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## Coverage and outcomes of antenatal tests for infections: a population based survey in the Province of Trento, Italy

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### ABSTRACT

**Background:** Rubella, syphilis, toxoplasmosis, cytomegalovirus (CMV), hepatitis B (HBV) and C (HCV), HIV, and Group B Streptococcus (GBS) infections may have very severe outcomes during pregnancy, and for this reason, monitoring of infections in pregnant women is a requirement of prenatal assistance.

**Aims:** To describe coverage and outcome of the screening for rubella, syphilis, toxoplasmosis, CMV, HBV, HCV, HIV, and Group B Streptococcus in pregnancy in the Autonomous Province of Trento, Northern Italy (538,600 inhabitants).

**Methods:** We analysed the coverage and outcome of the above-mentioned screenings among women who delivered in the hospitals of the Province of Trento between 2007 and 2014 ( $N = 38,712$ ). Screenings were grouped according to characteristics such as recommendation by national and local guidelines, scheduling of the tests, operating methods, and charge. We also estimated odds ratios (ORs) for missing screening for selected infections through multiple logistic regression.

**Results:** Estimated uptake of antenatal screening was 99.7% for rubella, 99.3% for syphilis, 99.7% for toxoplasmosis, 98.1% for HIV infection, 99.0% for HBV, 98.9% for HCV, 94.0% for GBS infection, and 75.4% for CMV infection. The overall prevalence of immunity was 94.1% for rubella, 24.2% for toxoplasmosis, and 64.2% for CMV. The rate of seroconversion in pregnant women was 0.02% for rubella, 0.29% for toxoplasmosis, and 0.75% for CMV. The overall prevalence of infection was 0.94% for HBV, 0.53% for HCV, 22.3% for GBS, 0.29% for syphilis, and 0.13% for HIV. We found a significant positive association for all screening tests, between lack of testing and late first medical examination in pregnancy (ORs ranging from 1.20 to 1.66 for the first medical visit in the second trimester and ORs ranging from 1.60 to 5.88 for the first medical visit in third trimester, compared to early medical visit in the first trimester). Compared to Italian citizenship, foreign citizenship of the mother was also positively associated with absence of screening (ORs ranging from 1.30 to 1.53). A significant inverse association was observed for calendar year of delivery (ORs ranging from 0.71 to 0.97, for 1 year increment). Less educated mothers and pluriparae were also at higher risks of not being tested. Analysis of the association with mother age showed different heterogeneous effects.

**Conclusions:** Our study indicates that the attention to screening and detecting infected cases is growing over the time. In addition, care delivered during pregnancy has a leading role in determining coverage of the examinations. Immigrant, pluriparous and less educated women need particular attention.

### ARTICLE HISTORY

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### KEYWORDS

Antenatal test; antenatal infection; risk factors; pregnancy; Italy


### Introduction

Rubella, syphilis, toxoplasmosis, cytomegalovirus (CMV), hepatitis B (HBV) and C (HCV), HIV, and Group B Streptococcus (GBS) infections may have very severe outcomes if contracted during pregnancy, and monitoring of infections in pregnant women is a fundamental requirement of prenatal assistance.

Prevention has the leading role in defeating prenatal infections, but early diagnosis is also crucial. Early detection of infected mothers allows timely intervention, first to reduce the risk of vertical transmission and second to treat for any damage that may result in the newborn.

We address here the coverage of selected investigations and their outcome in women who delivered in

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 Supplemental data for this article can be accessed [here](#).

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the Autonomous Province of Trento (with a population of 538,600 people in the North-East Italy) in the years 2007–2014. The Autonomous Province of Trento, through the Local Health Trust (Azienda Provinciale per i Servizi Sanitari – APSS, Servizio Epidemiologia clinica e valutativa), provided the update of its CedAP (Certificato di Assistenza al Parto, 1996) informative service, including additional information related to investigations for infections carried out by women during pregnancy, which are therefore systematically collected on all deliveries taking place in the Province.

## Materials and methods

### Study population

Out of a total of 39,787 deliveries registered in CedAP between 2007 and 2014, we excluded cases of birth in extraregional structures, home or rushing deliveries, and women who wanted to keep anonymity at birth (1039 women in total). In addition, 36 cases without registration of information on investigations were also excluded.

The final population is thus composed of 38,712 women who had given birth in all the provincial hospitals ( $N = 7$ ) in the years 2007–2014.

### Investigations groups

The infections were studied by dividing them into four groups, distinct for diversity and testing timing.

1. Toxoplasmosis, rubella, syphilis, and HIV infections. National and local guidelines for prenatal care recommend the screening for these infections at the beginning of pregnancy, at the first visit during pregnancy, possibly within the 12-gestational week. All these examinations are free of charge according to Italian law. The tests for Rubella, Toxoplasmosis, HIV infection, and Syphilis evaluate the presence of specific antibodies.
2. HBV and HCV. National guidelines recommend screening for HBV in the third trimester, while screening for HCV should be proposed only to women with related risk factors. Local guidelines actually propose both those screenings in the third trimester. The aforementioned screenings are included among those free of charge between 33 and 37 gestational weeks. The HCV test evaluates the presence of specific antibodies while the HBV test assess the HBsAg antigen.
3. GBS examination. National and local guidelines recommend to perform this test between 36–37 gestational weeks. This test is not free of charge

according to Italian law. Given the timing of the examination, it is sometimes performed at the birth point chosen for delivery. For this reason, the performance of this examination depends even on logistic and organizational aspects of the care setting. Research for GBS is performed through vaginal and rectal swab.

4. CMV screening is the only one not routinely recommended in pregnancy either by national or local guidelines. Local guidelines promote it in selected cases since the first visit (12–13 gestational weeks). CMV testing is also not free of charge. The CMV test evaluates specific antibodies.

### Statistical analysis

We estimated the relative risks (RRs) of not getting tested for all the infections of each group, through the odds ratios (ORs) and related 95% confidence intervals (CIs). We fitted a multiple logistic regression model including terms for calendar year of delivery, time of the first visit in pregnancy, citizenship, age class, parity, and education level of the women.

## Results

**Table 1** shows the demographic characteristics of women who delivered in the Autonomous Province of Trento over the years considered. Women were mainly Italian, resident in the Province, aged between 15 and 53 years with a median of 32 years and with a high school degree and a bachelor/master degree.

CedAP data show strong adherence to screening for infectious diseases during pregnancy (**Supplementary Table 1**). Rubella, HIV infection, toxoplasmosis, Syphilis: the coverage rate for each one is over 97% each year, with an increase over the years. The percentage of women who got tested for all these infections was 97.2% over the 8 years of observation.

As regards rubella, most of the women who had been tested were found immune (94.1%) and the proportion remained similar throughout the years. Approximately 5–6% of women were susceptible, with seven cases of seroconversion in pregnancy, respectively, in 2007 (one case), 2008 (three cases), 2013 (one case), and 2014 (two cases).

Women who were not immune to toxoplasmosis were 75.5% of the women tested (99.7%, 38,575 women) and 24.2% were immune. Over time, there was a decrease in the proportion of immune cases in favour of an increase in nonimmune ones. Women who had a seroconversion in pregnancy were 110, with a range of 10–18 cases per year.

**Table 1.** Distribution of the study population ( $N=38,712$ ) according to selected characteristics in Italy, 2007–2014.

	<i>n</i>	%
Age group (years)		
<26	5440	14.05
26–30	10,348	26.73
31–35	13,373	34.54
36–40	7946	20.53
>40	1605	4.15
Citizenship		
Italian	29,475	76.14
European	5265	13.60
Extra-European	3972	10.26
Residence		
Italy (province of Trento)	36,814	95.10
Italy (extra-province)	1294	3.34
Abroad	604	1.56
First check in pregnancy timing		
1° trimester	32,789	84.70
2° trimester	5412	13.98
3° trimester	511	1.32
Education level		
University	10,545	27.24
High school	20,709	53.50
Medium high school	6568	16.97
Licenza elementary/none	890	2.30
Parity		
Primiparous	18,324	47.33
Pluriparous	20,388	52.67
Year of delivery		
2007	4862	12.56
2008	5070	13.10
2009	4967	12.83
2010	5018	12.96
2011	4905	12.67
2012	4804	12.41
2013	4592	11.86
2014	4494	11.61

Syphilis test was performed on 99.3% of women: positive cases were between 8 and 19 per year, for a total of 112 cases. HIV test was performed on 98.1% of women. Among these, cases of HIV positivity were 49 (range of 4–9 cases per year).

HBV and HCV: the coverage for HBV and HCV investigations increased from about 97% in 2007 to over 99% in 2014. During the 8 years, 98.7% of the women had been tested for both diseases during pregnancy. Most of the women were negative for HBV or vaccinated (98.8 and 0.3%, respectively). The total number of cases of HBV positivity was 362 with a slight increase over the years: from a minimum of 37 cases per year (2009) to a maximum of 54 cases per year (2014). Positivity cases for HCV were in total 203, with a range of 19–36 cases per year.

GBS screening shows a 94% adherence over the 8 years. The proportion of women positive to GBS was 22.3% (8117 women) of the screened ones with a range of 914 (2014) to 1106 (2012) annual cases.

In total, 75.4% of women got tested for CMV. However, the proportion of screening among women increased significantly over the years, from 59.6% in 2007 to 95.6% in 2014. Women with prepregnancy

infection were 64.2% in the considered years while the CMV-negative case were 35.1%. Women who had reinfection/reactivation in pregnancy were 97, from a minimum of three cases per year (2008) to a maximum of 33 (2013). New infections registered in pregnancy were 123, with a range of 5–24 cases per year.

Table 2 shows the ORs, and corresponding 95%CI, for not being tested in relation to groups of infections by demographic characteristics of the woman and some features related to the health care assistance.

Foreign women had a higher risk (OR: 1.37, 95%CI: 1.18–1.59) than Italian of not being tested for either Rubella, HIV, Toxoplasmosis, and Syphilis. First pregnancy (OR: 0.63, 95%CI: 0.55–0.72) was inversely related to the risk of not getting tested compared to subsequent pregnancies. The two middle age classes also exhibited lower risk (OR: 0.73, 95%CI: 0.60–0.88 for women between 26 and 30 years and OR: 0.71, 95%CI: 0.58–0.86 for women between 31 and 35 years) compared to women aged  $\leq 25$ . Delay of the first medical examination in pregnancy significantly increased the risk of not being tested: compared to women who attended the first visit in the first trimester, those who made it in the second trimester had an OR of 1.66 (95%CI: 1.41–1.97) and visit in third trimester is associated to an OR of 5.88 (95%CI: 4.54–7.60). The year of birth was inversely associated with the lack of testing (1 year increase implies a 14% lower OR, 95%CI of OR: 0.83–0.88).

Foreign citizenship (OR: 1.30, 95%CI: 1.04–1.62) increased the risk of not being screened for both HBV and HCV compared to Italian women. First-parity (OR of 0.80, 95%CI: 0.66–0.97) was inversely associated with the risk of not taking the examinations compared to subsequent pregnancies. Late first check (OR for third trimester visit: 2.04, 95%CI: 1.24–3.37) was associated to a higher risk with respect to early check. Giving birth in recent years (OR for 1 year increase: 0.76, 95%CI of OR: 0.73–0.80) was inversely associated with the risk of not taking both tests.

Regarding to GBS screening, foreign citizens (OR: 1.51, 95%CI: 1.36–1.67) exhibit a higher risk of not getting tested with respect to Italian women. Lower academic qualification (OR: 1.17, 95%CI: 1.05–1.31 for high school graduates and OR: 1.42, 95%CI: 1.25–1.62 for women with even lower education level compared to highest degrees), older age (OR: 1.25, 95%CI: 1.07–1.45 for women between 36 and 40 and OR: 1.53, 95%CI: 1.23–1.91 for women over 40 years compared to women aged  $\leq 25$ ) and the timing of first visit (OR for first visit in the second trimester: 1.35, 95%CI: 1.19–1.53, OR for first visit in the third trimester: 2.12,

**Table 2.** Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for lack of testing in pregnancy according to selected covariates<sup>a</sup>.

	Toxoplasmosis & Syphilis & Rubella & HIV infection		HBV & HCV infection		GBS infection		CMV infection	
	N (%)	OR (95%CI)	N (%)	OR (95%CI)	N (%)	OR (95%CI)	N (%)	OR (95%CI)
Citizenship								
Italian <sup>b</sup>	688 (2.33)	1	335 (1.14)	1	1536 (5.21)	1	6561 (22.26)	1
Foreign	399 (4.32)	1.37 (1.18–1.59)	160 (1.73)	1.3 (1.04–1.62)	777 (8.41)	1.51 (1.36–1.67)	2977 (32.23)	1.53 (1.44–1.63)
Education level								
University <sup>b</sup>	253 (2.40)	1	101 (0.96)	1	505 (4.79)	1	1865 (17.69)	1
High school	503 (2.43)	0.86 (0.74–1.01)	253 (1.22)	1.08 (0.85–1.36)	1196 (5.78)	1.17 (1.05–1.31)	5171 (24.97)	1.32 (1.24–1.40)
Lower	331 (4.44)	1.14 (0.95–1.37)	141 (1.89)	1.35 (1.02–1.78)	612 (8.21)	1.42 (1.25–1.62)	2502 (33.55)	1.65 (1.53–1.78)
Parity								
Primiparous	396 (2.16)	0.63 (0.55–0.72)	210 (1.15)	0.80 (0.66–0.97)	953 (5.20)	0.85 (0.77–0.93)	4347 (23.72)	0.89 (0.85–0.94)
Pluriparous <sup>b</sup>	691 (3.39)	1	285 (1.40)	1	1360 (6.67)	1	5191 (25.46)	1
Age group (years)								
≤25 <sup>b</sup>	224 (4.12)	1	99 (1.82)	1	371 (6.82)	1	1706 (31.36)	1
26–30	263 (2.54)	0.73 (0.60–0.88)	129 (1.25)	0.78 (0.59–1.03)	559 (5.40)	0.95 (0.82–1.09)	2685 (25.95)	1.31 (1.13–1.51)
31–35	325 (2.43)	0.71 (0.58–0.86)	153 (1.14)	0.72 (0.54–0.96)	737 (5.51)	1.04 (0.90–1.19)	3117 (23.31)	1.21 (1.06–1.39)
36–40	227 (2.86)	0.83 (0.67–1.02)	99 (1.25)	0.81 (0.59–1.12)	518 (6.52)	1.25 (1.07–1.45)	1698 (21.37)	1.08 (0.95–1.24)
>40	48 (2.99)	0.85 (0.61–1.19)	15 (0.93)	0.62 (0.35–1.09)	128 (7.98)	1.53 (1.23–1.91)	332 (20.69)	1.02 (0.89–1.17)
First check up <sup>c</sup>								
1° trimester <sup>b</sup>	805 (2.36)	1	405 (1.19)	1	1886 (5.54)	1	7977 (23.41)	1
2° trimester	195 (4.72)	1.66 (1.41–1.97)	72 (1.74)	1.20 (0.92–1.56)	354 (8.57)	1.35 (1.19–1.53)	1347 (32.62)	1.30 (1.20–1.40)
3° trimester	87 (17.03)	5.88 (4.54–7.6)	18 (3.52)	2.04 (1.24–3.37)	73 (14.29)	2.12 (1.64–2.75)	214 (41.88)	1.60 (1.32–1.94)
Year of delivery								
1 year increment		0.86 (0.83–0.88)		0.76 (0.73–0.80)		0.97 (0.95–0.99)		0.71 (0.71–0.72)

<sup>a</sup>ORs and 95%CIs derived from multiple logistic models, one for each screening group, including all variables listed.

<sup>b</sup>Reference category.

<sup>c</sup>The variable was categorized as following: 1° trimester (up to 13 gestational weeks), 2° trimester (from 13+1 gestational weeks to 27 gestational weeks), 3° trimester (from 27+1 gestational weeks on).

95% CI: 1.64–2.75 compared to early check) were associated to a higher risk of not getting tested.

Factors positively associated to the risk of not being tested for CMV infection were foreign citizenship (OR: 1.53, 95%CI: 1.44–1.63), lower educational level (OR: 1.32, 95%CI: 1.24–1.40 for high school graduates and OR: 1.65, 95%CI: 1.53–1.78, for women with an even lower degree with respect to higher degrees) and the timing of the first visit (OR for visit in the second trimester: 1.30, 95%CI: 1.20–1.40 and OR for first visit in the third trimester: 1.60 95%CI: 1.32–1.40 compared to early first check). Delivering in recent years is a protective factor: 1 year increase had an OR of 0.71 (95%CI: 0.71–0.72) of not getting tested.

## Discussion

This analysis shows a high rate of coverage for all tests in the Province of Trento, and the rate of coverage for nonrecommended/nonfree of charge tests is also increasing over time. For all types of tests, there is a strong influence of the care setting in determining the coverage of the investigations. In addition to the year of delivery, the time of the first medical visit in pregnancy is an important predictor of whether or not a woman will get the test. For each of the four groups of infections, which refer to tests to be made at different moment of pregnancy, women who undergo their first

check in the second or third trimester are penalized, even for tests to be performed in the third trimester such as hepatitis or towards the end of pregnancy such as GBS. Further, low education and foreign citizenship were associated with an increased risk of not being screened for most of infections. Ethnic or economic disadvantage has been reported associated with lower screening rates also in other populations [1]. These results are in general agreement (or possibly showing higher rates of coverage) with data from other populations. The European Centre for Disease Prevention and Control delivered a survey on antenatal screening for HIV, HBV, syphilis and rubella. Twenty-six EU/EEA countries participated in the survey. Testing coverage was over 95% in 12 out of the 18 European countries for HIV, in eight out of the 13 countries for HBV, in 14 out of the 18 countries for syphilis and in four countries out of the five countries for rubella [2]. In an analysis of a large administrative database in USA including 98,709 Medicaid-insured pregnant women, 96.3% were screened for syphilis, 96.3% for HBV, 82.4% for HIV [3].

Another interesting finding of this analysis is the opportunity of analyse the frequency of infections in pregnancy. Our findings are generally in agreement with available data from Italy or other populations.

Studies on Rubella infection in Italy reported rates of sero-prevalence among women of childbearing age and pregnant women in Italy about 90%, with higher



values in the North than in the South [4–9]. At the international level, 27 EU/EEA countries reported 38,847 cases of rubella, with 12.6% cases in females [2]. Most of them derived from a large rubella outbreak which occurred in Poland [10]. In Romania, 119 rubella cases in pregnant women were reported in 2013, after an outbreak in 2011–2012 [11].

The prevalence of syphilis infection was comparable to that reported in the Italian literature, which ranges from 0.22 to 0.49% in various Italian regions [12–15]. The rate of registered syphilis among woman in EU/EEA countries was 1.6 per 100,000 in 2013, with a minimum in Croatia/Slovenia (0.3) and a maximum in Lituania (7.7) [2].

The frequency of toxoplasmosis infection in pregnancy was also comparable with the Italian literature, which reported ranges between 0.09 and 4.8% [13,16,17]. The reported rate of toxoplasmosis infection in pregnancy varied in different European countries from 0.17 to 0.24% with maternal-fetal transmission in 23–44% of cases not treated [17–21].

Studies on HIV infection in pregnancy in Italy show slightly lower values than those found in this study, with a maximum of 0.09% [13,22]. From 2000 to 2004, HIV infection in pregnant women was below 0.1% in 16 European countries. The highest values were reported for Estonia and Ireland (over 0.3%), and between 0.1 and 0.2% in Latvia, Romania, Spain, and the UK [2,23].

Results for HBV and HCV are also comparable with other Italian datasets reporting ranges, respectively, from 0.79 to 1.7% (HBV) and between 0.4 and 2.4% (HCV) [13,24–27]. The reported HBV prevalence among pregnant women ranges between 0.14% (Finland) and 1.15% (Greece) [28]. Limited data on HCV in pregnant women in Europe are available [29]. A study in the Netherlands reported a seroprevalence of 0.33% in 2003 [30], while in a Russian study it was 3% [31].

CMV infection estimate in Italy varies between 0.28 and 0.9% [13,32] with a range comparable with our result. Reported rates of CMV primary infection in pregnancy in the world range from 0.5 to 4% [33,34], and the incidence of seroconversion among pregnant women ranges from 0.4 to 2% [32,35–38] depending on the prevalence of infection in the populations.


The frequency of GBS infections was also similar to those reported by literature, although higher with respect to Italian studies, ranging from 7.98 to 13.6% [13,39]. Limited data are available on GBS infection in pregnancy in Europe: in most countries, the prevalence of infection range between 10 and 20%, and the incidence of neonatal disease ranges from 0.5 to 2.0 per 1000 live births [40,41].


In summary, this work has allowed to see how the welfare setting has a strong influence on the coverage of the surveys, sometimes showing more importance than the individual characteristics of women that showed somewhat stronger effects in relation to tests which are less promoted/recommended in the prenatal assistance. An additional interest in our study was to provide data on adherence to investigations in relation to demographic characteristics of women. There are, in fact, aspects that are beyond the connotations of the setting of assistance and the characteristics of the screenings and outline specific groups of women who need greater attention. Among them, non-Italian citizens, pluriparous and less educated mothers are at risk for not uptaking pregnancy screening. These findings may be useful to focus specific preventive campaigns.


### Disclosure statement


The authors report no conflicts of interest.

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