach to abdominal entry led to less blood loss, a shorter duration of surgery (including a shorter duration from skin incision to delivery of the baby), and less postoperative fever and pain. More serious complications, including blood transfusion of the mother, were too few to analyse. The main challenge of interpreting these eponymous techniques is that, if done as intended, they include prescribed techniques for uterine incision closure and abdominal wound closure,[15] making interpretation of outcomes in relation solely to the method of abdominal entry difficult.

Exteriorisation of the uterus for repair versus intra-abdominal repair was the topic of a systematic review published in 2009, which included 11 trials with 3183 women in total.[16] The investigators found no evidence that one approach was superior to the other for several outcomes such as intraoperative or postoperative complications including endometritis, pain, and nausea and vomiting. There were no differences in the duration of the operation or in the duration of hospital stay. Since this study was published, a trial of 4925 women has been published.[17] This trial found an excess of uterine atony in the exteriorisation group (9·1% *vs* 3·8% in the intra-abdominal repair group), although there was no statistically significant difference in the incidence of blood transfusion. The intra-abdominal repair group had a shorter operating time and less postoperative pain and a lower incidence of wound infection (4·6% *vs* 11·5% in the exteriorisation group). This finding is in contrast to the CORONIS trial, which found no differences in these outcomes in 9795 women.

A Cochrane review of closure versus non-closure of the peritoneum (visceral or parietal or both) was last updated in 2008.[18] It incorporated 14 trials including 2908 women and found that non-closure reduced operating time, postoperative fever, use of pain relief, and hospital stay. Since this review was published, a further five trials have been published.[9,19–22] Four of these trials are moderate in size (between 80 and 340 women per trial),[19–22] whereas the CAESAR trial included 2995 women in this comparison.[9] Some of the smaller trials found similar findings to the Cochrane review, with shorter operating times and less postoperative febrile morbidity in the non-closure group. However, the CAESAR trial found no differences in any outcomes of postoperative morbidity but did suggest that non-closure of the pelvic peritoneum shortened the duration of the operation by a mean of 2·3 min. In CORONIS, by contrast, we found no difference in duration of surgery.

A Cochrane systematic review of surgical techniques involving the uterus at the time of caesarean section included trials of single-layer versus double-layer closure of the uterine incision (ten trials with 2531 women in total).[23] Two further trials that compared single-layer and double-layer uterine closure published since the Cochrane review was last updated have been identified, involving 208 women in one[24] and 2979 women in the other.[9] None of the existing studies suggest major differences in short-term outcomes between single-layer and double-layer uterine closure. There was a suggestion that single-layer closure might result in a decreased estimated blood loss at the time of caesarean section and shorter duration of the operative procedure, but the addition of the data from the large CAESAR trial suggests no differences in any of these outcomes. CORONIS, when added to the existing evidence, confirms this absence of short-term differences in maternal morbidity.

There are no published or ongoing trials comparing different suture materials for this element of the caesarean section operation.

Interpretation

The published trials of caesarean section surgical techniques are mostly small and inconclusive, and pooled estimates show, for some of the outcomes, substantial heterogeneity. With respect to the five pairs of interventions included in CORONIS, all the available evidence suggests that blunt abdominal entry is unlikely to offer any short-term benefits for postoperative morbidity; non-closure of the peritoneum might decrease the duration of the operation by a small amount, but this does not translate into improvements in morbidity outcomes; single-layer closure of the uterine incision does not improve short-term morbidity outcomes; and the use of chromic catgut might have moderate advantages over the use of polyglactin-910. With respect to whether intra-abdominal repair of the uterine incision improves outcome, the available evidence is still uncertain. We found no evidence of improved outcomes for women in this comparison pair, in contrast to the findings by Doganay and colleagues.[17]

The findings of CORONIS, when combined with the existing evidence, suggest that clinicians are free to carry on with their existing practices, at least with respect to their effect on short-term postoperative morbidity. However, particularly for interventions that involve closure of the uterine incision (single-layer versus double-layer closure or use of different suture materials) as well as closure or non-closure of the peritoneum, longer-term outcomes are needed to enable clinicians to make fully informed decisions about what surgical approaches to take.

tested intervention pairs in these settings is therefore likely to also apply to caesarean sections undertaken in high-income countries.

The potential effects of these surgical techniques on longer-term outcomes, such as the functional integrity of the uterine scar during subsequent pregnancies, is of increasing importance for guiding clinical practice. Long-term outcomes, even if uncommon, are likely to have a substantial effect on morbidity and can occasionally result in life-threatening events or even death. There have been few follow-up studies of existing trials of caesarean section techniques and these studies are small (a total of just over 350 women).[25–27] For important outcomes such as uterine rupture (incidence 0·4–0·6%) and dehiscence (1·1%),[28–30] detection of differences between alternative surgical techniques with adequate power is challenging. This absence of long-term follow-up data and the absence of short-term effects of these techniques raise important issues about present clinical guidance.

The short-term outcomes of the CORONIS trial might suggest that any of the five pairs of surgical techniques is acceptable. However, until we have information from the ongoing CORONIS follow-up study, which is assessing women's health at least 3 years after the CORONIS caesarean section, we cannot assume that the absence of evidence of short-term effects will translate into an absence of evidence of long-term effects.

Contributors

All members of the writing committee contributed equally to the development of the protocol and management and undertaking of the trial. EJ, PH, and PS did the analyses. PB wrote the report and revised it with input from all members of the writing committee. All members of the writing committee read and approved the final manuscript.

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Conflicts of interest

We declare that we have no conflicts of interest.

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