European Journal of Obstetrics and Gynecology 302 (2024) 65–72

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Full length article

The impact of cut-off values on the prevalence of short cervical length in pregnancy

Sofie H. Breuking [a,b,*], Charlotte E. van Dijk [a,b], Annabelle L. van Gils [a,b], Maud D. van Zijl [a,b], Brenda M. Kazemier [a,b,c], E. Pajkrt [a,b], for the Quadruple P research group

[a] Amsterdam UMC Location University of Amsterdam, Dept. of Obstetrics and Gynaecology, Meibergdreef 9, Amsterdam, the Netherlands
[b] Amsterdam Reproduction and Development Research Institute, Amsterdam, the Netherlands
[c] Department of Obstetrics, Wilhelmina's Children Hospital, UMC Utrecht, Utrecht, the Netherlands

ARTICLE INFO

Keywords:
Cervical length
Selection bias
Threshold value
Cut-off value

ABSTRACT

Background: A prior study suggested that implementing a cut-off value of ≤30 mm for a short cervical length (CL) could potentially introduce selection bias and alter the distribution of CL measurements. As such, the objective of this study is to evaluate how CL distribution and incidence of short CL are affected when using different cut-off values for a short CL.

Study design: This is a secondary analysis of the Quadruple P (QP) Screening study; a prospective cohort study that included low-risk patients with singleton pregnancies undergoing fetal anomaly scan at 18–22 weeks of gestation, including a CL measurement. Patients with a short cervix, defined as ≤35 mm, were subsequently counseled for the QP trial; a randomized controlled trial (RCT) comparing progesterone to cervical pessary for the prevention of preterm birth. If participation to the RCT was refused, patients with a CL ≤25 mm were advised to use progestogen. The primary objective of this current study was to assess the normal distribution of CL across the entire cohort and to assess the incidence of short CL when using the cut-off values of ≤35 and ≤25 mm. Normal distributions for CL were simulated based on mean and standard deviation(SD) of the original data. The Kolmogorov-Smirnov test was used to evaluate the distribution of the CL measurements. Moreover, to evaluate the motives behind ultrasound measurements around the cut-off value, sonographers were asked to fill out a qualitative questionnaire.

Results: The total cohort included 19.171 eligible participants who underwent CL measurement, with a mean CL of 43.9 mm (±8.1 SD). The distribution of all CL observed measurements deviated significantly from the normal distribution ($p < 0.001$). A total of 1.852 (9.7%) patients had short CL ≤35 mm, which was significantly lower than expected when compared to the simulated normal distribution (n = 2.661, 13.9%; $p < 0.001$). The incidence of short CL ≤25 mm in our cohort statistically differed from the simulated normal distribution (238, 1.2% vs 177, 0.9%; $p=0.003$). When comparing our data to the simulated normal distribution, the difference in distributions is most pronounced when examining the difference between 35 and 36 mm. Results of the questionnaire reveal sonographers claimed not to be influenced by a cut-off value for study participation or progesterone treatment.

Conclusion: This study demonstrates that using any cut-off value for a short CL influences the incidence and distribution of CL. When using a cut-off value of ≤35 mm for study inclusion, the incidence of measurements of a short CL is lower than the anticipated incidence compared to a normal distribution. However, when using a cut-off value of ≤25 mm for progesterone treatment, the frequency of CL measurements is higher than expected below this threshold compared to a normal distribution. This study highlights the risk of introducing selection bias, most likely unintentionally, when cut-off values for short CL are used, regardless of the specific value chosen. Therefore healthcare providers should measure the CL with caution if essential decisions depend on a specific cut-off value.

* Corresponding author at: Department of Obstetrics and Gynaecology, Amsterdam UMC, Meibergdreef 9, 1100 DD, Amsterdam, The Netherlands.
E-mail address: s.h.breuking@amsterdamumc.nl (S.H. Breuking).

https://doi.org/10.1016/j.ejogrb.2024.08.046
Received 17 June 2024; Received in revised form 29 August 2024; Accepted 30 August 2024
Available online 1 September 2024
0301-2115/

Introduction

The identification of patients at high risk of preterm birth (PTB) is crucial for implementing interventions aimed at delaying delivery or preventing PTB altogether [1]. An important risk factor for PTB is a midtrimester short cervical length (CL) based on transvaginal ultrasound (TVU) [1–4].

Worldwide, different cut-off values are used for a short CL to start preventive treatment, such as progesterone in order to prolong pregnancy [5,6], or as threshold in PTB prevention studies, ranging mostly from 20 to 35 mm [6–9]. A study by van der Ven et al. [1] showed an increased risk of PTB in Dutch nulliparous individuals with a CL between 25 and 35 mm that increased further to 34.2 % for a CL of 25 mm or shorter. Subsequently, the Quadruple P (QP) screening study was initiated: a multicenter prospective cohort study offering patients routinely CL measurements to assess the risk of PTB with a short CL. Based on the results from van der Ven [1], in this study a cut-off value for short CL was defined as ≤35 mm. Moreover, in July 2019, the guideline 'Progesterone for the Prevention of Preterm Birth in Singleton Pregnancies' was implemented in which was advised to start progesterone treatment in case of CL≤25 mm, thereby introducing another cut-off value. A study by van Os et al. [10] demonstrated that using a cut-off value of 30 mm for a short CL significantly affects the distribution of CL measurements and a pronounced difference ('the gap') of CL measurements around 30 mm was seen. Since the cut-off value of the QP screening study and the threshold to start progesterone treatment differ 5 mm from the value used by van Os et al. [10], it is plausible the gap will shift when assessing measurements around a new predefined cut-off value.

Given these considerations, it can be hypothesized that the measurement variability may impact the accuracy and reliability of identifying patients at risk for PTB when using any cut-off value. Therefore, the aim of this study is to examine the influence of a cut-off value for a short CL of ≤35 mm and ≤25 mm on the distribution and incidence of CL measurements in a cohort of low-risk, asymptomatic patients.

Methods

Study design

This is a secondary analysis of the Quadruple P (QP) Screening study; a prospective multicenter cohort study that included low-risk patients with singleton pregnancies undergoing fetal anomaly scan at 18–22 weeks of gestation, including a CL measurement. Exclusion criteria were a cervical cerclage in situ, identified major congenital abnormalities, previous spontaneous PTB < 34 weeks and previous participation in this trial.

Patients with a short cervix, defined as ≤35 mm, were subsequently counseled for the QP randomized controlled trial (RCT)[11]; a multicenter RCT that compared the effectiveness of vaginal progesterone and cervical pessary in the prevention of PTB in low-risk patients with a short CL. Patients refusing participating, were advised the use of progesterone treatment in case of short CL ≤25 mm according to the Dutch national guideline´prevention of preterm birth' unless there was an indication for a physical examined indicated cerclage (CL <10 mm with cervical dilation or bulging membranes).

Ethical consideration

Both the QP screening study and the QP RCT were registered and approved by the Medical ethical committee of the Amsterdam UMC at 8th of March 2018 (NL59156.018.17) and 9th of November in 2013 (NL42926.018.13), respectively.

All patients screened for eligibility for the QP screening study, were asked for informed consent to collect data using their medical records and pregnancy outcomes for research purposes.

Cervical length measurement

The QP screening study included a standardized protocol concerning the CL measurements. This protocol was formed according to the criteria for transvaginal CL measurement as proposed by the Society for Maternal and Fetal Medicine [7]. In short, this includes measurement by transvaginal sonography, where the probe was placed in the anterior fornix of the vagina and a sagittal view of the cervical canal was obtained. The distance from the external os and the V-shaped notch at the internal os was measured. Every time a cervical length was measured, it was done for three minutes to be able to observe any cervical changes due to contractions. The shortest measurement was recorded.

All participating sonographers were trained and qualified according to the national guidelines and the scans were performed on ultrasound systems that met the quality requirement composed by the National Institute of Health & Environment [12,13].

Data collection and extraction

A total of 25 institutions participated in the QP screening study. This included four primary obstetric healthcare ultrasound centers, 16 secondary level care hospitals and five tertiary academic hospitals. Cervical length measurements were extracted from this QP screen cohort and the measurements in relation to the cut-off values of 35 and 25 mm was analyzed. Institutions including 50 participants or less were excluded from this analyses, due to the requirement of a minimum number of CL measurements essential for the evaluation of a normal distribution.

Simulated cohort

To be able to compare the data to a cohort with normal distributions of the CL, a simulated cohort was created based on the mean and standard deviation(SD) of the original data and will be referred to as 'simulated cohort'.

Outcome measures

The primary objective was to assess the distribution across the entire cohort and to evaluate the incidence of CL measurements ≤35 and ≤25 mm compared between the observed and simulated cohort.

Distributions within groups were investigated as defined in the study by van Os et al. [10], including:

1. Measurements obtained at various levels of healthcare.
2. Institutions categorized based on patient inclusion volume, with low, intermediate and high volume centers defined as <500, 500–1000, and >1000 patients, respectively.

To compare the distribution affected by the implementation of the guideline 'progesterone for prevention of preterm birth in singleton pregnancies' and its influence on the cut-off of ≤25 mm, a subgroup analysis before and after July 2019 was conducted.

Qualitive questionnaire for sonographers

After reviewing the results of this current study, we aimed to further understand the reasoning of the sonographer when utilizing a cut-off value. In February 2024, a national symposium was organized for

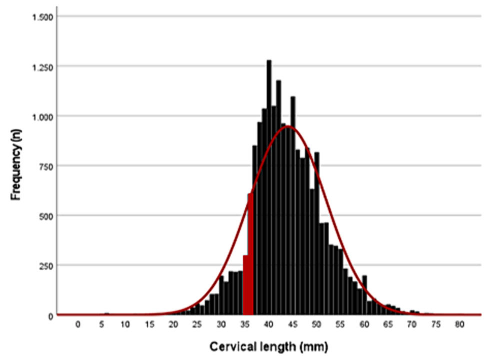

Fig. 1A. Distribution of cervical length (CL) measurement in total cohort (n = 19.171) compared to a normal distribution (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

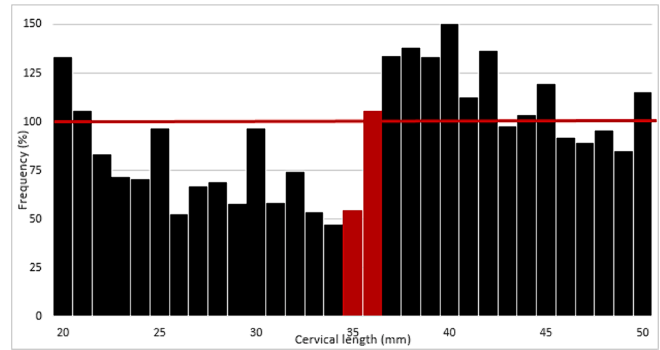

Fig. 1B. Number of cervical length(CL) measurements as a percentage of number of simulated CL measurements (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

sonographers for teaching purposes. The participants of the symposium included sonographers measuring CLs and including patients for the QP-screening study as well. Therefore, we asked all sonographers participating in this symposium to complete a questionnaire regarding CL measurement in two different scenarios.

1. A scenario detailing the methodology for measuring CL around a predetermined cut-off value for study eligibility.
2. A scenario detailing the methodology applied for measuring CL around a predetermined cut-off value for progestogen, a proven treatment aimed at preventing PTB.

In both scenarios, the focus was to capture the perspectives of the sonographers regarding their preferred approaches. The options included to measure objectively regardless of a cut-off value, to extend the CL beyond the cut-off value to alleviate stress on pregnant individuals, extend the cut-off value to reduce an administrative burden for themselves or, shorten the CL below the cut-off value to ensure no treatment or study inclusion is withheld. (Supplementary).

Statistical analysis

The Kolmogorov-Smirnov test was used to evaluate the distribution of the CL measurements. A Chi-square test was used to assess the statistical significance of incidence of measurements in the observed versus the simulated distribution. Statistical analysis and the simulated normal distribution was performed in SPSS (IBM SPSS Statistics v.28).

Results

Between April 2014 and March 2022, 19.288 patients were included in the QP screening study.

We excluded eight institutions (n = 117 patients) since the only CL measurement they provided, were of patients eligible for the QP RCT or the institution included less than 50 patients.

Finally, 19.171 patients were included for analysis. The total CL mean was 43.9 mm (±8.1SD) at a gestational age of 19 weeks and 6 days. The distribution of all CL measurements observed deviated significantly from the normal distribution ($p < 0.001$; Fig. 1A). A CL of ≤35 mm was measured in 1852 patients (9.7 %) which was significantly lower compared to the simulated cohort (2661 patients(13.9 %); $p < 0.001$). A total of 238 participants had a CL of ≤25 mm, which is significantly more than expected compared the simulated cohort (1.2 % vs 0.9 %; $p = 0.003$, Table 1).

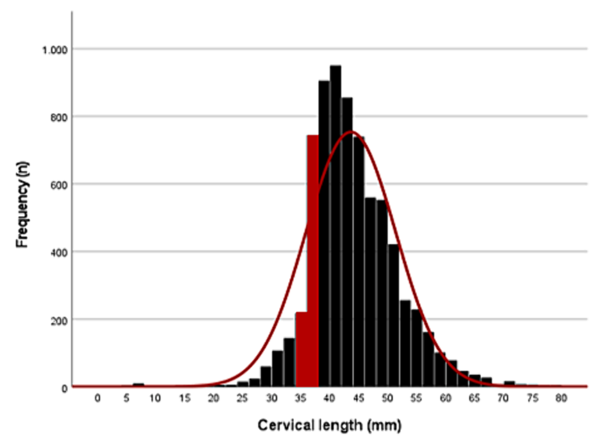

Fig. 2A. Distribution of cervical length (CL) measurement in institutions of primary care (n = 7323) compared to a normal distribution (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Measurements around 35 mm deviate the most from the normal distribution, with measurements below 35 mm being less common, while above 35 mm there is an increase in measurements. The difference, or 'the gap', in distributions is most pronounced when examining the difference between 35 and 36 mm, wherein there is a deviation of 51 % from the original data compared to the simulated data. When looking at the incidence of measurements between 25 and 26 mm, the gap is a

Table 1
Descriptive characteristics of cervical length measurements of total cohort.

	Number of institutions	Number of inclusions	Mean cervical length (mm)	Cervical length ≤35 mm n (%)	p-value	Cervical length ≤25 mm n (%)	P-value
observed simulated	17	19.171	43.9 ± 8.1	1852 (9.7) 2661 (13.9)	**<0.001**	238(1.2) 177(0.9)	**0.003**

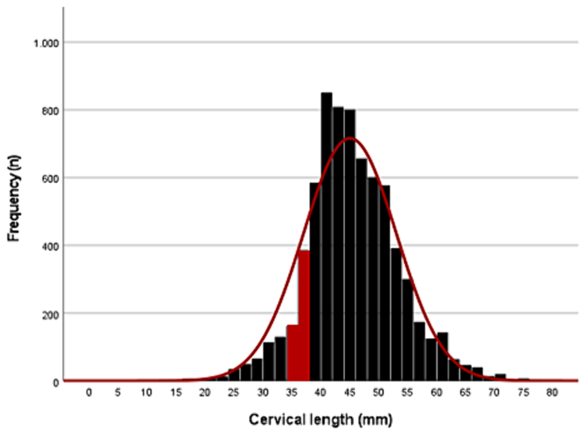

Fig. 2B. Distribution of cervical length (CL) measurement in institutions of secondary care (n = 6949) compared to a normal distribution (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

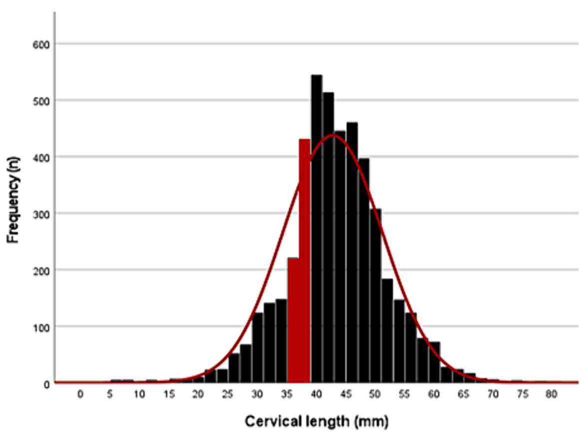

Fig. 2C. Distribution of cervical length (CL) measurement in institutions of tertiary care (n = 4573) compared to a normal distribution (red line).

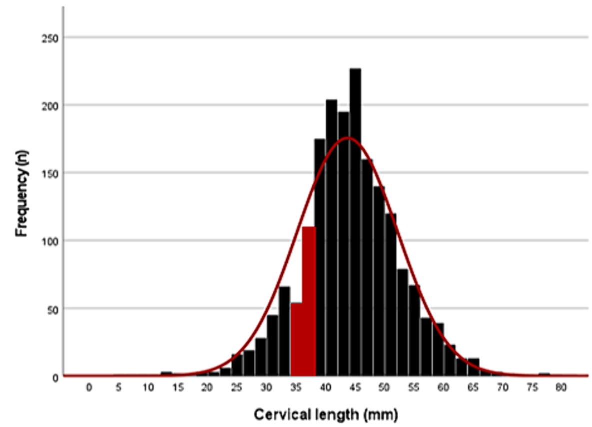

Fig. 3A. Distribution of cervical length (CL) measurement based on inclusion volume of cervical length measurements of > 1000 (n = 14.712) compared to a normal distribution (red line).

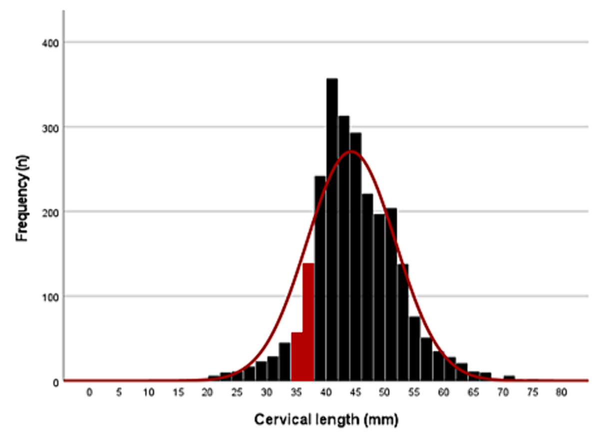

Fig. 3B. Distribution of cervical length (CL) measurement based on inclusion volume of cervical length measurements of 500–1000 (n = 2281) compared to a normal distribution (red line).

substantial difference of 44 %. (Fig. 1B).

The distribution of CL were not normally distributed in all institutions with different levels of care (Fig. 2; $p \leq 0.001$). For all levels, the gap between 35 and 36 mm was visible, but most pronounced in the primary care level institutions (Fig. 2A).

Also, the incidence of CL ≤35 mm was significantly less frequent in institutions for primary and secondary care when compared to the simulated cohorts (primary care 7.8 % vs 13.6 %; $p < 0.001$ and secondary care 8.2 % vs 13.8 %; $p < 0.001$). For tertiary care, the incidence of CL ≤35 mm was comparable to the simulated cohort(15.0 % vs 14.4 %; $p = 0.43$). When investigating the incidence of measurements ≤25 mm, observed measurements were significantly lower in the primary care settings (0.6 % vs 1.0 %; $p = 0.014$), while in secondary and tertiary care an increased trend of measurements were seen compared to the simulated cohort (secondary care 1.0 % vs 0.8 %; $p = 0.19$ and tertiary care 2.6 % vs 1.1 %; $p < 0.001$). (Table 2).

Table 2
Descriptive characteristics of cervical length measurements based on different level of care.

	Number of institutions	Number of inlcusions	Mean cervical length (mm)	Cervical length ≤35 mm N(%)	p-value	Cervical length ≤25 mm N(%)	P-value
Primary care observed simulated	4	7323	43.6 ± 7.7	568 (7.8) 995 (13.6)	**<0.001**	44 (0.6) 70 (1.0)	**0.014**
Secondary care observed simulated	9	7203	45.0 ± 8.0	588(8.2) 997 (13.8)	**<0.001**	73 (1.0) 58 (0.8)	0.19
Tertiary care observed simulated	4	4645	42.7 ± 8.5	696 (15.0) 669 (14.4)	0.43	121 (2.6) 49(1.1)	**< 0.001**

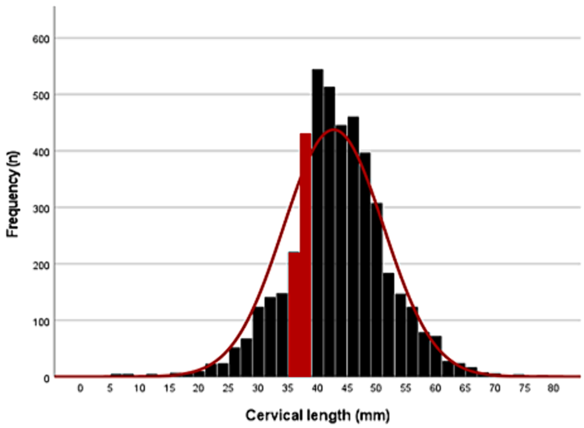

Fig. 3C. Distribution of cervical length (CL) measurement based on inclusion volume of cervical length measurements of <500 (n = 1867) compared to simulated normal distribution (red line).

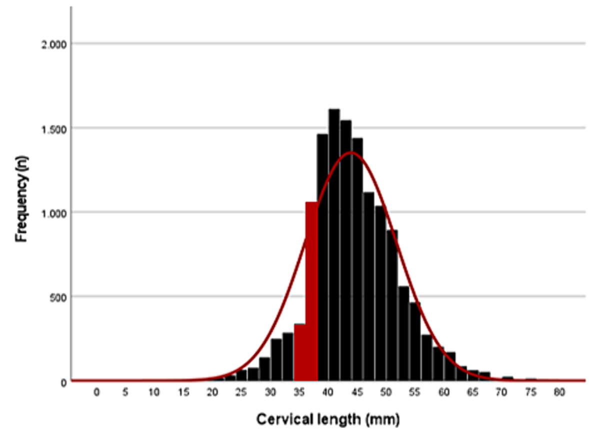

Fig. 4A. Distribution of cervical length (CL) measurement before 07–2019 implementation of prevention of preterm birth guideline (n = 12.926).

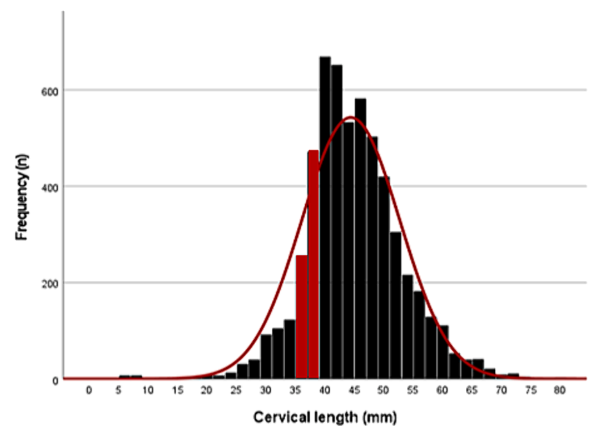

Fig. 4B. Distribution of cervical length (CL) measurement after 07–2019 implementation of prevention of preterm birth guideline (n = 5.637).

When categorizing the participating centers based on the number of inclusions into low, intermediate and high, all distributions were not normally distributed (Fig. 3; p ≤ 0.001). Lower incidences of CL ≤35 mm were found across all categories compared to the simulated cohort, whereas an increasing trend was noted for the incidence of CL ≤25 mm. Additional descriptive details can be found in Table 3.

In subgroup analyses on differences before and after the implementation of the guideline for the prevention of PTB in which progesterone was advised for short CL, we observed that both before and after, the distribution is not normally distributed (Fig. 4; P < 0.001). As demonstrated in Table 4, the number of patients with a CL of ≤35 mm was significant less in comparison to the simulated cohort both before and after implementation of the guideline(before implementation 9.2 % versus 13.9 %; p < 0.001, after implementation 8.8 % versus 13.7 %; p < 0.001). Conversely, the incidence of participants with a CL of ≤25 mm was comparable for both cohorts when comparing to the simulated cohort(before implementation 1.2 % versus 1.0 %; p = 0.24, after implementation 1.3 % versus 0.8 %; p = 0.25).

Qualitative results from sonographers perspective

A total of 54 sonographers completed the questionnaire. Among them, 34 sonographers (55.6 %) practiced in primary care settings, 13 (24.1 %) in secondary care hospitals and 11 (20.4 %) in tertiary hospitals.

Regarding the methodology for measuring CL when a predefined cut-off value determined study eligibility, all 54 respondents (100 %) indicated measuring the CL objectively without considering the cut-off value.

When queried about measuring CL around a cut-off value where patients would receive a proven treatment, two sonographers (3.7 %) stated to measure just below the cut-off value to ensure treatment eligibility. In contrast, the remaining 52 sonographers (96.3 %) reported adhering to their standard practice of measuring the CL objectively.

Discussion

Main findings

This study demonstrates that the distribution of CL measurements in a large cohort of low-risk, asymptomatic singleton pregnancies, differs from a normal distribution when a predefined cut-off value is used. The decrease in CL measurements at ≤35 mm might be influenced by the cut-

Table 3
Descriptive characteristics of cervical length measurements based on volume of cervical length measurements.

	Number of institutions	Number of inlcusions	Mean cervical length (mm)	Cervical length ≤35 mm N (%)	p-value	Cervical length ≤25 mm N (%)	p-value
<500 observed simulated	7	1867	43.6 ± 8.5	244 (13.0) 253 (13.5)	0.67	36 (1.9) 17 (0.9)	**0.009**
500–1000 observed simulated	3	2281	44.0 ± 7.4	200 (7.9) 346 (13.6)	**< 0.001**	33 (1.3) 19 (0.7)	0.051
>1000 observed simulated	6	14,752	43.9 ± 8.1	1408 (9.5) 2062 (14.0)	**< 0.001**	169 (1.1) 141 (1.0)	0.11

Table 4
Descriptive characteristics of cervical length measurements before and after implementation of progestogen treatment.

	Number of inlcusions	Mean cervical length (mm)	Cervical length ≤35 mm N(%)	p-value	Cervical length ≤25 mm N(%)	p-value
<08–2019						
observed	13.362	43.8 ± 7.9	1224 (9.2)	**< 0.001**	154 (1.2)	0.24
simulated			1862 (13.9)		134 (1.0)	
>08–2019						
observed	5663	43.4 ± 8.3	501 (8.8)	**< 0.001**	33 (1.3)	0.25
simulated			776 (13.7)		43 (0.8)	

off value for study eligibility, while the incidence in CL measurements at ≤25 mm appears to be influenced by the cut-off value for treatment with progestogens.

Strengths and limitations

The study's strength lies in the inclusion of multiple settings at primary, secondary and tertiary levels of care, allowing a broader representation of diverse care settings and patient groups, increasing the relevance of the results for generalization. In addition, this is a specific low-risk cohort, which is less often described separately and involves a large number of inclusions, which contributes to the reliability and validity of the study.

One limitation is that sonographers did not have additional specific training before being allowed to measure the CL. However, the protocol included standardized guidelines as described by the SMFM [7] that the CL measurement needed to adhere to in order to achieve the same quality for all measurements. Despite these specific guidelines, we still observe a gap around cut-off values in this study, which further emphasizes the value of standardizing the method of obtaining the image and measuring.

Another limitation is that ethnicity or socioeconomic background could not be considered, since variations in the distribution of CLs exist across diverse populations, ethnicities and income levels [6,14]. The mean CL of this cohort (43.9 mm) is substantially higher compared to studies by Iams et al. [15] (mean 35.2 mm) and Heath et al. [16] (median 38 mm). A closer examination of Fig. 1.A reveals a rightward shift in the distribution, suggesting systematic overmeasurement of CL or differences in ethnicity across the studies. The hypothesis of CL differences in ethnicity is supported by the comparable mean CL in the study by van Os et al. [10] (mean 44.2 mm), also examining a Dutch cohort.

Additionally, since this study is focused on the effect of using a cut-off value, these limitations do not contradict the conclusion of this study.

Interpretation (in light of other evidence)

The findings of this study are in line with van Os et al. [10] investigating the cut-off value of ≤30 mm, where a significantly deviation from the normal distribution and a low prevalence of CL ≤30 mm was found (1.8 % versus 4.9 %; $p < 0.0001$). Both studies demonstrate that the most pronounced deviations from a normal distribution arise just below the cut-off value. Therefore, it can be concluded that the gap shifts with the cut-off value. This also supports the hypothesis that the use of any specific cut-off value introduces observer bias and consequently affects the normal distribution.

The study of v Os et al. [10] hypothesized that sonographers may measure the CL above 30 mm in order to prevent referral that may cause distress to patients, as this cut-off value was the threshold for participation in a study. Similar observations are noted in the present study, where the gap between 35 and 36 mm is most pronounced, precisely aligning with the threshold for participation in the RCT [11]. On the contrary, the incidence of a short cervix increases significantly when using the cut-off value of ≤25 mm, which appears to be influenced by the threshold for treatment with progesterone. This could imply sonographers might underestimate the length of ≤25 mm to avoid withholding treatment from their patient. Also, the finding that the incidence of CL ≤25 mm is lower only in primary care setting supports the hypothesis that measurements near the cut-off value may be slightly adjusted to avoid referral, as midwives must refer patients to the hospital for progesterone prescription.

This underscores that measurements around cut-off values present a clinical dilemma for the sonographer, making them more alert. In this context, it's important to recognize that cut-off values may not fully capture the complexity of individual patient risk profiles, potentially leading to oversimplification. Taking into account individual patient characteristics within the broader clinical context is essential for making well-informed decisions.

Previous studies have demonstrated that the significant risk of selection bias is more likely when the assessor is not blinded to the treatment options.[17,18] Moreover, in studies where investigators take measurements, people tend adjust values based on the preexisting ideas about treatments, often unintentionally.[19] Since the sonographers in the QP Screen were aware of the cut-off values and the consequences, the incidence and difference to a normal distribution could be explained. This phenomenon could potentially lead to over- or under-treatment, thereby imposing a costly burden on society and mentally on patients, who may undergo unnecessary stress and anxiety. Women who are not at risk of PTB may receive treatment and subsequently not deliver prematurely, leading to an distorted perception of progesterone's effectiveness. However, since progesterone has proven to be effective in multiple double blinded RCTs [5], this theory remains speculative.

When reviewing sonographers' questionnaires, the majority reported not to be influenced by cut-off values for study participation or progesterone treatment. However, our results reveal a substantial discrepancy between measurements at 35 mm and 36 mm, with fewer measurements below 35 mm. Conversely, the incidence of measurements increases at 25 mm. The discrepancy between results and questionnaire responses suggest unintentional influence from cut-off values. In fact, of those surveyed, 96.3 % (n = 51) indicated that they measure objectively, while there is clearly bias in the measurement process. The higher frequency of measurements below 25 mm could be explained by the theory that healthcare professionals are more inclined to make sure not to withhold someone from treatment and tend to rather overtreat than deny treatment. Especially if the treatment is not surgical and does not entail serious side effects. For example, 3.7 %(n = 2) admitted to intentionally measuring slightly shorter to start progesterone.

This study highlights the introduction of selection bias, most likely unintentionally, irrespective of the chosen cut-off value. This bias may extend to any subjective ultrasound measurement, underscoring the importance of measuring with caution when cut-off values are used.

Research implications

An optimal approach for future studies could involve a similar design aligning with Kuusela et al. [20] where sonographers maintained independent from treatment decisions. However, in clinical practice, this might not be feasible. We should be aware that there is a high risk on selection bias when a cut-off value of a short cervical length is used.

The only entity capable of measuring completely objectively and avoiding selection bias, by disregarding potential treatments, is a computer. A recent study by Sarno et al. [21] introduced the role of artificial intelligence (AI) to reduce inter-and intraobserver variability in fetal ultrasound. However, AI for CL measurement has not been evaluated yet, although a study performed in 2004 did propose an image processing algorithm that provides anatomic landmarks of the cervix for TVU, reducing the intraobserver variability by 75 %[22]. Therefore, AI may help providing an objective CL measurement, without the introduction of selection bias when a cut-off value is used. However, this should be validated through further research, keeping in mind that cut-off values may not fully capture the complexity of individual patient risk profiles.

Conclusion

Using a cut-off value for a short CL influences the distribution and incidence of a short CL. When using a cut-off value of ≤35 mm for study eligibility, the incidence of measurements ≤35 mm is less than expected compared to a normal distribution. Nevertheless, employing a cut-off value of ≤25 mm for progesterone treatment increases the incidence of CL measurements below this threshold. This study highlights the risk if cut-off values are used for a short CL, regardless of the used value, selection bias is introduced. Healthcare professionals should be aware of this and measure the CL with caution when essential decisions depend on a cut-off value for a short CL.

Financial support of the research

No financial support was received for this study.

Paper presentation

Abstract presented at Society for Maternal Fetal Medicine (SMFM) 44th annual meeting February 10-14th 2024.

Tweetable statement

The use of any cut-off value for a short cervical length in pregnancy introduces selection bias and affects the normal distribution and incidence of a short cervix.

CRediT authorship contribution statement

Sofie H. Breuking: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Visualization, Writing – original draft, Project administration. **Charlotte E. van Dijk:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Annabelle L. van Gils:** Writing – review & editing, Data curation. **Maud. D. van Zijl:** Writing – review & editing, Data curation. **Brenda M. Kazemier:** Writing – review & editing, Supervision. **E. Pajkrt:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2024.08.046.

References

[1] van der Ven J, van Os MA, Kazemier BM, et al. The capacity of mid-pregnancy cervical length to predict preterm birth in low-risk women: a national cohort study. Acta Obstet Gynecol Scand 2015;94(11):1223–34. https://doi.org/10.1111/aogs.12721.
[2] van Zijl MD, Koullali B, Mol BW, Pajkrt E, Oudijk MA. Prevention of preterm delivery: current challenges and future prospects. Int J Womens Health 2016;8:633–45. https://doi.org/10.2147/IJWH.S89317.
[3] Iams JD, Goldenberg RL, Mercer BM, et al. The Preterm Prediction Study: recurrence risk of spontaneous preterm birth. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 1998;178(5):1035–40. https://doi.org/10.1016/s0002-9378(98)70544-7.
[4] Hessami K, D'Alberti E, Mascio DD, Berghella V. Universal cervical length screening and risk of spontaneous preterm birth: a systematic review and meta-analysis. Am J Obstet Gynecol MFM 2024. https://doi.org/10.1016/j.ajogmf.2024.101343.
[5] Group E. Evaluating Progestogens for Preventing Preterm birth International Collaborative (EPPPIC): meta-analysis of individual participant data from randomised controlled trials. Lancet 2021;397(10280):1183–94. https://doi.org/10.1016/S0140-6736(21)00217-8.
[6] Bortoletto TG, Silva TV, Borovac-Pinheiro A, et al. Cervical length varies considering different populations and gestational outcomes: Results from a systematic review and meta-analysis. PLoS One 2021;16(2):e0245746.
[7] Society for Maternal-Fetal Medicine, 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(3):B2–7. https://doi.org/10.1016/j.ajog.2016.04.027.
[8] Nicolaides KH, Syngelaki A, Poon LC, et al. A randomized trial of a cervical pessary to prevent preterm singleton birth. comparative study multicenter study randomized controlled trial research support, non-U.S. Gov't. N Engl J Med 2016;374(11):1044–52. https://doi.org/10.1056/nejmoa1511014.
[9] Hui AS, Lao TT, Ting YH, Leung TY. Cervical pessary in pregnant women with a short cervix. Lancet 2012;380(9845):887. https://doi.org/10.1016/S0140-6736(12)61504-9. author reply 887.
[10] van Os MA, Kleinrouweler CE, Schuit E, et al. Influence of cut-off value on prevalence of short cervical length. Comparative Study Multicenter Study Randomized Controlled Trial. Ultrasound Obstet Gynecol 2017;49(3):330–6. https://doi.org/10.1002/uog.15967.
[11] van Dijk CE, van Gils AL, van Zijl MD, et al. Cervical pessary versus vaginal progesterone in women with a singleton pregnancy, a short cervix, and no history of spontaneous preterm birth at less than 34 weeks' gestation: open label, multicentre, randomised, controlled trial. BMJ 2024;384. https://doi.org/10.1136/bmj-2023-077033. e077033.
[12] Rijksinstituut voor Volksgezondheid en Milieu. Kwaliteitseisen tweede trimester SEO (structureel echoscopisch onderzoek). . 2022.
[13] Rijksinstituut voor Volksgezondheid en Milieu. Kwaliteitseisen echoapparatuur en beeldopslag voor prenatale screening. 2020.
[14] Costantine MM, Ugwu L, Grobman WA, et al. Cervical length distribution and other sonographic ancillary findings of singleton nulliparous patients at midgestation. Am J Obstet Gynecol. 2021;225(2). https://doi.org/10.1016/j.ajog.2021.02.017. 181 e1–181 e11.
[15] 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(9):567–72. https://doi.org/10.1056/NEJM199602293340904.
[16] Heath VC, Southall TR, Souka AP, Elisseou A, Nicolaides KH. Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery. Ultrasound Obstet

Gynecol Nov 1998;12(5):312–7. https://doi.org/10.1046/j.1469-0705.1998.12050312.x.
[17] Hrobjartsson A, Thomsen AS, Emanuelsson F, et al. Observer bias in randomized clinical trials with time-to-event outcomes: systematic review of trials with both blinded and non-blinded outcome assessors. Int J Epidemiol 2014;43(3):937–48. https://doi.org/10.1093/ije/dyt270.
[18] Mahtani K, Spencer EA, Brassey J, Heneghan C. Catalogue of bias: observer bias. BMJ Evid Based Med 2018;23(1):23–4. https://doi.org/10.1136/ebmed-2017-110884.
[19] Braithwaite RS, Ban KF, Stevens ER, Caniglia EC. Rounding up the usual suspects: confirmation bias in epidemiological research. Int J Epidemiol 2021;50(4):1053–7. https://doi.org/10.1093/ije/dyab091.
[20] 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(2):195–206. https://doi.org/10.1111/1471-0528.16519.
[21] Sarno L, Neola D, Carbone L, et al. Use of artificial intelligence in obstetrics: not quite ready for prime time. Am J Obstet Gynecol MFM 2023;5(2):100792. https://doi.org/10.1016/j.ajogmf.2022.100792.
[22] Wu M, Fraser RF, Chen CW. A novel algorithm for computer-assisted measurement of cervical length from transvaginal ultrasound images. IEEE Trans Inf Technol Biomed 2004;8(3):333–42. https://doi.org/10.1109/titb.2004.832548.