### MODELLING THE PROGRESSION OF CERVICAL DILATION IN SPONTANEOUS LABOUR

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#### Introduction

The first attempt to model the progression of cervical dilation during spontaneous labour of pregnant women dates back to 1955 [1]. From the graphical analysis of the time profiles of dilation observed in 500 women aged 13 to 42 years, the Author derived a mean labour sigmoid curve, consisting in a latent phase followed by an active phase ending in a deceleration phase. This cervimetric graph, or cervicogram, is still reported in current manuals of obstetrics. Zhang *et al* [2, 3] fitted cervical dilation profiles with mixed models based on 10<sup>th</sup> or 8<sup>th</sup> degree polynomials, and concluded that the duration of latent and active phase. For this reason, these Authors supply charts reporting the empirical 95<sup>th</sup> centile of the distribution of labour duration for different values of cervical dilation. The aim of this presentation is to show the use of parsimonious nonlinear mixed models to trace cervimetric charts, reporting current cervical dilation *vs* time to full dilation.

#### Data and methods

Data here used derive from an observational study including 328 low-risk women (146 primiparae and 182 multiparae), who delivered at Buzzi Children's Hospital between April and June 2013 [4]. All women delivered vaginally at term, after uncomplicated single pregnancy and spontaneous labour managed by midwives, without any kind of medical intervention.

We had to take into account a lot of difficulties and hindrances to construct a model for the progression of cervical dilation. The time of the beginning of labour is unknown (1); women are admitted to labour room at different degrees of dilation (2); cervical dilation measures are taken at irregular intervals as required by clinical practice (3); midwives usually assess cervical dilation with fingers, though the measure is reported in cm, from 0 (no dilation) to 10 (full dilation) (4); full cervical dilation is not indicated with a measure, but with a value of 10 cm, arbitrarily assigned to all women (5); individual dilation profiles are largely incomplete, a maximum of 5 measures per woman was recorded before full dilation, and only 60 women (18%) were assessed twice or more (6); the progression of cervical dilation is extremely erratic (7).

Since dilation cannot be related to the unknown time from the onset of labour, we considered, as already suggested by Zhang *et al* [2], the time remaining to the attainment of full cervical dilation (t, time to full dilation), and expressed current dilation ( $y_i(t)$ , from 1 to 9 cm) observed in the i<sup>th</sup> woman as a function of a parsimonious nonlinear model (3 parameters only), instead of the 9 to 11 parameters of the polynomials used by Zhang *et al* [2, 3]:

$$logit(y_i(t)/10) = \alpha_i + \beta_i \times log(t + \delta_i) + \varepsilon_{i(t)}$$
<sup>{1}</sup>

In {1},  $logit(y_i(t)/10)$  is a linear function of the log-transformation of time: parameter  $\beta_i$  is the dilation velocity constant, the ratio  $\alpha_i/\beta_i$  determines the time at maximum dilation velocity, and  $\delta_i$  modulates the shape of

the log-transformation of time; intra-individual random terms  $\varepsilon_{i(t)}$  were assumed to approximate a normal distribution, with variance proportional to  $\{[E(y_i(t))/10][1-E(y_i(t))\}^{-1}\}$ . When back-transformed to the original scale, expression {1} defines a family of strongly asymmetrical never-decreasing (since cervical dilation is an irreversible process) sigmoid curves, with a slight slowdown of dilation velocity a little before, or at full dilation, in this latter case the curve presents an exponential shape.

Because cervical dilation profiles were largely incomplete, we could not resort to the usual two-stage models [5] to trace cervimetric charts, but we were forced to adopt a nonlinear mixed model [6], which can obtain estimates of the parameters of the individual cervical dilation curves also for the women with profiles made up by a number of observations lower the number of parametes (in our case 1 or 2 assessments only):

$$logit(y_i(t)/10) = \alpha_0 + \alpha_i + \alpha_P x + (\beta_0 + \beta_i + \beta_P x) log(t + \delta_0 + \delta_P x) + \varepsilon_{i(t)}$$
<sup>{2}</sup>

Parity (x=0 for primiparae, x=1 for multiparae) was included as a covariate into model {2}, since multiparae are known to progress somewhat faster in active-phase labour [7]. Parameters  $\alpha_0$  and  $\beta_0$  refer to primiparae,  $\alpha_P$  and  $\beta_P$  refer to the difference between multiparae and primiparae, whereas  $\delta_0$  and  $\delta_P$  modulate the log-transformation of time by parity. Random terms  $\alpha_i$  and  $\beta_i$ , which model inter-individual differences, are assumed to have bivariate normal distribution with  $E(\alpha_i)=E(\beta_i)=0$  and unstructered covariance matrix  $Cov(\alpha_i,\beta_i)=[\sigma_{\alpha}^2,\sigma_{\alpha\beta},\sigma_{\beta}^2]$ .

Models {1} and {2} were fitted using PROC NLIN and NLMIXED of SAS/STAT® software (SAS Institute, Cary, NC; v.9.4, 2013).

#### Results

Although based on 3 parameters only, model {1} proved to be flexible enough to describe cervical dilation profiles of rather different shape. As shown in figure 1 (left), concerning primiparous women, profiles may present an inflection point (i.e. a maximum dilation velocity) already 4 hours before the attainment of full dilation (orange curve) or at about 1 hour (dark red and green curves) or in the last half hour of the dilation process (the remaining profiles). Ten hours before the attainment of full dilation there are women with no more than 1 cm dilation and women with so much as 4 cm dilation. During the labour, dilation velocity may vary considerably from woman to woman: 10 hours before the attainment of full dilation, dilation velocity is always less than 0.5 cm/hr, but maximum velocity may be more than 3.5 cm/hr when initial dilation is 1 cm (red and blue curves) or be about 1 cm/hr when initial dilation is 4 cm (green curve). It is worth noting that women with different initial dilation (red curve: 1.7 cm, olive green curve: 2.7 cm) may present the same maximum velocity (1.7 cm/hr), since their dilation profiles differ in convexity.

Figure 1 (right) shows, plotted on the cervicometric charts traced with mixed model {2}, the cervical dilation profiles (green lines) of the 95 primiparous women with 2 or more assessments and the dilation values (green dots) of the 51 women with 1 assessment only, predicted on the basis of model {2}.

Green dots As expected, though individual profiles differ largely, the large majority of them lies completely within the interval 3<sup>rd</sup> – 97<sup>th</sup> centile of the cervicometric charts. At 10 hours, the distribution of dilation values conditional on time to full dilation is highly right skewed, then positive skewness decreases and the distribution becomes symmetrical when median dilation is 5 cm, and left skewed subsequently. The same results were observed in the 182 multiparous women included in the study.

We observe that a 4 cm dilation is the  $97^{\text{th}}$  centile 10 hours before the attainment of full dilation, and is the  $3^{\text{rd}}$  centile at 0.5 hours. This means that, at 10 hours, 3% of women present more than 4 cm dilation, but that another 3% of women still present a 4 cm dilation half an hour before the end of dilation process. So

a 4 cm dilation observed from 10 to 0.5 hours before the attainment of full dilation cannot be regarded as unusual. Analogously, at 10 hours, 10% and 25% of women present more than 3 and 2 cm dilation, respectively, but 10% and 25% of women still present a 3 or 2 cm dilation, 1 and 3 hours before the end of dilation process.

Our data confirm that labour progresses faster in multiparae than in primiparae: e.g. a 5 cm dilation is achieved 45 min *vs* 1 hour and half before the end of dilation process in multiparae. Primiparae present a wider variability (+30% in terms of interquartile range) in the distribution of dilation values conditional on time to full dilation.

#### Conclusions

In 1955 Friedman [1] wrote: "The dynamic nature of parturitional change has, in the past, rendered exceedingly difficult the detailed and critical analysis of its vagaries". Actually, try to model the kinetics of the cervical dilation process turned out still to be a very hard task. Nonetheless some important points were established: (1) a parsimonious nonlinear parametric model is suitable to describe very different shapes of the dilation process, (2) mixed nonlinear models allow to trace plausible cervimetric charts even in the case of dilation profiles largely incomplete, (3) the above model provide quantitative estimates of the inter-individual variability and of the difference in the progression of cervical dilation between primiparae and multiparae.

Unfortunately, the classical cervicograms give an unrealistic and useless picture of labour progression when referred to a single patient, the course of cervical dilation being largely erratic even in the case of spontaneous labour in uncomplicated pregnancies. In the first place, during labour the time remaining to the attainment of full cervical dilation is unknown, so the charts cannot be used in obstetric practice; in the second place a subsequent value of dilation cannot be predicted on the basis of the previous assessments. For these reasons, Ferrazzi *et al* [4] proposed cervimetric charts reporting the distribution of time needed to gain 1 cm in cervical dilation as a function of current dilation. Although theoretically usable, the practical value of these charts remains very low. In primiparous women, the time needed to gain 1 cm in dilation ranges from 10 (10<sup>th</sup> centile) to 110 min (90<sup>th</sup> centile) when current dilation is 1 cm, and from 5 to 70 min when current dilation is 9 cm. In multiparous women, the reference interval is somewhat narrower, the time needed ranging from 3 to 70 min when current dilation is 1 cm, and from 2 to 45 min when current dilation is 9 cm. On the basis of these results they concluded that the progression of cervical dilatation in normal human labour is unpredictable.

#### References

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**Figure 1.** Left: examples of individual cervical dilation profiles, observed (solid circles) in 7 primiparous women, and predicted by model {1} (continuous lines). Right: cervical dilation profiles (green lines) of the 95 primiparous women with 2 or more assessments and dilation values (green dots) of the 51 women with 1 assessment only, predicted on the basis of mixed model {2}, and plotted on the cervicometric charts traced with model {2}. Time to full dilation denotes the time remaining to the attainment of full cervical dilation.



# TEMA DELLA COMUNICAZIONE:

o metodi biostatistici

## PREFERENZA TIPO DI PRESENTAZIONE: Comunicazione Orale

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