

# Is cerclage safe and effective in preventing preterm birth in women presenting early in pregnancy with cervical dilatation?

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27 *Uncertainties*

28 **Is cerclage safe and effective in preventing preterm birth in**  
29 **women presenting early in pregnancy with cervical dilatation?**

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40 This is one of a series of occasional articles that highlight areas of practice where  
41 management lacks convincing supporting evidence. The series adviser is David Tovey, editor  
42 in chief, the *Cochrane Library*. This paper is based on a research priority identified and  
43 commissioned by the National Institute for Health Research's Health Technology  
44 Assessment programme on an important clinical uncertainty. To suggest a topic for this  
45 series, please email us at [uncertainties@bmj.com](mailto:uncertainties@bmj.com).

46 **Box Start**

47 **What you need to know**

- Emergency cervical cerclage is a potential treatment for women presenting with cervical dilatation and exposed unruptured fetal membranes before 28 weeks of pregnancy in the absence of bleeding, uterine activity, or infection
- There is limited low quality evidence mainly from retrospective studies that emergency cervical cerclage may prolong pregnancy duration, but concerns regarding selection bias and reporting of complications restrict their clinical interpretation.
- There is no evidence to support the use of progesterone, NSAIDs, pessary, prophylactic antibiotics, or tocolytics as independent treatments in these women

**Box End**

Preterm birth is an important cause of maternal and neonatal morbidity and neonatal mortality globally accounting for almost 1 million neonatal deaths each year (Liu et al 2016). Women who present with a dilated cervix in the second trimester with minimal or no preceding symptoms are at increased risk of pregnancy loss and preterm birth (fig 1). Emergency cervical cerclage, or rescue cerclage, is performed to prevent this. The National Institute for Health and Clinical Excellence (NICE) guidelines recommend considering this procedure for women presenting with cervical dilatation and exposed fetal membranes between 16 and 28 weeks of gestation if there are no signs of bleeding, infection, or uterine activity (see box 1).<sup>1</sup>

**Fig 1.** Premature cervical dilatation and exposed unruptured fetal membranes

**Box Start**

**Box 1. NICE guidelines for management of preterm labour and birth (NG25)<sup>1</sup>**

**Women with a closed cervix**

- For women with a history of spontaneous preterm birth or second trimester miscarriage, plus a cervical length of <25 mm on transvaginal ultrasound (TVUSS): offer a choice of prophylactic cervical cerclage or progesterone.
- For women with a history of spontaneous preterm birth or second trimester miscarriage, or a cervical length of <25 mm on TVUSS (but not both): consider progesterone.
- For women with a history of preterm premature rupture of the membranes (PPROM) or cervical trauma, plus a cervical length of <25 mm on TVUSS: offer prophylactic cervical cerclage.

**Women with cervical dilatation and exposed unruptured fetal membranes\***

- Do not offer “rescue” cerclage if there are signs of infection, bleeding, or uterine activity.
- Consider rescue cerclage for women between 16+0 and 27+6 weeks of gestation, taking into account gestational age and degree of dilatation, and in discussion with consultant obstetrician and paediatrician.
- Explain to women the risks of the procedure and that the aim is to delay birth to increase the likelihood of survival and decrease neonatal morbidity.

\*NICE guidance does not discuss any interventions other than emergency cervical cerclage (rescue cerclage) for women with cervical dilatation and exposed membranes.

**Box End**

Asymptomatic women with a history of preterm birth or spontaneous miscarriage and a short cervix may be considered for prophylactic cervical cerclage (performed when the cervix

90 is closed and the membranes are not exposed); this procedure is not the focus of this paper.  
91 Likewise, management of women presenting early in gestation with contractions, vaginal  
92 bleeding, or ruptured membranes is not part of this article.

93 Emergency cervical cerclage (ECC) tends to be complex as membranes must be replaced  
94 within the uterus and a stitch placed around any remaining cervix. The procedure carries a  
95 risk of complications such as membrane rupture, maternal or fetal infection, sepsis, cervical  
96 trauma, and worsening clinical scenario.

97 There is uncertainty about the benefits and risks of ECC and other management options to  
98 prevent preterm birth and pregnancy loss in women with dilated cervix and exposed  
99 unruptured fetal membranes.

## 100 **What is the evidence of uncertainty?**

101 There is limited, low quality evidence that ECC prolongs pregnancy duration and reduces  
102 pregnancy loss in these women. It is unclear how variable presentations, gestation, infection,  
103 and add-on treatments influence outcomes with emergency cervical cerclage and risks for  
104 mother and baby.<sup>2,3</sup>

105	<b>Box start</b>
106	<b>GRADE quality of evidence and definitions</b>
107	<i>High quality</i> —Further research is very unlikely to change our confidence in the estimate of
108	effect
109	<i>Moderate quality</i> —Further research is likely to have an important impact on our confidence
110	in the estimate of effect and may change the estimate
111	<i>Low quality</i> —Further research is very likely to have an important impact on our confidence in
112	the estimate of effect and is likely to change the estimate
113	<i>Very low quality</i> —Any estimate of effect is very uncertain
114	<b>Box end</b>

115 A systematic review and meta-analysis published in 2020 (12 observational studies, 1021  
116 participants) found that ECC in singleton pregnancies decreased preterm birth (odds ratio  
117 0.25 (95% confidence interval 0.16 to 0.39), 5 studies, n=392) and pregnancy loss (OR 0.26  
118 (0.12 to 0.56), 8 studies, n=455) compared with expectant management.<sup>2</sup> Emergency cervical  
119 cerclage was found to increase mean pregnancy duration by 47.45 days (95% CI 39.89 to  
120 55.0). The evidence is of low to very low quality.

121 However, unlike other options, the consequences of ECC may shorten the pregnancy (due  
122 to rupture of membranes or infection). The reporting of complication rates in existing  
123 literature is very poor. Reported rates of rupture or membranes vary from 5-25%  
124 (Olatunbosun et al 1995, Proctor et al 2021). Depending on gestation, this may cause loss of  
125 the pregnancy or limit the chance of survival. It is also possible for ECC to prolong

126 pregnancy without meaningful improvement in the chance of live birth or survival to  
 127 childhood particularly at earlier gestations of presentation (box 2). Advances in neonatal care  
 128 mean a significant number of extremely preterm babies (22-27 weeks) will survive to  
 129 neonatal unit admission but overall, mortality, and significant morbidity, in surviving infants  
 130 remains very high (Mactier et al 2019).

131 **Box Start**

132 **Box 2. Gestation calculator**

133 At 24 weeks, 6 out of every 10 babies are expected to survive; at 28 weeks, 9 out of 10 babies  
 134 will survive; and at 34 weeks, survival is equivalent to that of full term babies<sup>4 5</sup>

Gestation at presentation	Prolongation required to reach gestation		
	24/40	28/40	34/40
16+0	56 days	84 days	126 days
18+0	42 days	70 days	112 days
20+0	28 days	56 days	98 days
22+0	14 days	42 days	84 days
24+0	0	28 days	70 days
26+0	0	14 days	56 days
28+0	0	0	42 days

135 *Green*—The mean pregnancy prolongation\* for emergency cervical cerclage (ECC) and bed  
 136 rest are expected to result in reaching the given gestation

137 *Yellow*—The mean pregnancy prolongation\* for ECC but not bed rest is expected to result in  
 138 reaching the given gestation

139 *Red*—The mean pregnancy prolongation\* for neither ECC or bed rest are expected to result in  
 140 reaching the given gestation

141 \*The trial by Althusius et al<sup>6</sup> found mean prolongation of pregnancy of 54 days in the ECC arm and 20 days in  
 142 the bed rest arm.

143 **Box End**

144 A small randomised controlled trial (23 women (16 singleton and 7 twin pregnancies)),  
 145 found that ECC led to a statistically significant improvement in time to delivery compared  
 146 with bed rest (54 v 20 days, P=0.46) and composite neonatal outcome (risk ratio 1.6 (95% CI  
 147 1.1 to 2.3)).<sup>6</sup> It lowered preterm birth before 34 weeks (7/13 in ECC group v 10/10 in bed rest  
 148 group, P=0.2). Both groups received antibiotic prophylaxis. Women in the cerclage group  
 149 received indomethacin in addition.<sup>6</sup> Results should be interpreted with caution because of  
 150 fewer twin pregnancies and use of indomethacin in the cerclage group. There was no long  
 151 term follow-up of mothers or babies. A trial of ECC compared with no cerclage in women  
 152 with twin pregnancy (30 women) found similar reduction in preterm birth at <34 weeks (risk  
 153 ratio 0.71 (95% CI 0.52 to 0.96)) and perinatal mortality.<sup>7</sup> All women in the cerclage group  
 154 received indomethacin and antibiotics.

155 Progesterone, non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin,  
 156 pessaries, and prophylactic antibiotics have been variably used as adjuncts to ECC in small  
 157 studies (box 3). There is little evidence to recommend their use as independent treatments for

158 this condition. Urinary tract infection and bacterial vaginosis may cause cervical dilatation  
159 and increase the risk of preterm birth. Antibiotics may be used if infection is suspected or  
160 confirmed, but there is no evidence for prophylactic antibiotic use.

161 **Box Start**

162 **Box 3. Summary of evidence for interventions in women with cervical dilatation and**  
163 **exposed fetal membranes (in the absence of uterine contractions)**

164 **Antibiotics**

165 A Cochrane review of prophylactic antibiotics in women in spontaneous preterm birth with  
166 intact membranes found no significant reduction in birth within 48 hours (relative risk 1.02  
167 (95% CI 0.89 to 1.18), 4 trials, n=6800) or preterm birth <36 weeks (RR 0.98 (0.92 to 1.04),  
168 8 trials, n=7185). Antibiotic use was associated with increased risk of harm to neonates.<sup>8</sup>  
169 There was an increased risk of neonatal death with any antibiotic compared with placebo (RR  
170 1.57 (1.03 to 2.40), 9 studies, n=7248).

171 One randomised controlled trial<sup>9</sup> (n=84) in women with painless cervical dilatation and  
172 exposed membranes found no significant difference in preterm birth <34 weeks (25.6% in  
173 antibiotic group v 40% in placebo group, P value not significant, not otherwise specified) or  
174 in composite neonatal outcome (2.6% v 17.5%, P value not significant). There was also no  
175 evidence of benefit of antibiotics in preventing preterm birth or neonatal outcome in the  
176 subgroup with confirmed microbial invasion of the amniotic cavity (preterm birth <34 weeks  
177 50% in antibiotic group v 100% in placebo group, P value not significant).

178 One small single centre RCT (n=53) randomised women undergoing emergency cervical  
179 cerclage (ECC) to either ECC alone or ECC plus indomethacin and antibiotics.<sup>10</sup> Adjunctive  
180 use of indomethacin and antibiotics were associated with a significant increase in the  
181 percentage of women with an ongoing pregnancy at 28 days (92.3% (n=24) v 62.5% (n=15),  
182 P=0.01). There was no difference in gestation at delivery overall or neonatal outcomes.

183 **Arabin pessary**

184 Low quality evidence from one retrospective observational study comparing pessary, ECC,  
185 and expectant management in women with an open cervix (n=112) suggests no significant  
186 difference in gestation at delivery between pessary and expectant management.<sup>11</sup> ECC was  
187 associated with a significant increase in gestational age at delivery (mean 22.9 (SD 4.5)  
188 weeks with pessary, 25.6 (6.7) weeks with expectant management, and 29.2 (7.5) weeks with  
189 cerclage, P=0.015). There is no RCT or meta-analysis evidence for the use of cervical  
190 pessaries in women with an open cervix.

191 **Cervical cerclage**

192 One small RCT at high risk of bias compared ECC with bed rest.<sup>6</sup> ECC was found to increase  
193 pregnancy length (mean time from intervention to delivery 54 v 20 days, P=0.46) and reduce  
194 neonatal morbidity (compound outcome) compared with controls (risk ratio 1.6 (95% CI 1.1  
195 to 2.3)).<sup>12</sup> 2020 systematic review and meta-analysis of observational data (12 observational  
196 studies, 2 at low risk of bias) supports a reduction in preterm birth and prolongation of  
197 pregnancy with ECC compared with expectant management, but most of these studies are  
198 small, retrospective, and at high risk of bias. ECC was associated with a reduction in risk of  
199 preterm birth <28 weeks (odds ratio 0.25 (95% CI 0.16 to 0.39), 5 studies, n=392).

200 **Indomethacin**

201 Indomethacin is an NSAID and potential uterine muscle relaxant sometimes used at the time  
202 of ECC. There is no role for indomethacin as a stand-alone treatment for women with  
203 cervical dilatation.

204 One small single centre RCT (n=53) randomised women undergoing ECC to either ECC  
205 alone or to ECC plus indomethacin and antibiotics.<sup>10</sup> Adjunctive use of indomethacin and  
206 antibiotics were associated with an increase in the percentage of women with an ongoing

207 pregnancy at 28 days (92.3% (n=24) v 62.5% (n=15), P=0.01). There was no significant  
208 difference in gestation at delivery overall or neonatal outcomes.

209 A retrospective observational study (n=222) of women undergoing ECC compared women  
210 who received indomethacin (31%) with those who did not and found no significant difference  
211 in risk of preterm birth <32 or <35 weeks.<sup>12</sup>

#### 212 **Progesterone**

213 There is no RCT or meta-analysis evidence for the use of progesterone in the prevention of  
214 preterm birth or late miscarriage in women with an open cervix and exposed fetal  
215 membranes.

216 A small observational study (n=69) which included women with a short cervix or an open  
217 cervix (22% of study population) undergoing cerclage found no difference with progesterone  
218 and cerclage (prophylactic or emergency) compared with cerclage alone (odds ratio 2.83  
219 (95% CI 0.58 to 13.89)).

#### 220 **Tocolysis**

221 There is no role for tocolysis alone in women with an open cervix and exposed membranes in  
222 the absence of uterine activity.

223 Tocolytics have been given as an adjunct to ECC in RCT but their role as an intervention has  
224 not been individually assessed.<sup>6</sup>

#### 225 **Box End**

### 226 **Is ongoing research likely to provide relevant evidence?**

227 We searched ISRCTN, PROSPERO, and NIHR registries for ongoing studies on  
228 emergency cervical cerclage. We found two ongoing randomised controlled trials in the  
229 United Kingdom.

230 We are conducting the C-STICH2 trial to assess effect of ECC on pregnancy loss in  
231 singleton pregnancies (50 women), the risks of ECC, and maternal and neonatal outcomes  
232 over a two year follow-up. An accompanying prospective observational cohort study (120  
233 women) will inform on the incidence of the condition.

234 ENCIRCLE aims to assess the effect of ECC on time to delivery, preterm birth,  
235 pregnancy loss, and maternal and neonatal outcomes in (a) women with a twin pregnancy  
236 with an open cervix and exposed fetal membranes and (b) women with a short cervix after  
237 laser treatment for twin-to-twin transfusion syndrome. ENCIRCLE aims to recruit 31 women.

238 There are no registered trials assessing progesterone, antibiotics, or bed rest for women  
239 with an open cervix and exposed fetal membranes.

#### 240 **Box Start**

#### 241 **Recommendations for further research**

- 242 • Effectiveness of emergency cervical cerclage (ECC) in earlier or later gestations (than 16-  
243 28 weeks), and in women with different causes for preterm birth (multiple pregnancies,  
244 structural uterine anomalies, previous full dilatation caesarean section, or cervical  
245 surgery)
- 246 • Women's views and experiences on options for prevention and management of preterm  
247 birth to develop optimal care pathways

- 248 • Future studies must report on all preterm birth core outcomes and include long term follow-  
249 up of surviving children.

250 **Box End**

## 251 **What should we do in light of the uncertainty?**

252 This is a challenging emergency to manage with a high risk of a poor outcome for  
253 mothers and babies and few proven effective treatments.

254 Women, their partners, and families must be offered counselling by a consultant  
255 obstetrician and paediatrician, taking into consideration the woman's wishes, to choose  
256 between expectant management or bed rest and emergency cervical cerclage. It is important  
257 that they receive information about possible outcomes of the condition, interventions, and  
258 potential adverse effects for mother and baby. A calculation tool has been developed based  
259 on the results of a previous RCT to demonstrate graphically to women and clinicians the  
260 likelihood of reaching specific gestations dependent on the timing of intervention.

261 Antibiotics may be used if urinary tract infection or chorioamnionitis is suspected or  
262 confirmed. Women with exposed membranes may have increased risk of subclinical infection  
263 within the amniotic fluid (microbial invasion of the amniotic cavity). This is thought to cause  
264 some cases of painless cervical dilatation,<sup>9</sup> but it is not routinely investigated (by  
265 amniocentesis) or treated.

266 ECC is not available within all maternity settings due to local policies and availability of  
267 experienced practitioners. We recommend establishing local networks such that women can  
268 be offered appropriate interventions regionally.

269 **Box Start**

### 270 **What patients need to know**

- 271 • Sometimes the neck of the womb can start to open early and the bag of waters around the  
272 baby can come through the neck of the womb (fig 1).
- 273 • If this happens too early in pregnancy (before 28 weeks), there are a limited number of  
274 options to prolong the pregnancy. These include expectant management or bed rest  
275 (combined sometimes with antibiotics, progesterone, or medicines to stop the womb  
276 contracting) or emergency cervical cerclage (ECC).
- 277 • An ECC is the placement of a stitch around the neck of the womb after replacement of the  
278 bag of waters.
- 279 • There is some evidence from small studies that ECC may prolong pregnancy, preventing  
280 some of the complications of being born too early. The evidence is of low quality, and  
281 there are no long term data on pregnancy outcomes in the mother and newborn.

282 **Box End**

### 283 **Date search**

284 We searched the ISRCTN, PROSPERO, and NIHR research registries to identify any  
285 ongoing studies.



286 **Search strategy**  
287 We searched the Cochrane Library for systematic reviews on emergency cervical cerclage,  
288 progesterone, tocolysis, and bed rest.  
289 When there was no Cochrane review, we searched for systematic reviews, randomised  
290 control trials, or observational studies in PubMed.  
291 **Query results**  
292 • ((open cervix) OR (cervical dilatation) OR (exposed fetal membranes)) AND (bedrest)—33  
293 results  
294 • ((open cervix) OR (cervical dilatation) OR (exposed fetal membranes)) AND  
295 (progesterone)—159 results  
296 • ((open cervix) OR (cervical dilatation) OR (exposed fetal membranes)) AND (cervical  
297 pessary)—77 results  
298 • ((open cervix) OR (cervical dilatation) OR (exposed fetal membranes)) AND (antibiotics)—  
299 190 results  
300 • (physical exam indicated cerclage) OR (emergency cervical cerclage)—277 results

301 **Box End**

302 **Box Start**

303 **Education into practice**

- 304 • How would you discuss management options with pregnant women at risk of preterm birth?  
305 • How would you ensure your practice is linked with local or regional maternity services that  
306 offer emergency cervical cerclage?

307 **Box End**

308 **Box Start**

309 **How patients were involved in the creation of this article**

310 We asked a patient representative on our trial group to contribute to this paper. The patient  
311 representative has contributed extensively in the context of the trial regarding use of language  
312 and what parents wish to know, and has reviewed the manuscript to ensure the language used  
313 is supportive and appropriate and parent's priorities are addressed.

314 **Box End**

315 Advisers to this series are Nai Ming Lai, Win Sen Kuan, Paula Riganti, and Juan Franco.

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