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## Integration of Preventing Mother-To-Child Transmission of HIV and Syphilis Testing and Treatment in Antenatal Care Services in the Northern Cape and Gauteng Provinces, South Africa

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### Abstract

**Background:** South Africa recommends universal syphilis and HIV testing in pregnancy, with prompt antiretroviral therapy or penicillin treatment for women testing positive.

**Methods:** We used a multistage, purposeful sampling strategy to retrospectively identify clinical records from a sample (7.3%) of 32,518 women delivering from January 2005 to June 2006 at 6 public clinics in the Northern Cape and Gauteng. Descriptive analyses and logistic regression were used to assess coverage and factors related to testing and treatment of HIV and syphilis.

**Results:** Of 2379 women sampled, 93% accessed antenatal care (ANC) services during pregnancy and 71% before the third pregnancy trimester. Testing during pregnancy or delivery was 74% for HIV and 84% for syphilis; testing at the first ANC visit was 41% and 71%; and infection prevalence at delivery was 14% and 5%, respectively. Of 243 women with reactive HIV tests, 104 (43%) had treatment documented (single-dose nevirapine) before delivery. Of 98 women with reactive syphilis tests, 73% had documented receipt of 1 penicillin injection and 36% had all 3 recommended injections. Multivariable analysis found women tested for syphilis were almost 4

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times more likely to have had no HIV test compared with those without syphilis testing (adjusted odds ratios, 3.9; 95% confidence interval, 1.7–5.5).

**Conclusions:** Integration and provision of a package of HIV and syphilis testing at the first ANC visit and decentralizing treatments of both infections to primary care settings could increase the coverage of testing and treatment services, thus enhancing the effectiveness of current programs eliminating mother-to-child transmission of HIV and syphilis.

The World Health Organization (WHO) has called for the global elimination of pediatric HIV and congenital syphilis.<sup>1,2</sup> WHO's Prevention of Mother to Child Transmission (PMTCT) guidelines aim for reduction in mother-to-child transmission (MTCT) of HIV to less than 5% through the provision of efficacious antiretroviral (ARV) therapy for HIV-infected pregnant women from 28 weeks (2006 guidelines) or as early as 14 weeks (2010 guidelines) of gestational age.<sup>3–5</sup> The elimination of congenital syphilis initiative is based on the effectiveness of antenatal syphilis testing, coupled with prompt penicillin injections for women testing positive.<sup>6,7</sup> Rapid diagnostics that allow testing to be done in settings with limited laboratory capacity have made these interventions cost-effective and feasible almost everywhere.<sup>8</sup> Nonetheless, many women do not undergo syphilis or HIV testing in pregnancy or are not promptly treated.<sup>9</sup>

In South Africa (SA), national guidelines have recommended universal syphilis testing and HIV counseling and testing for ANC attendees since 2002.<sup>10</sup> Syphilis accounted for almost half of the cases of genital ulcer disease in 1991, whereas it currently accounts for less than 10% of cases.<sup>11,12</sup> Furthermore, the national prevalence of presumptive syphilis steadily declined from 11.2% in 1997 to 2.8% in 2007 in pregnant women attending ANC.<sup>13</sup> In contrast, during the same period, antenatal HIV prevalence increased from 17.0% to 28.0%.<sup>13</sup>

We sought to assess the coverage of syphilis and HIV testing and treatment for pregnant women and the extent to which syphilis and HIV screening was integrated into routine ANC services. We also attempted to identify factors associated with lack of HIV testing, at the first ANC visit.

## MATERIALS AND METHODS

We conducted a retrospective evaluation of women who gave birth from January 2005 to June 2006. Two provinces were purposively selected to be part of the evaluation: Northern Cape (NC), a rural province with 5 districts, moderate antenatal HIV (15.6%), and a high syphilis prevalence (6.9%),<sup>8</sup> and Gauteng (GP), an urban province with 12 districts, high HIV (30.8%), and a moderate syphilis (2.3%) prevalence.<sup>8</sup>

We randomly selected 3 districts from each province and then identified 1 maternity clinic that (1) reported deliveries from at least 100 pregnant women during the previous year, (2) served most antenatal women in its subdistrict, and (3) had ANC records that were available for the duration of the evaluation in each selected district. For each clinic, we assigned sample size proportionally to the number of women delivering at that clinic. A maternity record was sampled for every fifth woman logged into the clinic. If an assigned medical

record was missing, we used the record of the next consecutive woman listed in the register. This process achieved a total desired sample of 2379 maternity clinical records (7.3%) representing of the 32518 women who delivered at the study facilities during the study period.

We reviewed the entire maternal medical record including an original copy of the ANC card, the labor and delivery record on which all medical care was recorded, and available laboratory results and treatment. We assessed HIV and syphilis counseling, testing and treatment, and dates of services provided to the woman during pregnancy and at labor/delivery. Information from the ANC card was mostly copied to the labor/delivery records at the time of admission during labor.

We defined a pregnant woman as “syphilis infected” if her Rapid Plasma Reagins (RPR) assay was seroreactive and as “HIV infected” if her blood was seroreactive on 2 separate HIV rapid test assays. We considered “maternal adherence to single-dose nevirapine (sdNVP) prophylaxis” to occur in HIV-infected women whose ANC cards documented that nevirapine was dispensed and labor/delivery records documented that it had been taken before (rather than issued at) labor. For syphilis-infected women, we defined “treatment adherence” to include receiving treatment per national guidelines<sup>14</sup> (3 doses of intramuscular penicillin for asymptomatic women with infections of unknown or >2 years in duration). The ANC card had spaces and dates for each of the 3 penicillin doses.

Descriptive analyses were used to assess demographic characteristics and current and past obstetrical histories as well as current congenital syphilis prevention and PMTCT services provided. Logistic regression models were used to identify patterns associated with HIV and syphilis test uptake at the first ANC visit. The initial multivariable model included maternal age at delivery, marital status, urban versus rural location, primigravida, gestational age at the first ANC visit, HIV status, and screening for syphilis, all factors that presented some possible evidence of association in the univariate analysis ( $P < 0.05$ ). The final model included factors significant at  $P = 0.05$  in the multivariable model.

The evaluation protocol was approved by the human research ethics committee at the University of Witwatersrand in SA and the institutional review board at the US Centers for Disease Control and Prevention.

## RESULTS

Overall, 43% of the medical records in our original sampling frame were not found and were replaced with the next available record listed on the labor/delivery register. Rates of missing records varied widely, from 0% to 80%, among the 6 selected delivery facilities.

### Demographic Characteristics and Obstetric History

Overall, 76% ( $n = 1803$ ) of women sampled were 30 years or younger, 83% ( $n = 1732$ ) were “unmarried/single,” and 39% ( $n = 888$ ) had primigravida pregnancies (Table 1). Among 2267 women whose pregnancy history was known, 1379 (61%) had had prior pregnancies, of whom 51 women (4%) reported at least 1 stillborn pregnancy, 99 (8%) reported at least 1

miscarriage, and 3% ( $n = 40$ ) reported that they had at least 1 child who died within 1 month of birth. Among the current 2379 pregnancies, 2210 women (93%) went on to deliver healthy infants, 51 (2%) had stillbirths, 9 (G1%) experienced neonatal deaths, and 19 (1%) had unknown histories (data not shown).

### **HIV and Syphilis Testing**

Of all 2379 women whose medical records were reviewed, 93% of the women had at least 1 ANC visit documented and 71% indicated that the first ANC visit occurred before the third trimester (<28 weeks of gestation). Table 2 provides data on HIV and syphilis testing. Of all sampled women, 24 (1%) had HIV testing before the first ANC visit, 1747 (73%) were tested for HIV, and 2008 (85%) were tested for syphilis at some point during pregnancy or delivery. Based on records with testing data documented, test uptake at the first ANC visit was 41% for HIV ( $n = 733$ , excluding previously positive women) and 71% ( $n = 1434$ ) for syphilis (Table 2). However, data on HIV testing were missing from the clinical notes for 608 (26%) women and on syphilis testing for 371 (16%) women. Test uptake before the third trimester of pregnancy was 72% for HIV and 71.7% for syphilis, again based on records with testing data documented (Table 2).

Among sampled women who gave birth, the prevalence of HIV was 14% and the prevalence of syphilis was 5% (Table 3). The prevalence of HIV and syphilis coinfection was just less than 1%. There were no statistically significant differences in the prevalence of infections between 2 provinces.

### **ARV Prophylaxis to Reduce MTCT**

Of 243 pregnant women identified as HIV infected at some point before or during pregnancy or at labor, 104 (43%) had medical records documenting provision of sdNVP before delivery (Table 3). Among 268 newborns who received a sdNVP within 72 hours of birth, 104 (39%) had mothers who received sdNVP, 95 (35%) had mothers who did not receive sdNVP before delivery, and 69 (26%) had mothers whose sdNVP use was not documented (data not shown).

Of the subset of 219 pregnant women who learned their HIV-infected status during pregnancy, their ANC cards indicated that sdNVP was dispensed to 103 (48%); however, delivery records indicated that only 53 (52%) of these women took the dispensed sdNVP pill before delivery as instructed by ANC clinicians. The maternal adherence level among HIV-infected pregnant women from NC was 1.7 times higher than that who were from GP (57.1% vs. 34.6%,  $P = 0.07$ ).

### **Syphilis Treatment to Prevent Congenital Syphilis**

Among 98 women whose records indicated they had RPR reactive test results during ANC visits or at labor/delivery, all were asymptomatic, and 72 (74%) received at least 1 dose of benzathine penicillin at some point during their pregnancies. Of these 98 women with presumed untreated syphilis infections, receiving the full 3 weekly doses of intramuscular penicillin recommended in the South African national guidelines was documented in 26 (36%) of the women's medical records. Of the 72 women with seroreactive syphilis who

received some treatment, less than half (47%) began treatment within 2 weeks of the blood sample (Table 3). As true for HIV, the proportion with prompt treatment was higher in NC than that in GP (52.9% vs. 33.3%,  $P = 0.10$ ).

### Factors Associated With Lack of HIV Testing Uptake at the First ANC Visit

Adjusting for other factors, we found that women who had a syphilis test were about 4 times more likely not to have had an HIV test (ie, refused or lacked documentation of an HIV test) compared with women who had no syphilis test at the first ANC visit (adjusted odds ratio, 3.9; 95% confidence interval [CI], 2.7–5.5; Table 4). Other factors associated with lack of HIV testing at the first ANC visit were being legally married, residing in the NC, and having the first ANC visit before 26 weeks of gestation (third trimester).

## DISCUSSION

We found lower-than-anticipated testing rates at the first antenatal visit and very low or delayed treatment rates for both HIV and syphilis in 2 provinces in SA; however, the syphilis prevalence data (5.8% in NC and 4.0% in GP) are fairly consistent with the annual provincial estimates reported among pregnant women attending their first ANC visit in the national sentinel surveillance in 2005 and 2006.<sup>13</sup> We found HIV prevalence in our sample to be much lower in GP (13%) compared with the 2005 provincial estimates (95% CI, 30.6%–34.3%), although our estimate of HIV prevalence (15%) in NC was within the 95% CI estimate (14.6%–22.4%) reported in the 2005 sentinel surveillance.<sup>13</sup> Because our data were based on extracted data from ANC cards or labor/delivery records, the estimates reflect the status of pregnant women who agreed to be tested for HIV and received their test results. Because our HIV prevalence estimate does not include women who were not offered HIV testing, or were offered testing but refused testing, or accepted testing but did not receive their test results, the record results are likely to underestimate true HIV prevalence. In addition, HIV test results could be misclassified because of the HIV testing identification code system, which was used nationally before 2008. The higher HIV prevalence found from the anonymous, unlinked approach compared with this evaluation's estimate within GP province suggests that a significant proportion of pregnant women with HIV were still refusing or not offered testing or that the HIV coding system was not well implemented. Because most of HIV care and therapy would be based on HIV testing documented on ANC card, this is an important missed opportunity for women to learn their HIV status and receive ARV prophylaxis that could reduce HIV transmission to their babies.

The proportion of pregnant women having an HIV and RPR test during pregnancy was lower than expected (74% and 84%, respectively). Furthermore, only 42% and 71% of the women were tested for HIV and syphilis, respectively, at the first pregnancy visit as recommended in the national guidelines in 2005. Both lack of testing and late testing after the first ANC visit contributed to missed opportunities for reducing MTCT of HIV and syphilis, and both are amenable to quality improvement in existing ANC services. That almost 29% of women presented for their first ANC visit in the third trimester further limited the chance to provide effective prevention against syphilis and HIV transmission. These data highlight the need for community efforts to encourage women to attend for their

first ANC assessment early during pregnancy and to ensure that nurses are aware that each ANC visit may be the last opportunity to provide preventive services. Our multivariable analysis indicated that having an RPR test done was associated with lack of HIV testing at the first ANC visit, suggesting that the HIV and syphilis testing programs were not well integrated in the sites evaluated. Requiring separate blood tests at different locations, as was typical at most of the ANC clinics, may have led some women to assume that they had already been HIV tested or to not take the time to go for a second blood test for HIV. Syphilis testing in these clinics was provided as part of the routinely required laboratory tests at the first ANC visit, whereas HIV testing service was provided at a different location in the same clinic after specialized counseling with a trained counselor. These results suggest that HIV testing strategies could have been improved by promoting syphilis and HIV testing including other recommended blood work at the same time and at the first ANC visit.

Among the almost 14% of tested women who were found and told they had HIV infection, maternal sdNVP was dispensed to less than half of the women, and only half of those provided the pills actually took NVP before delivery. In other words, only approximately 22% of the HIV-infected women took the NVP as recommended in the national guidelines. These low treatment rates for syphilis and ARV prophylaxis for PMTCT are quite concerning and suggest that systems should be strengthened in ANC settings to ensure that women are appropriately followed up and provided prompt treatment.

Among 99 women testing positive for syphilis, 72 (74%) received treatment with at least 1 intramuscular penicillin dose, but only 34 did so within 2 weeks of diagnosis, that is, sufficiently early to prevent the most severe complications of syphilis, which can occur much earlier in pregnancy. Untreated or late-treated syphilis infection in these 65 fetuses could be expected to result in 34 to 52 adverse perinatal outcomes,<sup>2,15,16</sup> all of which could have been prevented with a stronger ANC program that included more rigorous quality control strategies. Because HIV testing was performed using rapid tests, women received their results on the same day. Some factors that may have explained the limited provision of sdNVP for HIV-infected women were that not all ANC nurses were trained on PMTCT, NVP supplies may have been limited, or the provision may not have been documented. For syphilis, because not all clinics have a laboratory at the site to perform an RPR test for syphilis, blood specimens had to be sent to outside laboratories and results were not available for a few days or, in some cases, for weeks. In addition, the test results were usually returned to the women at the second ANC visit, which could have been several weeks later, depending on her gestational age at the first visit, or not at all in some cases of late presentation. As a result, most (53%) of syphilis-infected pregnant women who received their test results and treatment did so more than 2 weeks after testing and sometimes months after the test results were completed. Rapid point-of-care tests and especially the dual-treponemal/nontreponemal point-of-care tests could avoid these delays.

Our findings suggest that late presentation to ANC, delayed testing, long turnaround time of test results, delays in treatment initiation for both infections, and low coverage of ARV dispensement have greatly limited the effectiveness of the prevention of congenital syphilis and MTCT of HIV programs. Although a substantial amount of time and effort is being

expended by ANC clinical staff in implementing these programs, some of these factors would require efforts beyond the clinics themselves, but many of these issues could be immediately addressed within these programs. Provider-initiative testing and integrating HIV testing as part of the basic ANC package would help ensure earlier HIV testing, in keeping with current PMTCT guidelines, which recommend the initiation of ARV prophylaxis from the 14th week of gestation. Documenting syphilis and HIV test results and treatment on the longitudinal ANC log books could help provide adequate and prompt continuum of care to syphilis and/or HIV-infected women during pregnancy and postpartum. Following global recommendations, SA has embarked on processes to improve the type and quality of data collected to better inform PMTCT programs. Making benzathine penicillin available to ANC clinics would greatly improve the likelihood that women received at least a single dose of long-acting penicillin, sufficient to treat the unborn baby (if not always the mother). Cross-training ANC clinicians on PMTCT and congenital syphilis prevention, with special emphasis on the urgency of early testing and prompt (ideally same day) treatment, could reduce perinatal transmission of both infections.<sup>15,17</sup>

Our findings are subject to several limitations. The results are based on retrospective paper-based medical record review and may overestimate or underestimate true program results, depending on how well the data were recorded. A purposeful sampling method was used to ensure feasibility and to meet national program needs, and it may not have yielded a true representation of ANC services within the province or in SA. That 43% of assigned medical records had to be replaced by the next available record may have further reduced representativeness of the sample. In addition, when records were available, some data elements were missing, which could dilute outcome estimates. We are also cautious with misclassification bias because some data may not have been well documented in the medical record; however, we cannot predict the directions of all these biases. These biases could have been limited if the medical records are carefully documented and stored in secured areas or if electronic medical record systems are used at facility levels.

In conclusion, coverage of HIV testing was lower than syphilis testing, and coverage of treatment was very low for both conditions, suggesting a lack of functional integration at the facility level and that treatment may not be immediately available at the clinic when the test results were returned to the women. Provision of a package of HIV and syphilis testing and treatments delivered at the primary health care center setting could enhance the effectiveness of current programs on elimination of MTCT of HIV and congenital syphilis. In addition, ongoing quality improvement of these programs could make a difference in reducing maternal and infant morbidity and mortality caused by both HIV and syphilis.

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Demographic Characteristics and Obstetric History of the Women by Province, SA, January 2005 to June 2006

TABLE 1.

Characteristic	Overall (N = 2379)			GP (n = 1167)			NC (n = 1212)		
	n	%	n	%	n	%	n	%	
Age at delivery documented, y									
14–18	280	11.9	113	9.7	167	13.9			
19–25	1007	42.6	481	41.2	526	43.9			
26–30	516	21.9	246	21.2	270	22.5			
31–35	350	14.9	198	17.0	152	12.7			
36+	208	8.8	124	10.7	84	7.0			
Age at delivery not documented									
18	18	5	5	13					
Marital status documented									
Unmarried	1732	83.0	905	781.8	827	84.3			
Married	354	17.0	200	18.1	153	15.6			
Widowed/divorced	2	<0.1	1	0.1	1	0.1			
Marital status not documented	291	60	231						
Obstetric history									
No. prior births documented									
0	888	39.2	399	36.2	489	42.0			
1	694	30.6	349	31.6	345	29.6			
2+	685	30.2	354	32.0	331	28.4			
No. prior births not documented	112	64	47						
No. live births documented									
0–1	710	75.6	404	76.7	306	74.3			
2+	229	24.4	123	23.3	106	3.7			
No. live births not documented	1440	640	800						
No. stillborns documented									
0	1237	96.0	705	97.2	532	94.5			
1+	51	4.0	20	2.8	31	5.5			
No. stillborns not documented	1091	442	649						
No. miscarriages documented									

Characteristic	Overall (N = 2379)		GP (n = 1167)		NC (n = 1212)	
	n	%	n	%	n	%
0	1185	92.3	642	89.2	543	96.6
1+	99	7.7	80	11.8	19	3.4
No. miscarriages not documented	1095		445		650	
No. infant deaths documented						
0	1248	96.9	695	95.9	553	98.2
1+	40	3.1	30	4.1	10	1.8
No. infant deaths not documented	1091		442		649	

HIV and Syphilis Testing by Antenatal Characteristics by Province, SA, January 2005 to June 2006

TABLE 2.

Characteristic	Overall (N = 2379)		GP (n = 1167)		NC (n = 1212)	
	n	%	n	%	n	%
Gestational age at 1 <sup>st</sup> ANC documented						
First trimester	146	8.4	57	6.6	89	10.1
Second trimester	1093	62.9	535	62.1	558	63.6
Third trimester	499	28.7	269	31.3	230	26.2
Gestational age at first ANC not documented						
Tested for HIV by ANC visit documented	641	306	335			
Before first ANC visit	24	1.4	10	1.1	14	1.6
At first ANC visit	733	41.4	315	35.7	418	47.1
At later ANC visit	970	54.8	557	63.1	413	46.5
During labor	44	2.5	1	0.1	43	4.8
Tested for HIV by ANC visit not documented	608	284	324			
Tested for syphilis by ANC visit documented						
First ANC visit	1434	71.4	674	68.6	760	74.1
Follow-up ANC visit	555	27.6	290	29.6	265	25.8
During labor	19	1.0	18	1.8	1	<0.1
Tested for syphilis by ANC visit not documented	371	185	186			
Tested for HIV by gestational age documented						
First trimester	128	9.2	53	7.8	75	10.5
Second trimester	872	62.8	418	61.8	454	63.7
Third trimester	389	28.0	205	30.2	184	25.8
Tested for HIV by gestational age not documented	990	491	499			
Tested for syphilis by gestational age documented						
First trimester	141	8.5	56	6.9	85	10.0
Second trimester	1055	63.3	509	62.3	546	64.2
Third trimester	471	28.3	252	30.8	219	25.8
Tested for syphilis by gestational age not documented	712	350	362			

TABLE 3.

Prevalence and Adherence to Medications Among HIV-Infected and Syphilis-Infected Women by Province, SA, January 2005 to June 2006

Characteristic	Overall (N = 2379)		GP (n = 1167)		NC (n = 1212)	
	n	%	n	%	n	%
HIV test uptake in ANC and labor/delivery*	1747	74.2	873	75.5	874	73.0
HIV prevalence among women tested	243	13.9	112	12.8	131	15.0
Syphilis test uptake in ANC and labor/delivery	2008	84.4	982	82.0	1026	84.7
Syphilis prevalence among women tested <sup>†</sup>	99	4.9	39	4.0	60	5.8
HIV prophylaxis						
Overall ARV prophylaxis uptake before delivery						
Yes	104	42.8	40	35.7	64	48.9
No	139	57.2	72	64.3	67	51.1
SdNVP provided to HIV+ women during ANC						
Yes	103	47.5	26	26.0	77	65.8
No	114	52.5	74	74.0	40	34.2
Adherence to sdNVP at labor <sup>‡</sup>						
Yes	53	51.5	9	34.6	44	57.1
No	50	48.5	17	65.4	33	42.9
Not documented						
Syphilis treatment						
Documented receipt of at least 1 dose of penicillin						
Yes	72	73.5	21	56.8	51	83.6
No	26	26.5	16	43.2	10	16.4
Time interval from test date to first dose of treatment						
<2 wk	34	47.2	7	33.3	27	52.9
2-4 wk	13	18.1	4	19.0	9	17.6
>4 wk	25	34.7	10	47.6	15	29.4
Adherence to 3 weekly doses <sup>§</sup>						
Yes	26	36.1	10	47.6	16	31.4
No	20	27.8	4	19.0	16	31.4

Characteristic	Overall (N = 2379)		GP (n = 1167)		NC (n = 1212)	
	n	%	n	%	n	%
Not documented	26	36.1	7	33.3	19	37.2

\* Calculation excludes previously tested women, n = 24 (1.0% overall).

<sup>†</sup> Based on RPR seroreactivity.

<sup>‡</sup> Assumes adherence if sdNVP treatment occurred at labor or during ANC.

<sup>§</sup> National guidelines recommend 3 weekly doses of intramuscular benzathine penicillin.

TABLE 4.

Factors Associated With Not Being Tested for HIV at the First ANC Visit Among ANC Attendees, SA, January 2005 to June 2006

Variable Assessed	Univariable Analysis			Multivariable Analysis*		
	Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Age at delivery (continuous)	1.0	1.0-1.0				
Married status						
Married	1.5	1.1-1.9	1.4	1.1-1.9		
Not married	Reference	—	Reference	—	—	
Location (rural vs. urban)						
NC	1.5	1.2-1.8	1.7	1.4-2.1		
GP	Reference	—	Reference	—	—	
Primigravida <sup>†</sup>						
Yes	1.2	1.0-1.5				
No	Reference	—				
Gestational age						
26 wk	1.3	1.1-1.6	1.5	1.2-1.9		
>26wk	Reference	—	Reference	—	—	
HIV status						
Positive	1.2	0.9-1.6				
Negative	Reference	—				
Syphilis screened						
Yes	10.3	7.5-14.0	3.9	2.7-5.5		
No	Reference	—	Reference	—	—	

\* Findings from the final model. Factors significant at  $P=0.05$  in the univariate analysis were included in the multivariable model. The final model included factors significant at  $P=0.05$  in the multivariable model.

<sup>†</sup> Excluded from the final model because the factor was not significant in a reduced model.