



HAL
open science

The introduction of a universal transvaginal cervical length screening program is associated with a reduced preterm birth rate

Aude Figarella, Cécile Chau, Anderson Loundou, Claude D'ercole, Florence Bretelle

► To cite this version:

Aude Figarella, Cécile Chau, Anderson Loundou, Claude D'ercole, Florence Bretelle. The introduction of a universal transvaginal cervical length screening program is associated with a reduced preterm birth rate. *American Journal of Obstetrics and Gynecology*, 2023, 228 (2), pp.219.e1-219.e14. 10.1016/j.ajog.2022.07.046 . hal-04279310

HAL Id: hal-04279310

<https://amu.hal.science/hal-04279310v1>

Submitted on 12 Apr 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

The introduction of a universal transvaginal cervical length screening program is associated with a reduced preterm birth rate

Aude Figarella, MD; Cécile Chau, MD; Anderson Loundou, PhD; Claude d'Ercole, MD, PhD; Florence Bretelle, MD, PhD

BACKGROUND: Midtrimester sonographic short cervix is a good predictor of preterm birth in singleton pregnancies.

OBJECTIVE: This study aimed to assess the impact of implementing a universal transvaginal cervical length screening program on preterm birth rate.

STUDY DESIGN: This study consisted of 2 parts: a before-and-after multicenter study and a study on the ECHOCOL (“echo”=“ultrasound” and “col”=“cervix” in French) prospective cohort. We compared the rate of preterm birth before and after the introduction of universal cervical length screening at the time of midtrimester anatomy ultrasound. The multicenter before-and-after regional study included all women with a singleton pregnancy who gave birth after 24 weeks’ gestation in the South East of France from January 1, 2012 to April 30, 2018. In parallel, the ECHOCOL cohort study was prospectively conducted from May 2015 to July 2018, including 17 maternity hospitals in the South East region of France. In case of asymptomatic short cervix <25 mm, treatments offered included 200 mg of vaginal progesterone, or cerclage, or a pessary until 34 weeks’ gestation.

RESULTS: We observed a significant decrease rate of preterm birth between periods A and B after multivariate analysis. (respectively, 5.8% vs

5.6%; adjusted odds ratio, 0.92; 95% confidence interval, 0.89–0.95; $P<.0001$). In parallel, the percentage of cervical length screening significantly increased from 28.9% in period A to 52.9% in period B (odds ratio, 2.76; 95% confidence interval, 2.71–2.80; $P<.0001$). Among the 3468 patients of the ECHOCOL prospective cohort, 38 (1.1%) asymptomatic short cervixes were detected, and 192 patients gave birth prematurely (11 with an asymptomatic short cervix and 181 without). In the ECHOCOL cohort, a marked but statistically insignificant tendency toward a reduced rate of preterm birth before 37 weeks of gestation was observed (from 5.8% to 5.5%; adjusted odds ratio, 0.72; 95% confidence interval, 0.51–1.03; $P=.068$).

CONCLUSION: This study showed a significantly lower rate of preterm birth after the implementation of a universal cervical length screening and treating policy during the second trimester of pregnancy. The clinical trial was registered under NCT02598323.

Key words: cervical length measurement, ECHOCOL, implementation research, preterm birth, preterm labor, screening, short cervix, vaginal progesterone

Introduction

Preterm birth is birth before 37 weeks of gestation.¹ It can be induced or spontaneous (two-thirds of cases).² In 2014, 14.84 million infants were born prematurely worldwide, comprising 10.6% of live births.³ In France, preterm birth represented 6% of singleton live births in 2016 (vs 4.5% in 1995).⁴ Preterm birth is associated with a significant increase in short- and long-term neonatal and infantile morbidity.⁵ Risk factors for spontaneous preterm birth are previous preterm birth, multiple gestations and

abnormalities of the reproductive organs, vaginal infections, underweight or obesity before pregnancy, placenta previa, diabetes mellitus and gestational diabetes mellitus, maternal age, drug use, and smoking. Among the risk factors, a midtrimester sonographic short cervix is a good predictor of preterm birth.^{6–8} Thus, a previous study on asymptomatic patients with a singleton pregnancy and no history of preterm birth showed that cervical length ≤ 15 mm exposed them to a risk of delivery before 32 weeks of gestation of $\geq 50\%$.⁹ In France, cervical length screening of singleton pregnancies is recommended for women with a history of preterm birth but not systematically in other cases.¹ In the United Kingdom and the United States, the National Institute for Health and Care Excellence (NICE) guidelines and the American College of Obstetricians and Gynecologists recommend midtrimester cervical length screening in case of singleton pregnancy and previous preterm birth

or midtrimester loss.^{10,11} However, most guidelines except 2 advised against universal cervical length screening in singleton pregnancy.^{12,13} In the absence of previous preterm birth when an asymptomatic short cervix is detected (cervical length ≤ 25 mm without regular and painful uterine contractions), vaginal progesterone is recommended.^{1,14–17} Progesterone is known for its immunomodulatory and antiinflammatory effects, and for its inhibitory effects on uterine contractions and the production of prostaglandins, responsible for cervical ripening.¹⁸ Administration of vaginal progesterone acts on the adaptive immune system by increasing the proportion of decidual CD4+ regulatory T cells.¹⁹ A 2012 meta-analysis showed that the use of vaginal progesterone in cases of singleton pregnancies with an asymptomatic short cervix significantly reduced the rate of preterm birth before 33 weeks’ gestation (12.4% vs 22.0%; odds ratio [OR], 0.58; 95% confidence

Why was this study conducted?

To the best of our knowledge, no study has evaluated the effect of introducing a universal transvaginal cervical length screening program on the preterm birth rate in a European country.

Key findings

In a before-and-after study, the introduction of a universal transvaginal cervical length screening program in the South East of France was associated with a significant reduction in the singleton preterm birth rate (from 5.8% to 5.6%; adjusted odds ratio, 0.92; 95% confidence interval, 0.89–0.95; $P < .029$). In the prospective cohort study (ECHOCOL), the introduction of a universal transvaginal cervical length screening program was associated with a nonsignificant decrease in the rate of preterm birth at < 37 weeks' gestation (from 5.8% to 5.5%; adjusted odds ratio, 0.72; 95% confidence interval, 0.51–1.03; $P = .068$).

What does this add to what is known?

Our study showed a decrease in the rate of preterm birth within a large cohort in France after the implementation of a universal policy of cervical length screening to identify asymptomatic short cervix and provide preterm birth preventive treatment.

interval [CI], 0.42–0.80).²⁰ In the case of an asymptomatic short cervix with a history of preterm birth or late miscarriage, cervical cerclage is also recommended.^{1,15,21–23} In France, pessary is not recommended for this indication because of contradictory results concerning its efficacy. Vaginal progesterone and cerclage are equally effective in preventing preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix.^{15,24} However, a combination of these methods seems to give better results in reducing preterm birth rates, including those of pregnancies with a short cervix < 10 mm.²⁵ Spontaneous preterm birth with a personal history of preterm birth currently represents 10% of spontaneous preterm births in France.¹ Therefore, 90% of spontaneous preterm births occur in patients without a history of preterm birth, but these are not detected because there is currently no universal cervical length screening program.²⁶ Two retrospective studies showed that a universal cervical length screening program enabled to significantly reduce the rate of preterm birth.^{27,28} However, these results need to be verified in larger prospective cohorts. On this background, our study

prospectively assessed the impact of a program for universal transvaginal ultrasound cervical length screening and treatment in cases of asymptomatic short cervix on the preterm birth rate, and its medical consequences.

Materials and Methods

Ethical and regulatory issues

The ethics committee provided approval on July 21, 2014 (reference number 2014-A00920-47). The ClinicalTrials.gov website was updated when ethical and regulatory approvals were obtained (identifier: NCT02598323). An informed consent form was given to the patients to harmonize the information given (research goals, procedure, benefits, and risks). All women provided informed signed consent to be included in the study. Research on the ECHOCOL prospective cohort was performed in accordance with the Declaration of Helsinki (World Medical Association) stating the ethical principles that apply to medical research involving human subjects, and was also defined according to article L.1121-2 of the French public health regulations (Code de la santé publique) of research in current health-care practice.

Trial design

This study consisted of 2 parts: a before-and-after multicenter study and a study on the ECHOCOL prospective cohort. We compared the rate of all preterm births before (period A) with the rate after (period B) the introduction and promotion of universal transvaginal ultrasound measurement of cervical length at the time of the second-trimester anatomy scan in the whole Mediterranean network and in a prospective study of a cohort of patients (ECHOCOL prospective cohort).

The multicenter before-and-after regional study concerned all women with a singleton pregnancy who gave birth after 24 weeks' gestation in the South East of France (the Mediterranean Network; <https://www.reseaperinatmed.fr/>) from January 1, 2012 to April 30, 2018. The “before” period or A (January 1, 2012–December 31, 2014) corresponded to the control group and the “after” period or B (May 1, 2015–April 30, 2018) corresponded to the treatment group. The study was based on data from the French Programme de médicalisation des systèmes d'information (PMSI) national database and delivery procedure codes available from the regional health agency (agence régionale de santé [ARS]) for all women with singleton pregnancies in the South of France from 2012 to 2018.

The PMSI assigns specific codes to different delivery procedures; for example, the rate of preterm birth was assessed using the PMSI code O60 (preterm labor and delivery). The rate of spontaneous preterm labor with preterm birth was determined using the PMSI code O60.1. To check if the rate of induced preterm birth was stable over periods A and B, the rates of the different causes of induced preterm birth were calculated and compared between periods.

We recorded the following data to assess the impact of the cervical length screening program: number of cervical length measurements before 37 weeks of gestation with no hospitalization, number of hospital admissions for threatened preterm labor, number of cervical length measurements with a prescription for

vaginal progesterone and/or cerclage and/or pessary and/or sick leave before 37 weeks' gestation, number of cervical length measurements with a prescription for vaginal progesterone and/or cerclage and/or pessary and preterm birth at <37 weeks, length of hospital stay for threatened preterm labor with cervical length measurement with or without a prescription or performance of cerclage and/or pessary and/or vaginal progesterone, and finally hospital admissions and average length of stay for premature newborns.

ECHOCOL prospective cohort

The study on the ECHOCOL prospective cohort was multicenter and observational. Inclusions took place from May 19, 2015 to July 12, 2018. The study was originally proposed to the 41 maternity hospitals belonging to the Mediterranean perinatal network during a network training day on June 11, 2012. The universal transvaginal cervical length screening program was introduced in the study area between January 1, 2015 and April 30, 2015. Each of the 41 maternity hospitals were given a 2-hour training session including the quality analysis of ultrasound cervical measurement with the visibility of the endocervical canal. The measurement technique was also available on the Mediterranean Network website including the potential benefits of transvaginal cervical length measurement and treatment to prevent preterm birth (<https://www.reseaperinatmed.fr/>). Among the 41 centers, 17 accepted to participate in the ECHOCOL prospective cohort study, and received, in 2014, according to Iams, special training (in groups of 3 maternity hospitals) on ultrasound measurement, including the potential benefits of transvaginal cervical length measurement and treatment.⁸ Because of the number of sonographers in the study area, there was no individual accreditation of sonographers or retrospective quality analysis of scans. All patients aged >18 years with a singleton pregnancy between 16 and 26 weeks of gestation and no signs of preterm labor were eligible for the study.

Transvaginal ultrasound cervical length measurement was performed after obtaining the patient's consent. In case of detection of an asymptomatic short cervix (cervical length ≤ 25 mm), patients were treated with vaginal progesterone (200 mg daily) or cerclage or a pessary according to the usual local practice and had regular follow-up until 34 weeks' gestation, or rupture of membranes, or birth. The data from this cohort were compared with those from the A period using PMSI data from the southern regional health agency.

Exclusion criteria were: existing maternal pathology (preeclampsia), uterine malformation, fetal malformation or fetal chromosome anomaly, preterm labor (cervix dilated >2 cm and/or regular painful uterine contractions), existing signs of chorioamnionitis, allergy to progesterone (for B-period patients), and having taken progesterone within the month before inclusion (for B-period patients).

Outcome measures and data collection

The primary outcome was the rate of preterm delivery before 37 weeks' gestation.

The secondary outcomes were the following.

For the comparison of period A (before) with period B (after implementation of universal screening) in the whole Mediterranean Network, the secondary outcomes included induced preterm birth rate, length of hospital stay for threatened preterm labor with cervical length measurement with or without prescription or performance of cerclage and/or pessary and/or vaginal progesterone, number of hospital admissions, and length of stay in intensive care and/or neonatal resuscitation for premature newborns.

For the ECHOCOL prospective cohort, the secondary outcomes included rate of preterm birth before 37 weeks' gestation for asymptomatic patients without a short cervix, rate of preterm birth before 37 weeks for asymptomatic patients with a short cervix (comparing the subgroups: cervical length ≤ 15 mm, cervical length from

16–25 mm, active smoker, personal history of preterm birth, and personal history of miscarriage during the second trimester of pregnancy), and rate of preterm birth before 28 and 32 weeks' gestation (patients with and without a short cervix).

Statistical analysis

In 2013, the rate of preterm birth in France was 7.4% (reference available at the time of study design).⁴ We estimated that to obtain a 1.5% reduction with 80% power, we would need 3500 patients in the ECHOCOL prospective cohort for a total of 44,000 births per year in the maternity network. We also estimated that 10% (350) of patients would have a short cervix.

Statistical analysis was performed using IBM SPSS Statistics, version 20.0 software (SPSS Inc, Chicago, IL). Quantitative data are given as averages \pm standard deviation or as medians with range (min, max). Categorical data are given as numbers and percentages. Percentages were compared between the 2 groups using the chi-square or Fisher exact test if theoretical numbers were <5. Averages were compared between the 2 groups with the Student *t* test or a nonparametric Mann–Whitney test. For all tests, statistical significance was set at $P < .05$.

Multivariate analysis was performed using a logistic regression model. Variables that were found to be significantly associated with outcome or to be marginally significant in bivariate analysis, or that had clinical relevance were included into the logistic regression model. Calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test to evaluate the discrepancy between observed and expected values. ORs are presented with 95% CIs.

Results

Comparison of period A (before) with period B (after implementation of universal screening) in the whole Mediterranean Network

Multivariate analysis of data from all the maternity hospitals belonging to the Mediterranean Network revealed that there was a significant decrease in the rate of preterm birth for singleton

TABLE 1
Data on singleton pregnancy deliveries in a before-and-after study covering the Mediterranean Network (41 maternities)

Variables (number)	Period A					Period B					Pvalue				
Total deliveries	171,079					165,524									
Age (y)															
<20	3437 (2.0%)					2793 (1.7%)					1				
20–35	132,782 (77.5%)					125,828 (75.9%)					<.0001				
≥35	35,219 (20.5%)					37,237 (22.5%)					<.0001				
BMI >30 kg/m ²	3755 (2.2%)					5509 (3.3%)					<.0001				
Smoker	281 (0.2%)					44 (0.01%)					<.0001				
Use of psychoactive substances	63 (0.1%)					91 (0.1%)					.05				
Social precariousness	385 (0.2%)					1022 (0.6%)					<.0001				
History of pathologic pregnancies	1259 (0.7%)					1362 (0.8%)					<.0001				
Gestational diabetes mellitus	9378 (5.5%)					13,285 (8.0%)					.53				
Singleton pregnancy <37 WG	24–25+6	26–27+6	28–31+6	32–36+6	Still born	24–25+6	26–27+6	28–31+6	32–36+6	Stillborn	24–25+6	26–27+6	28–31+6	32–36+6	Stillborn
Placenta previa	5	9	29	93	5	9	10	39	102	7	0.12	0.18	0.02	0.03	0.18
Chorioamnionitis	24	27	37	39	12	34	24	40	53	12	0.04	0.11	0.06	0.02	0.16
Preeclampsia	13	19	65	254	21	14	26	77	251	20	0.15	0.06	0.01	0.03	0.13
Placental abruption	4	4	32	36	17	10	13	34	45	14	0.06	0.02	0.08	0.04	0.14

(continued)

TABLE 1
Data on singleton pregnancy deliveries in a before-and-after study covering the Mediterranean Network (41 maternities) (continued)

Variables (number)	Period A					Period B					P value				
	27	26	65	93	10	28	25	86	151	7		0.11	0.12	0.002	<.0001
Premature rupture of membranes	0	1	1	12	0	0	0	1	33	0	/	0.5	0.5	0.0004	/
Intrahepatic cholestasis	124	153	435	950	144	105	139	384	953	111	0.03	0.04	0.04	0.006	0.01
Fetal growth restriction	83	103	327	2666	83	70	76	277	2521	32	0.04	0.01	0.03	0.01	<.0001
Preterm labor	341	339	1004	8219	794	332	331	889	7723	741	aOR (95% CI)				
Total (at least 1)	9903/171,079 (5.79%)														
Preterm birth (<37 WG)	9275/165,524 (5.60%)					0.92 (0.89–0.95); P<.0001 ^a									

aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; WG, weeks of gestation.

^a Multivariate analysis.

pregnancies from period A (5.79%; 9903 preterm births out of 171,079 births) to period B (5.6%; 9275 preterm births out of 165,524 births) (adjusted OR, 0.92; 95% CI, 0.89–0.95; $P<.0001$) (Table 1). We also observed a significant decrease in the rate of spontaneous preterm birth from period A (1.9%; 3262/171,079) to period B (1.8%; 2976/165,524) (OR, 0.94; 95% CI, 0.88–0.99; $P=.02$). In parallel, a significant increase of cervical length measurements from 28.9% in period A (49,504/171,079) to 52.9% in period B (87,546/165,524) (OR, 2.76; 95% CI, 2.71–2.80; $P<.0001$) was observed for the whole Mediterranean Network. This increase was also detected when cervical length measurement was associated with prescription of vaginal progesterone and/or cerclage and/or pessary and/or sick leave from work before 37 weeks of gestation (12.9% [14,875/114,994] vs 22.4% [37,030/165,524]; OR, 1.94; 95% CI, 1.90–1.98; $P<.0001$ for the entire region) (Table 2). There was no difference in the main factors for induced preterm birth between the 2 periods, except in preterm labor, which significantly decreased with time (Table 1). Hospitalization rates for threatened preterm labor remained stable over the 2 periods. It was necessary to screen and treat 1250 women to prevent 1 preterm delivery during period B.

ECHOCOL prospective cohort

Between May 19, 2015 and July 12, 2018, 3757 patients were included in the ECHOCOL cohort from the 17 centers participating in the southern French neonatal network. A total of 289 (7.7%) patients were lost to follow-up or did not meet criteria (2 twin pregnancies included by error).

Among the 3468 patients with analyzable outcomes, 38 were asymptomatic with a short cervix. In total, 192 of the 3468 (5.5%) patients gave birth prematurely (including 11 cases of asymptomatic short cervix and 17 infants who died before 37 weeks of gestation). In comparison

TABLE 2**Socioeconomic assessment of the management of asymptomatic short cervix over periods A and B in South East France**

PMSI data	South East France			
	Number	Period A (n=171,079)	Period B (n=165,524)	Significance OR (95% CI)
Hospital admission for threatened preterm labor		17,254 (9.2%)	16,698 (9.2%)	1
Cervical length at <37 WG outside hospitalization		49,504 (22.4%)	87,546 (34.6%)	0.55 (0.54–0.55); <i>P</i> <.0001
Cervical length+progesterone and/or cerclage and/or sick leave at <37 WG		14,875 (11.5%)	37,030 (18.3%)	0.58 (0.57–0.59); <i>P</i> <.0001
Cervical length+progesterone and/or cerclage and delivery at <37 WG		381 (0.02%)	835 (0.05%)	0.44 (0.39–0.50); <i>P</i> <.0001
Hospital length for preterm labor+cervical length+progesterone and/or cerclage (d)				
- Before delivery		9.9	9.2	<i>P</i> =.21
- Before 34 WG		11.9	10.8	<i>P</i> =.28

Population studied: all patients who gave birth and/or had a stay for preterm labor in one of the maternity hospitals of the network (last stay defining the classification in or outside the network). CI, confidence interval; OR, odds ratio; WG, weeks of gestation.

with period A (9903 preterm births out of 171,079 births; 5.79%), in the prospective cohort study (ECHOCOL) the introduction of a universal transvaginal cervical length screening program was associated with a nonsignificant decrease in the rate of preterm birth at <37 weeks of gestation (from 5.8% to 5.5%; adjusted OR, 0.72; 95% CI, 0.51–1.03; *P*=.068).

Patients with an asymptomatic short cervix

In this group, the rate of preterm birth was 28.9% (11/38), and 54.5% (6/11) for patients with cervical length ≤15 mm (OR, 4.2; 95% CI, 0.94–18.70; *P*=.068). The rate of preterm birth before 32 weeks of gestation was 72.7% (8/11); 63.6% (7/11) before 28 weeks of gestation and 9.1% (1/11) before 22 weeks of gestation (Table 3).

Concerning the treatment of patients with a short cervix, 25 patients were treated with vaginal progesterone alone (65.8%; 25/38), 3 were told to rest (7.9%; 3/38), 7 were given nothing (18.4%; 7/38), 2 had a combination of vaginal progesterone and rest or vaginal progesterone and cervical cerclage (5.2%;

2/38), and 1 had cervical cerclage (2.6%; 1/38) (Table 3).

Patients without an asymptomatic short cervix

In total, 3249 patients gave birth at term, and 181 (ie, 5.3% of preterm births [181/3430]) gave birth before 37 weeks of gestation. There was no significant difference in parity, age, or smoking.

However, patients who gave birth prematurely had a significantly higher rate of history of preterm delivery (9.0% [16/181] vs 2.5% [80/3260]; OR, 3.94; 95% CI, 2.24–6.85; *P*<.001) or of miscarriage during the second trimester of pregnancy (6.2% [11/181] vs 1.0% [31/3260]; OR, 6.88; 95% CI, 3.40–13.92; *P*<.001). In 81.8% (148/181) of cases, preterm birth was moderately premature, occurring between 32 and 36+6 weeks of gestation.

Discussion

Principal findings

Our study showed a –0.19% significant decrease in the rate of preterm birth between periods A and B after the promotion and implementation of a policy for universal cervical length screening

and treatment of asymptomatic short cervix (5.8% vs 5.6%).

Results in context

Our results are in line with previous studies (Table 4). In 2016, Son et al²⁷ showed in a retrospective cohort of 64,207 women with singleton pregnancies that the introduction of universal cervical length screening during the second-trimester anatomy ultrasound significantly reduced preterm birth from 6.7% to 6.0% (OR, 0.74; 95% CI, 0.62–0.90).

In the before-and-after study, induced preterm birth was stable between the 2 periods, but with a significant decrease in the item “preterm labor.” We observed a significant increase in the percentage of cervical length measurements in period B, from 28.9% to 52.9% for the entire South East region. The percentage of cervical length measurements also increased when it was associated with a prescription of vaginal progesterone and/or cerclage and/or pessary. We supposed, therefore, that the reduced rate of preterm birth was linked to the policy of cervical length screening and treatment of asymptomatic

TABLE 3

Characteristics and management of ECHOCOL patients with an asymptomatic short cervix

Asymptomatic short cervix (n=38)

Characteristics	Term delivery (n=27)	Preterm birth (n=11)	OR (95% CI)	Pvalue
Parity				
- Primiparous	11 (42.3%)+1 missing data	6 (54.5%)	1.64 (0.40–6.76)	.495
- Multiparous	15 (57.7%)	5 (45.5%)	0.61 (0.15–2.53)	
Mother's age				
- 19–34 y	19 (70.4%)	9 (81.8%)	1.89 (0.33–10.80)	
- ≥35 y	8 (29.6%)	2 (18.2%)	0.53 (0.09–3.01)	
Smoker				
- Yes	2 (7.4%)	1 (10%)+1 missing data	1.39 (0.11–17.24)	.999
- No	25 (92.6%)	9 (90%)	0.72 (0.06–8.94)	
Prematurity (wk of gestation)				
<22	0	1 (9.1%)	/	
22–27+6	0	6 (54.5%)	/	
28–31+6	0	1 (9.1%)	/	
32–36+6	0	3 (27.3%)	/	
≥37	27 (100%)		/	
Cervical length on inclusion				
- ≤15 mm	6 (22.2%)	6 (54.5%)	4.2 (0.94–18.70)	.068
- 16–25 mm	21 (77.8%)	5 (45.5%)	0.24 (0.05–1.06)	
Previous spontaneous preterm birth				
- Yes	1 (3.8%)	1 (9.1%)	2.5 (0.14–43.97)	.512
- No	25 (96.2%)+1 missing data	10 (90.9%)	0.4 (0.02–7.03)	
Previous miscarriage during the second trimester of pregnancy				
- Yes	2 (7.4%)	3 (27.3%)	4.69 (0.66–33.22)	.134
- No	25 (92.6%)	8 (72.7%)	0.21 (0.03–1.51)	
Therapeutic care				
- Progesterone	19 (70.4%)	6 (54.5%)	0.51 (0.12–2.15)	.457
- Cerclage	0	1 (9.1%)	/	
- Pessary	0	0	/	
- Rest	3 (11.1%)	0	/	
- Combination	0	2 (18.2%)	/	
- Nothing	5 (18.5%)	2 (18.2%)	0.98 (0.16–6.0)	.999

CI, confidence interval; OR, odds ratio.

short cervix initiated during implementation of the ECHOCOL cohort. Therefore, if all health professionals adhered to cervical length screening, there would be an even greater impact on reducing the rate of preterm birth.

Among the patients with an asymptomatic short cervix in the prospective ECHOCOL cohort, our results showed that the only identified predictor was an asymptomatic short cervix. Furthermore, among patients who gave

birth prematurely, cervical length on inclusion was frequently ≤15 mm (54.5% vs 22.2%; OR, 4.2; 95% CI, 0.94–18.70; $P=.068$). These data are concordant with those of Rozenberg and Miller et al^{9,30}: the criterion

TABLE 4

Summary of studies for screening, interventions, and results for prevention of preterm birth

Cohort	Implementation of universal cervical length screening	Vaginal progesterone	Cervical cerclage	Cervical pessary	Results
Singleton pregnancy at low risk with spontaneous preterm delivery From 2013 to 2016 13,396 inclusions Retrospective cohort Green et al, ²⁸ 2017	Indicated from Oct 2014 Transvaginal ultrasound	Unspecified	Unspecified	Unspecified	Decrease of overall preterm birth rate from 3.8% to 2.4% ($P < .001$)
Singleton pregnancy with preterm delivery (n=227,020) From 2013 to 2015 Prospective cohort Newnham et al, ²⁹ 2017	Indicated at 18–20 WG from 2015 Transvaginal or abdominal	Recommended when transvaginal cervical length <25 mm from 16–36 weeks of gestation	Recommended when cervical length <10 mm, alone or both with vaginal progesterone	Not indicated	Significantly lower rate of preterm birth in 2015 ($P < .001$ compared with 2013 and 2014)
Singleton pregnancy with no previous preterm birth From 2007 to 2014 64,207 eligible women Retrospective cohort Son et al, ²⁷ 2016	Indicated at 18–24 WG from 2011 Transvaginal ultrasound	Recommended for cervical length ≤ 20 mm	Recommended when there is a cervical dilatation on digital examination at <24 weeks of gestation	Not indicated	Significant decrease in the rate of preterm birth: <37 weeks of gestation: 6.7% vs 6.0%; OR, 0.82 (0.76–0.88); <34 WG: 1.9% vs 1.7%; OR, 0.74 (0.64–0.85); <32 WG: 1.1% vs 1.0%; OR, 0.74 (0.62–0.90)

OR, odds ratio; WG, weeks of gestation.

“asymptomatic short cervix” seems to be an independent major predictor for preterm birth, especially with cervical length ≤ 15 mm. These results are also in line with those of Souka et al³¹ that showed that the risk of preterm birth exponentially increased when cervical length was ≤ 9 mm.

Strengths and limitations

Our study identified a decrease in the rate of preterm birth in a large cohort after implementation of universal cervical length screening (a total of 336,603 patients in the before-and-after study). Given that the Mediterranean Network is the largest network of maternity hospitals in mainland France, we may postulate that our cohort is representative of the French population.

Nevertheless, our results were not significant within the ECHOCOL prospective cohort. This could be explained by a lack of power due to the number of patients lost to follow-up and the low prevalence of asymptomatic short cervix. In our study, only 1.1% of the cohort

had an asymptomatic short cervix, which is 4 times lower than the prevalence found in the study by Kuusela et al.³² This low prevalence could also be explained by the low cervical length threshold used in our study (25 mm) and the fact that we did not perform any quality control of cervical length measurement. A recent prospective study suggested that identification of cervical length ≤ 30 mm during the second trimester of pregnancy could prevent 35% of spontaneous preterm births before 35 weeks’ gestation (OR, 9.1; 95% CI, 3.5–23.5; $P < .001$).³³

However, the major bias in the comparison of period A (before) with period B (after implementation of universal screening) in the whole Mediterranean Network is related to the database coding modalities. PMSI (national health system) codes are dependent on each center, but also on the training and the appreciation of the person assigning the code. One main code was retained for preterm birth, whereas preterm birth can result from several different

pathologies. Likewise, the exact cause of prematurity can be difficult to define and can have different neonatal consequences.³⁴ Moreover, mainly the design of our study did not enable us to link the lower rate of preterm birth in period B (after) to the implementation of universal screening for cervical length.

Research implications

Our results should lead to further research programs including cervical length screening to identify asymptomatic short cervix, with focus on spontaneous preterm birth and very short cervical length <15 mm using a health economics approach. It would therefore be interesting to improve and homogenize our practices to perform further studies more targeted to this population of patients.

Clinical implications

Our results contribute to evidence on the usefulness of universal transvaginal cervical length screening and encourage its use.

Conclusions

Our study showed a decrease in the rate of preterm birth within a large cohort in France after the implementation of a universal policy of cervical length screening to identify asymptomatic short cervix and provide preterm birth preventive treatment. Our results suggest that further studies focusing on the impact of cervical length ≤ 15 mm should be performed to adapt screening and current treatments. ■

Acknowledgments

We thank the women enrolled in the trial. In addition, we thank the Mediterranean Network, the agence régionale de santé (ARS)—regional agency of Provence-Alpes-Côte d'Azur, the 17 maternity hospitals in the network that participated in the ECHOCOL study, and the following individuals who contributed to this trial: Hervé Meur; Meriem Ait-Ouali; Marika Larose; Jean Francois Cocalleman; Michèle Marcot; Julie Blanc, MD; Nicolas Gourheux, MD; Isabelle Mortier, MD; Sandrine Lobelle, MD; Carole Mourey, MD; Imke Zerrhan, MD; Xavier Danoy, MD; Raoul Desbriere, MD; Dounia Souames, MD; Franck Mauviel, MD; Marion Gioan, MD; Caroline Adrados, MD; Françoise Germain, MD; Pauline Vignoles, MD; Francois Lisik, MD; Emmanuelle Collette, MD; Nicolas Menager, MD; Catherine Lechevallier, MD; Brigitte Viviani-Bourgeois, MD; Raha Shojai, MD; Catherine Lota, MD; Armelle Bertrand, MD; Agnes Pavard, MD; Nicolas Fontanarosa, MD; Eliane Simon.

References

1. Sentilhes L, Sénat MV, Ancel PY, et al. Prevention of spontaneous preterm birth: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). *Eur J Obstet Gynecol Reprod Biol* 2017;210:217–24.
2. Committee on Practice Bulletins—Obstetrics. The American College of Obstetricians and Gynecologists. Practice bulletin no. 130: prediction and prevention of preterm birth. *Obstet Gynecol* 2012;120:964–73.
3. Chawanpaiboon S, Vogel JP, Moller AB, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019;7:e37–46.
4. Blondel B, Coulm B, Bonnet C, Goffinet F, Le Ray C. National Coordination Group of the National Perinatal Surveys. Trends in perinatal health in metropolitan France from 1995 to 2016: results from the French National Perinatal Surveys. *J Gynecol Obstet Hum Reprod* 2017;46:701–13.
5. Rotteveel J, van Weissenbruch MM, Twisk JWR, Delemarre-Van de Waal HA. Infant and childhood growth patterns, insulin sensitivity, and blood pressure in prematurely born young adults. *Pediatrics* 2008;122:313–21.
6. Heath VCF, Southall TR, Souka AP, Elisseou A, Nicolaidis KH. Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery. *Ultrasound Obstet Gynecol* 1998;12:312–7.
7. Andersen HF, Nugent CE, Wanty SD, Hayashi RH. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. *Am J Obstet Gynecol* 1990;163:859–67.
8. Iams JD, Goldenberg RL, Meis PJ, et al. The length of the cervix and the risk of spontaneous premature delivery. National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. *N Engl J Med* 1996;334:567–72.
9. Rozenberg P. Universal cervical length screening for singleton pregnancies with no history of preterm delivery, or the inverse of the Pareto principle. *BJOG* 2017;124:1038–45.
10. Preterm labour and birth. London: National Institute for Health and Care Excellence (NICE); 2019.
11. Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, McIntosh J, Feltovich H, Berghella V, Manuck T. The role of routine cervical length screening in selected high- and low-risk women for preterm birth prevention. *Am J Obstet Gynecol* 2016;215:B2–7.
12. Minakami H, Maeda T, Fujii T, et al. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2014 edition. *J Obstet Gynaecol Res* 2014;40:1469–99.
13. Medley N, Poljak B, Mammarella S, Alfirevic Z. Clinical guidelines for prevention and management of preterm birth: a systematic review. *BJOG* 2018;125:1361–9.
14. Hassan SS, Romero R, Vidyadhari D, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. *Ultrasound Obstet Gynecol* 2011;38:18–31.
15. Alfirevic Z, Owen J, Carreras Moratona E, Sharp AN, Szychowski JM, Goya M. Vaginal progesterone, cerclage or cervical pessary for preventing preterm birth in asymptomatic singleton pregnant women with a history of preterm birth and a sonographic short cervix. *Ultrasound Obstet Gynecol* 2013;41:146–51.
16. Romero R, Nicolaidis KH, Conde-Agudelo A, et al. Vaginal progesterone decreases preterm birth ≤ 34 weeks of gestation in women with a singleton pregnancy and a short cervix: an updated meta-analysis including data from the OPPTIMUM study. *Ultrasound Obstet Gynecol* 2016;48:308–17.
17. Quibel T, Bultez T, Nizard J, Subtil D, Huchon C, Rozenberg P. [In utero fetal death]. *J Gynecol Obstet Biol Reprod (Paris)* 2014;43:883–907.
18. Elovitz M, Wang Z. Medroxyprogesterone acetate, but not progesterone, protects against inflammation-induced parturition and intrauterine fetal demise. *Am J Obstet Gynecol* 2004;190:693–701.
19. Furcron AE, Romero R, Plazyo O, et al. Vaginal progesterone, but not 17 α -hydroxyprogesterone caproate, has antiinflammatory effects at the murine maternal-fetal interface. *Am J Obstet Gynecol* 2015;213:846. e1–19.
20. Romero R, Nicolaidis K, Conde-Agudelo A, et al. Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data. *Am J Obstet Gynecol* 2012;206:124. e1–19.
21. Jarde A, Lutsiv O, Beyene J, McDonald SD. Vaginal progesterone, oral progesterone, 17-OHPC, cerclage, and pessary for preventing preterm birth in at-risk singleton pregnancies: an updated systematic review and network meta-analysis. *BJOG* 2019;126:556–67.
22. Alfirevic Z, Stampalija T, Medley N. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. *Cochrane Database Syst Rev* 2017;6:CD008991.
23. Berghella V, Odibo AO, Tolosa JE. Cerclage for prevention of preterm birth in women with a short cervix found on transvaginal ultrasound examination: a randomized trial. *Am J Obstet Gynecol* 2004;191:1311–7.
24. Conde-Agudelo A, Romero R, Da Fonseca E, et al. Vaginal progesterone is as effective as cervical cerclage to prevent preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix: updated indirect comparison meta-analysis. *Am J Obstet Gynecol* 2018;219:10–25.
25. Enakpene CA, DiGiovanni L, Jones TN, Marshalla M, Mastrogiannis D, Della Torre M. Cervical cerclage for singleton pregnant patients on vaginal progesterone with progressive cervical shortening. *Am J Obstet Gynecol* 2018;219:397. e1–10.
26. Adams MM, Elam-Evans LD, Wilson HG, Gilbert DA. Rates of and factors associated with recurrence of preterm delivery. *JAMA* 2000;283:1591–6.
27. Son M, Grobman WA, Ayala NK, Miller ES. A universal mid-trimester transvaginal cervical length screening program and its associated reduced preterm birth rate. *Am J Obstet Gynecol* 2016;214:365. e1–5.
28. Green PM, Argyelan A, Mutual F, Nynas J, Williams J, Keeton K. Implementation of universal cervical length screening is associated with a reduction in the rate of spontaneous preterm delivery in a low-risk cohort. *Am J Obstet Gynecol* 2017;216:S10.
29. Newnham JP, White SW, Meharry S, et al. Reducing preterm birth by a statewide multifaceted program: an implementation study. *Am J Obstet Gynecol* 2017;216:434–42.

30. Miller ES, Tita AT, Grobman WA. Second-trimester cervical length screening Among asymptomatic women: an evaluation of risk-based strategies. *Obstet Gynecol* 2015;126:61–6.
31. Souka AP, Papastefanou I, Pilalis A, Kassanos D, Papadopoulos G. Implementation of universal screening for preterm delivery by mid-trimester cervical-length measurement. *Ultrasound Obstet Gynecol* 2019;53:396–401.
32. Kuusela P, Jacobsson B, Hagberg H, et al. Second-trimester transvaginal ultrasound measurement of cervical length for prediction of preterm birth: a blinded prospective multicentre diagnostic accuracy study. *BJOG* 2021;128:195–206.
33. Guerby P, Girard M, Marcoux G, Beaudoin A, Pasquier JC, Bujold E. Midtrimester cervical length in low-risk nulliparous women for the prediction of spontaneous preterm birth: should we

consider a new definition of short cervix? *Am J Perinatol* 2021 [Epub ahead of print].

34. Delorme P, Goffinet F, Ancel PY, et al. Cause of preterm birth as a prognostic factor for mortality. *Obstet Gynecol* 2016;127:40–8.

Author and article information

From the Department of Gynecology, Obstetrics and Reproductive Medicine, Assistance Publique-Hopitaux de Marseille (AP-HM) Hôpital de la Conception, Pôle femmes parents enfants, Marseille, France (Drs Figarella and Bretelle); Aix-Marseille University, Marseille, France (Dr Figarella); Avignon Université, Centre national de la recherche scientifique, Institut de Recherche pour le Développement, Institut Méditerranéen de Biodiversité et d'Ecologie marine et continentale, Marseille, France (Dr Figarella); Department of Gynecology, Obstetrics and Reproductive Medicine, AP-HM Hôpital Nord, Pôle femmes parents enfants, Marseille, France (Dr Chau); Center for Studies and Research on Health Services and

Quality of Life (CEReSS), Aix-Marseille University, Marseille, France (Dr Loundou); Department of Gynecology, Obstetrics and Reproductive Medicine, AP-HM Hôpital Nord, Aix-Marseille Université, Marseille, France (Dr d'Ercole); and Microbes, Evolution, Phylogénie et Infection, L'institut hospitalo-universitaire en maladies infectieuses de Marseille (IHU Méditerranée Infection), Aix-Marseille Université, Marseille, France (Dr Bretelle).

Received Jan. 12, 2022; revised July 25, 2022; accepted July 27, 2022.

The authors report no conflict of interest.

The agence régionale de santé (ARS) regional agency supported this program (number 20140650 conv C2014000343).

ClinicalTrials.gov identifier: NCT02598323. Date of registration: November 5, 2015. First participant enrolled on May 19, 2015. <https://clinicaltrials.gov/ct2/show/NCT02598323>

Corresponding author: Aude Figarella, MD. aude.figarella@ap-hm.fr

Supplemental File
Results from the 17 maternity hospitals participating in the ECHOCOL prospective study (PMSI data)

The network covers 41 maternity hospitals. The before-and-after study was implemented using the Programme de médicalisation des systèmes d'information (PMSI) data for all singleton pregnancies. Data were collected either from all of the maternity hospitals belonging to the Mediterranean network or only from the 17 maternity hospitals in the network that participated in the ECHOCOL study (Aix/Pertuis, Aubagne, Carpentras, Clinique Bouchard, Clinique de l'Etoile, Polyclinique

Urbain V, Clinique de Vitrolles, Draguignan, Grasse, Hôpital de la Conception, Hôpital Nord, Hôpital Saint-Joseph, La Ciotat, Martigues, Nice L'Archet, Salon-de-Provence, Toulon) [Supplemental Table 1](#).

Results

We observed a lower rate of preterm birth in the 17 maternity hospitals from the network that participated in the ECHOCOL study, but it was not significant (6.63% in period A vs 6.43% in period B, a -0.20% difference; odds ratio [OR], 1.03; 95% confidence interval [CI], 0.99–1.06; $P=10$). There was no difference in the main factors for induced preterm birth between the 2

periods, except in “preterm labor,” which significantly decreased with time ([Supplemental Tables 2 and 3](#)). Hospitalization rates for threatened preterm labor remained stable over the 2 periods. However, we noticed a significant increase in the number of cervical length measurements from 24.7% to 49.6% (OR, 3.0; 95% CI, 2.94–3.05; $P<.0001$). This increase was also detected when the PMSI code for cervical length measurement was associated with the PMSI data for the prescription of progesterone and/or cerclage and/or pessary and/or for sick leave from work before 37 weeks of gestation (10.6% vs 20.9%; OR, 2.24; 95% CI, 2.18–2.31; $P<.0001$) ([Supplemental Table 4](#)).

SUPPLEMENTAL TABLE 1
Numbers of inclusions, patients lost to follow-up, and stillbirths by center

Center	Number of inclusions	Number of patients lost to follow-up	Number of asymptomatic short cervixes	Number of stillbirths
Aix/Pertuis	51	2	1	1
Aubagne	64	2	3	0
Bouchard	119	7+1 except criterion	0	0
Carpentras	90	1+1 except criterion	1	2
Conception	540	38	3	6
Draguignan	209	12	0	1
Etoile	419	18	7	1
Grasse	113	4	0	0
La Ciotat	169	11	3	0
Martigues	128	6	3	1
Nice	243	8	2	0
Nord	857	113	10	7
Saint-Joseph	319	10	0	1
Salon	51	11	1	0
Toulon	210	12	4	2
Urbain V	41	17	0	0
Vitrolles	134	4	0	0
Totals	3757	278	38	21

SUPPLEMENTAL TABLE 2**Data on singleton pregnancy deliveries in the 17 Mediterranean Network maternity hospitals that participated in ECHOCOL**

PMSI data	17 Mediterranean network maternity hospitals		
	Period A	Period B	
Total deliveries	100,333	100,202	OR (95% CI)=1.03 (0.99–1.06)
Preterm birth (<37 weeks of gestation)	6648 (6.63%)	6447 (6.43%)	<i>P</i> =.10

CI, confidence interval; *OR*, odds ratio.

SUPPLEMENTAL TABLE 3

Before-and-after study: main causes of singleton premature deliveries over periods A and B in the 17 Mediterranean Network maternity hospitals that participated in ECHOCOL

PMSI data		Period A				Period B					Comparison periods A and B					
		5	9	25	74	4	9	10	36	77	6	0.12	0.18	0.02	0.06	0.2
	Prævia placenta	5	9	25	74	4	9	10	36	77	6	0.12	0.18	0.02	0.06	0.2
	Chorioamnionitis	24	27	37	32	12	32	22	39	44	9	0.06	0.09	0.08	0.03	0.15
	preeclampsia	13	19	61	207	19	12	26	75	217	18	0.16	0.07	0.02	0.03	0.13
	Placental abruption	4	3	30	27	15	10	13	34	37	13	0.06	0.008	0.07	0.04	0.15
	Premature rupture of membranes	27	26	64	73	10	28	25	85	129	7	0.11	0.12	0.005	<.0001	0.16
	Intrahepatic cholestasis	0	1	1	10	0	0	0	1	25	0	/	0.5	0.5	0.004	/
	Fetal growth restriction	119	150	427	777	130	104	136	376	790	105	0.03	0.04	0.02	0.01	0.02
	Preterm labor	83	94	292	1858	78	68	70	253	1642	28	0.03	0.007	0.03	<.0001	<.0001
	Total (at least 1)	292	303	854	5199	620	293	302	792	5060	594					

SUPPLEMENTAL TABLE 4

Socioeconomic assessment of the management of asymptomatic short cervix over periods A and B in the 17 Mediterranean Network maternity hospitals that participated in ECHOCOL

PMSI data	17 Mediterranean Network maternity hospitals		
	Period A	Period B	Significance
Number of			
Total deliveries	100,333	100,202	/
Total deliveries (minus 2012)	68,070	100,202	/
Hospital admission for threatened preterm labor	10,853 (9.8%)	10,646 (9.6%)	OR (95% CI)=1.01 (0.991-1.05); <i>P</i> =.21
Cervical length measurement at <37 weeks of gestation outside hospitalization (reported to total deliveries)	24,777 (24.7%)	50,571 (49.6%)	OR (95% CI)=3.0 (2.94–3.05); <i>P</i> <.0001
Cervical length measurement with progesterone and/or cerclage and/or pessary and/or sick leave before 37 weeks of gestation (general health insurance regime) (reported to total deliveries minus 2012)	7178 (10.6%)	20,930 (20.9%)	OR (95% CI)=2.24 (2.18–2.31); <i>P</i> <.0001
Cervical length measurement with progesterone and/or cerclage and/or pessary and delivery at <37 weeks of gestation (reported to total deliveries)	210 (0.2%)	538 (0.5%)	OR (95% CI)=2.57 (2.19–3.01); <i>P</i> <.0001
Average length of hospital stay for threatened preterm labor with cervical length measurement ± cerclage and/or pessary and/or progesterone (d)			
- Before delivery	10.7	10.1	<i>P</i> =.30
- Before 34 weeks of gestation	12.6	12.4	<i>P</i> =.43

Population studied: all patients who gave birth and/or had a stay for preterm labor in one of the maternity hospitals of the network (last stay defining the classification in or outside the network).
CI, confidence interval; *OR*, odds ratio.