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Validity of preeclampsia registration in the Medical Birth Registry of Norway for women participating in the Norwegian Mother and Child Cohort Study, 1999-2010

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Abstract

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Background—The Norwegian Mother and Child Cohort study (MoBa), a prospective population-based pregnancy cohort, is a valuable database for studying causes of preeclampsia. Preeclampsia data in MoBa comes from the Medical Birth Registry of Norway (MBRN), thus, we wanted to study the validity of MBRN preeclampsia registration for MoBa women.

Methods—We selected all MoBa pregnancies with preeclampsia registered in the MBRN (n=4081) and a random control group (n=2000) without preeclampsia registrations. After excluding two delivery units not participating in MoBa and one no longer operating, units were asked to provide copies of antenatal charts with blood pressure and urinary measurements from all antenatal visits during pregnancy, and hospital discharge codes from the delivery stay. We received data for 5340 pregnancies delivered 1999-2010 (87% of all eligible). We calculated positive predictive value (PPV), sensitivity and specificity of MBRN registration, using hypertension and proteinuria on the antenatal charts and/or hospital discharge codes indicating preeclampsia as gold standard.

Results—Overall PPV was 83.9% (95% confidence interval 82.7, 85.1), and was higher when women were primiparous, or delivered preterm or low birth weight infants. Severe preeclampsia in the MBRN was found to be a true severe preeclampsia in 70% of cases. Extrapolating to the total MoBa population, the estimated sensitivity was low: 43.0% (38.7, 48.2), while specificity was high: 99.2% (99.2, 99.3). False negative cases seemed to have mild forms of preeclampsia.

Conclusions—PPV and specificity of preeclampsia registration in the MBRN during 1999-2010 was satisfactory, while sensitivity was low.

Preeclampsia is a serious pregnancy complication associated with maternal and neonatal morbidity and mortality. [1-4] Despite evidence of familial aggregation, [5-8] few consistent genetic predictors have been identified. Similarly, although some environmental and clinical characteristics show strong and consistent associations with preeclampsia (maternal smoking, maternal pre-pregnancy overweight, primiparity, multiple births, diabetes, renal disease, and long intervals between pregnancies),[2,4,9-11] they have not substantially clarified the etiology of this complex disorder.

The clinical course of preeclampsia can be quite variable. In the majority of cases, hypertension and proteinuria develop close to term, the mother has few other symptoms, and the infant is delivered with normal birth weight. In other cases, the symptoms may start early in pregnancy, and the mother can develop severe complications like HELLP (Hemolysis, Elevated Liver enzymes, Low Platelets), eclampsia, and/or multi organ failure. Although it is likely that “preeclampsia” actually represents more than one disease,[11-13] at present the diagnosis is based on syndromic criteria and clinical findings including new onset hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg) after 20 gestational weeks, along with proteinuria (protein excretion of ≥0.3 g in a 24 hour period).[14-16] However, there is variation in clinical guidelines across countries, and criteria have been revised a number of times in recent years, complicating comparison among research studies over time. [17]

Because of its unknown aetiology and its impact on maternal and fetal health, preeclampsia is subject to a large research interest. Moreover, because preeclampsia is a relatively rare condition (3-6% in developed countries), large studies are required to accrue a sufficient

number of cases with prospective exposure data and/or biological specimens. The Norwegian Mother and Child Cohort study (MoBa) is a large prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health.[18,19] It was established with a primary goal of providing data for the study of environmental and genetic risk factors for diseases in pregnancy and childhood. Information has been collected through questionnaires during and after pregnancy, and blood samples have been obtained from both parents during pregnancy and from the mother and child (umbilical cord) at birth. Clinical information on birth outcome is provided through data linkage with the Medical Birth Registry of Norway (MBRN), a population based registry established in 1967 with country-wide compulsory notification of the clinical course and outcome characteristics of all births, including pregnancy complications such as preeclampsia. [20] Together these sources of data make MoBa a valuable database for studying genetic and environmental causes of preeclampsia.

Although preeclampsia data from the MBRN have been used in numerous studies in high impact journals, describing aspects of this complication,[5,7,21-26] only one small study has examined the validity of preeclampsia registration in the MBRN from five hospitals. [27] The aim of the present study was to examine the validity of preeclampsia registration in the MBRN for all women who participated in MoBa and were registered with preeclampsia in the MBRN. In addition, a proportion of MoBa participants without registered preeclampsia were also studied, to enable estimation of the sensitivity and specificity of preeclampsia registration.

Methods

Pregnant women from all over Norway were invited to participate in MoBa during the years 1999-2008.[18] In Norway, approximately 98% of pregnant women present for ultrasound examinations in the second trimester, and invitations to participate in MoBa were sent by mail together with the appointment for ultrasound examination. MoBa expanded to national recruitment by 2005, with 50 of 52 eligible hospitals participating, ultimately recruiting 90,700 mothers, 71,500 fathers and 108,000 children.

In Norway, pregnant women carry a standardized antenatal chart to all antenatal examinations during pregnancy, where blood pressure, results from urinary tests, body weight, and edema are among variables recorded. At the time of delivery, the woman brings this chart to the delivery unit where it is kept for documentation purposes. The midwife transfers information requested by the MBRN (such as diagnosed pregnancy complications, maternal smoking habits, drugs taken during pregnancy) from the antenatal chart to the MBRN notification form. The MBRN also includes information about the course of delivery and birth outcomes, obtained by chart review or abstracted electronically from the medical records. The MBRN is routinely matched with the files of the Central Person Registry, to ensure medical notification of all newborns in Norway, and to obtain information on dates of death.

Since 1999, preeclampsia is notified to the MBRN by marking one or more of the following tick boxes on the MBRN notification form: “Preeclampsia, mild”, “Preeclampsia, severe”

and “Preeclampsia, before 34 weeks”. In addition, the form includes tick boxes for “HELLP syndrome” and “Eclampsia”, as well as for “Gestational hypertension (without proteinuria)” and “Pre-existing hypertension”. There are also separate tick boxes for “Preexisting diabetes type 1”, “Preexisting diabetes type 2” and “Gestational diabetes”. In addition to tick boxes, a considerable amount of free text information is received, which is coded at the MBRN using the International Classification of Diseases (ICD), 10th Revision (from 1999). Since 2006, an increasing proportion of births are notified electronically to the MBRN (close to 90% in 2012), but the content remains largely unchanged since 1999.

All women participating in MoBa who were registered with preeclampsia in the MBRN were selected for the study, a total of 4081 women. In addition, a random sample of 2000 MoBa participants without registered preeclampsia, were added. Invitations to participate in the validation study were sent to the delivery units where these women had given birth, requesting a copy of the antenatal charts and a list of hospital discharge codes (ICD-10) from the delivery stay. Births took place in a total of 52 delivery units. Two of these units, with a total of 103 selected women, were not participating hospitals in MoBa, and did therefore not respond. Another two delivery units, with 553 selected women, declined participation. One unit with three selected women was no longer operating, and a total of five women gave birth outside institutions. A total of 47 delivery units agreed to participate, and were requested to provide information for 5417 pregnancies. A total of 78,811 MoBa women gave birth from 22 gestational weeks at participating hospitals.

Data from antenatal charts and discharge codes provided by the hospitals were entered into an electronic database. Systolic and diastolic blood pressure as well as urinalysis and gestational age (weeks) at the time of visit was registered from 55,210 antenatal visits for 5104 pregnancies where antenatal charts were received (94% of all pregnancies received, Table 1). Values were assessed for inconsistent or implausible entries and corrected when possible through inspection of the paper antenatal charts. Following data cleaning, systolic blood pressure was missing for 1330 visits (2.4%), diastolic blood pressure was missing for 1365 visits (2.5%), urinalysis was missing for 8651 visits (15.7%) and the gestational week of visit was missing for 5175 visits (9.4%).

As the gold standard for “true preeclampsia” we considered positive blood pressure and protein criteria noted on the antenatal chart, or presence of preeclampsia/eclampsia ICD-10 codes on the hospital discharge form. Positive blood pressure and protein criteria were defined by 140 mmHg or more systolic and/or 90 mmHg or more diastolic after the 20th week of gestation and proteinuria of ≥ 0.3 g per 24 hours (≥1 + on dip-stick) at the same visit.[14] A single antenatal visit with these criteria was considered adequate. Women with evidence of hypertension before the 20th week who later met criteria for preeclampsia were considered to have preeclampsia superimposed on chronic hypertension and were included among the ”true preeclampsia” cases. For women where either the antenatal charts were missing, or where hypertension and proteinuria criteria were not fulfilled, we included women as “true preeclampsia” cases if ICD-10 codes indicating preeclampsia/eclampsia were present on the hospital discharge forms (O14 or O15). Hospital discharge codes capture the clinical information after hospital admittance and are particularly important when an acute onset of severe symptoms results in emergent transfer to hospital or when

preeclampsia presents at the time of delivery. The ICD10 code O13 may be used for both "mild preeclampsia" and "gestational hypertension with little or no proteinuria". We therefore did sub-analyses where we also included women with only O13 on the hospital discharge codes as "true preeclampsia" cases.

A true case of "severe preeclampsia" was defined as women whose blood pressure increased to at least 160 mmHg systolic and/or 110 mmHg diastolic along with proteinuria of at least 2+ on dip-stick, or if the ICD-10 codes O14.1 (severe preeclampsia), O14.2 (HELLP syndrome) or O15 (Eclampsia) were included among hospital discharge codes.

Preeclampsia in the MBRN was defined by one or more of the alternatives "Preeclampsia, mild", "Preeclampsia, severe", "Preeclampsia, before 34 weeks", "HELLP syndrome" or "Eclampsia" (tick boxes or corresponding free text). "Severe preeclampsia" in the MBRN was defined in three ways: (1) By the tick boxes "Preeclampsia, severe", "HELLP syndrome" or "Eclampsia" or free text coded with the corresponding ICD-10 codes (O14.1, O14.2 or O15); (2) As the previous and including "Preeclampsia, before 34 weeks"; (3) Any preeclampsia combined with preterm delivery.

We calculated the positive predictive value (PPV) of preeclampsia registration as the number of MBRN preeclampsia cases found to be true divided by the total number of MBRN preeclampsia cases (multiplied by 100%). The PPV was calculated using two definitions of gold standard preeclampsia: one excluding and one including the ICD-10 code O13 (light preeclampsia). Further, we also stratified by maternal age (<35 years versus >=35 years), parity (primipara versus para 1+), low birth weight (LBW, <2500 grams; yes/no), preterm delivery (<37 weeks; yes/no) and maternal pregestational diabetes (yes/no). Finally, we calculated the PPV of severe preeclampsia registration in the MBRN.

Given the sampling used in this study, estimation of sensitivity and specificity needed to account for the control sampling fraction. Among the underlying population of 78,811 eligible MoBa deliveries, all pregnancies registered with preeclampsia in the MBRN were identified, therefore calculation of PPV was straightforward. However, only a small subset of the remaining pregnancies was sampled as controls among those without a preeclampsia registration. Therefore the observed false negatives and true negatives were up weighted proportionally to account for the estimated 75,311 pregnancies without preeclampsia, which presumably would have been observed had records from the entire MoBa population been reviewed. Estimated sensitivity was then calculated as the number of true MBRN preeclampsia registrations divided by the estimated total number of true preeclampsia cases in the total eligible population (multiplied by 100%). The estimated specificity was calculated as the estimated number of truly negative preeclampsia registrations among the estimated total number of true negative preeclampsia cases (multiplied by 100%). Calculations of 95% confidence intervals (CI) around the proportions and differences were based on the normal approximation to the binomial distribution, except when calculating the estimated sensitivity and specificity. Here, 95% confidence intervals were calculated as bootstrap percentiles using 5000 bootstrap samples. Resampling was conditional on PE status in the MBRN.

Analyses were done using PASW (Predictive Analytics Software, formerly Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 18 and SAS 9.3 (Cary, NC, USA). The MBRN regulation requires the Registry to carry out quality control such as validation of received information, and such studies are exempt from Ethical Review.

RESULTS

Data was received from a total of 47 hospitals and for a total of 5,340 pregnancies (98.6% of 5,417 requested from participating hospitals, 87.8% of the 6,081 identified pregnancies). Hospitals returned incorrect charts in 57 pregnancies (different pregnancies for the requested women), however these charts could still be validated through linkage to the MBRN. For 4,348 (81.4%) women, we received both antenatal charts and hospital discharge codes, for 756 (14.2%) women we only received antenatal charts, and for 218 (4.1%) only hospital discharge codes (Table 1). For 18 women we only received written notes with insufficient information from the hospital stay.

Table 1 also shows the distribution of the received data by region of Norway. The West had the most complete set of gold standard data, with as much as 91.8% of the women being covered by both antenatal charts and hospital discharge codes. The East had the lowest proportion of complete gold standard data, 60% of the women had both antenatal charts and hospital discharge codes and 38% had antenatal charts alone.

Among the 5,340 women, 3,500 were registered with preeclampsia in the MBRN. Table 2 shows some characteristics of the women and their infants by preeclampsia status as defined by the MBRN and by the gold standard. For the latter, the table displays results when preeclampsia criteria were met by both antenatal charts and hospital discharge codes (not including O13), by charts alone or by discharge codes alone. There were no significant differences in the proportion of women aged 35 years or more at delivery across categories of preeclampsia diagnosis, whereas the proportion of primiparous women was lower if women had their preeclampsia diagnosis based on antenatal charts only (difference −6.2 [95% confidence interval (CI) −10.4, −2.1]) or on hospital discharge codes only (difference −6.1 [95% CI −10.4, −1.7]) rather than on both. Further, the proportions of preterm delivery (difference −18.5[95% CI −21.7, −15.2]) and infant LBW (difference −15 [95% CI −18.1, −12.0]) were significantly lower if the gold standard preeclampsia was based only on antenatal charts rather than on both charts and hospital discharge codes, whereas the proportion of women with pregestational diabetes was significantly lower if the gold standard preeclampsia was based only on hospital discharge codes (difference −1.2[95% CI −2.1, −0.2]).

Table 3, upper part (A), shows the overall positive predictive values of preeclampsia registration in the MBRN using two slightly different definitions of “true preeclampsia”: When the ICD-10 codes O14 (preeclampsia) or O15 (eclampsia) were added to hypertension and proteinuria criteria as “true” preeclampsia, registration of preeclampsia in the MBRN was found true in 83.9% of the cases (95% CI 82.7, 85.1]). When also including O13 (ICD-10), the PPV increased to 87.3% (95% CI 86.2, 88.4).

The lower part of Table 3 (B) shows the PPV in the five regions of Norway. The West had significantly higher PPV than all the other regions (88.4%), however, in all regions the PPV was above 80%.

Table 4 shows the PPV by some maternal and infant characteristics. We found no significant differences in the percentage of correct preeclampsia registration by maternal age, whereas there were slightly better values among primiparous than parous women. The PPV was further significantly higher when mothers delivered preterm or LBW infants compared to their counterparts (93.5% vs 80.7% and 93.8% vs 81.4%, respectively). Although there were relatively few cases, PPV appeared independent of maternal pregestational diabetes.

Although overall PPV was good, the results did reveal false positive preeclampsia registrations in the MBRN. Looking more closely at the 564 women with false positive registrations (overall results), 510 had sufficient clinical data after week 20 to evaluate the diagnostic components of preeclampsia based on antenatal records. Among these, 119 (23.3%) had an O13 hospital discharge code, indicating mild preeclampsia/ gestational hypertension, 294 (57.6%) had hypertension and/or proteinuria during pregnancy (157 only hypertension, 83 only proteinuria, and 54 both hypertension and proteinuria, but never at the same visit), while 97 women (19%) had no data suggesting preeclampsia/hypertension.

We examined the PPV of severe preeclampsia registration in the MBRN, defining severe preeclampsia in three ways. When defined by “Preeclampsia, severe”, “HELLP syndrome” or “Eclampsia” (Definition 1), 70.7% of severe MBRN cases were verified as true severe cases (PPV=70.7 [95% CI 67.9,73.5]). When we added “Preeclampsia before 34 weeks” into the case definition (Definition 2), PPV decreased slightly to 68.1% [95% CI 65.5,70.7]), while defining severe preeclampsia as any preeclampsia with preterm delivery (Definition 3) provided a PPV at 68.5 [95% CI 65.5,71.7].

Table 5 shows the sensitivity and specificity of preeclampsia registration, generalized to the underlying population of 78,811 eligible MoBa deliveries in the delivery units participating in the study. Extrapolated to this population, the estimated sensitivity was low (43%) and specificity was high (99.2%). The low sensitivity was driven by 95 false negative preeclampsia registrations in the studied subpopulation. Overall, these pregnancies had less of the risk characteristics known to be associated with preeclampsia than those that were correctly registered with preeclampsia: Mothers with false negative registrations were more often multiparous than those with correct registrations (53.7% vs 36.2%), and they had a higher proportion of vaginal delivery without induction (63% vs 26%). The pregnancy outcomes were also more favorable, with a lower proportion of LBW (4% vs 23%), preterm birth (2% vs 27%) and fewer transfers to neonatal intensive care units (10% vs 28%). The proportion of complete gold standard data differed between regions, with the West having the highest proportion (92%) of pregnancies covered by both antenatal charts and hospital discharge codes. Since the West also had the highest PPV compared to the other regions (Table 3), we analyzed the observed and estimated sensitivity and specificity based on numbers in the Western region alone. The sensitivity then increased from 43% to 53%, while the specificity was unchanged at 99%.

COMMENTS

The present study examined the validity of preeclampsia registration in the MBRN for 5,340 women participating in MoBa, and giving birth during 1999-2010. The percentage of preeclampsia registrations found to be true preeclampsia cases (PPV) was satisfactory, with overall values above 83%. The estimated percentage of true preeclampsia cases in the total population that was registered with preeclampsia in the MBRN (sensitivity), was, however, less than 50%, while the estimated percentage of true negative cases that lacked a registration in MBRN (specificity) was above 99%. PPV did not vary with maternal age, but was higher among primiparous women, and pregnancies complicated by preterm delivery or low birth weight.

The strengths of the present study include a high participation rate. Records were received for 87% of the identified MoBa pregnancies and 98% of the women who delivered at participating hospitals, representing nearly all eligible delivery units in the country (47 of 52 eligible units; 90.4%). Furthermore, the gold standard was based on clinical data (blood pressure and urinary test results) for 55,210 recorded antenatal visits among 5,104 pregnancies (94% of all pregnancies received). However, based on the assumption that some women might be referred to hospital due to a sudden deterioration or emergence of preeclampsia, and that in some cases preeclampsia may be diagnosed at the time of delivery, we also included hospital discharge codes indicating preeclampsia as part of our gold standard definition. Unfortunately, clinical data was not available to us after women had been admitted to hospital, and we therefore had to assume hospital discharge codes were correct. This assumption may not always be valid.[28] However, only 23% of the gold standard preeclampsia cases were based on hospital discharge codes alone, and these women did not differ in the proportion of preterm delivery or infant LBW from those with a gold standard preeclampsia based on both antenatal charts and hospital discharge codes. On the other hand, proportions of preterm delivery and LBW were significantly lower among women whose gold standard preeclampsia diagnoses were based only on evidence from antenatal charts (25%). This may suggest that a preeclampsia diagnosis is more likely to be recorded with a hospital discharge code when additional complications related to the preeclampsia exist.

Both PPV and estimated specificity of preeclampsia registration in the MBRN were satisfactory in this study, while this was not the case for the estimated sensitivity, with values less than 50%. The study covered births during 1999-2010, which was after the MBRN notification form changed from being based totally on free text information (without specific questions about preeclampsia) to a form where tick boxes specifically cover preeclampsia. In a recent study describing time trends of preeclampsia prevalence in the MBRN, a significant increase was found in 1999. The increase was most evident for preeclampsia associated with term delivery, and may indicate increased notification of milder forms of preeclampsia. The low sensitivity was therefore surprising. Only one previous study has described the validity of preeclampsia registration in the MBRN. [27] This study covered five hospitals during the years 1967-2009, and demonstrated a slightly higher PPV than we found (88%), however, it could not calculate sensitivity.

The gold standard definition of preeclampsia applied in the present study accepted a single antenatal visit fulfilling preeclampsia criteria (hypertension and proteinuria) as adequate for ”true preeclampsia”. A total of 1087 of our gold standard preeclampsia cases (36%) only had one antenatal visit fulfilling preeclampsia criteria, and 187 of these also lacked hospital discharge codes indicating preeclampsia. Diagnostic criteria for preeclampsia used in Norway today requires that hypertension and proteinuria should be measured at least twice, at least 4-6 hours apart.[16] Our gold standard criteria may therefore have been too liberal, defining as preeclampsia some cases that in fact did not have the syndrome. However, among the 1087 women with only one antenatal criteria visit, 95% were also registered with preeclampsia in the MBRN. This suggests that the low sensitivity was not driven by the gold standard definition. In fact, the sensitivity we found using this gold standard is compatible with studies from the USA reporting the registration of gestational hypertension on birth certificates, where sensitivity was found to be less than 50%.[29, 30] Among our 95 false negative registrations, the proportions of induced delivery, LBW, preterm delivery and transfer to neonatal intensive care were much lower than among the correctly registered cases. This indicates that the preeclampsia cases missed by the MBRN tend to be milder forms with good neonatal outcome.

Based on the MBRN, the prevalence of registered preeclampsia among the 78,811 MoBa women was 4.4%. If we include the estimated false negative cases, the prevalence increases to 9.4%, which seems high. However, compared to the total population of women giving birth in Norway during 1999-2010, the MoBa population has some characteristics which may increase the preeclampsia prevalence: more primiparous women (44.5% versus 41.3% in the total population), less daily smokers (5.2% versus 14.6%) and higher mean age when delivering their first infant (28.3 versus 27.3 years). The prevalence of preeclampsia registered for all women giving birth in Norway during the same period was only 3.7%.

We also found false positive preeclampsia registration. A total of 564 women (16%) were registered with preeclampsia in the MBRN without verification by the gold standard. Although criteria for preeclampsia may seem clear, the distinction between gestational hypertension with traces of proteinuria and the full syndrome may be difficult to assess, and is perhaps not always meaningful. The two entities are therefore sometimes handled as one group of “pregnancy induced hypertension”.[31] We found that approximately 80% of the false positive cases with clinical data available had evidence of the components of preeclampsia (hypertension or proteinuria) although they never met the full clinical criteria.

The predictive value of the MBRN preeclampsia registration was dependent on maternal and infant characteristics, with higher values when factors known to be related to preeclampsia were present, for instance primiparity, LBW and preterm delivery. This may indicate that clinicians are more aware of the syndrome when the clinical picture is consistent with acknowledged risk factors. This is also supported by the lower proportions of LBW and preterm delivery among the false negative cases.

The registration of severe preeclampsia in the MBRN had lower PPV than total preeclampsia, and the different ways of defining severe preeclampsia did not change the PPV by much. It is, however, important to point out that the gold standard definition of

severe preeclampsia employed in this study might be less accurate than the definition of overall preeclampsia, since the clinical criteria for severe preeclampsia include a wider variety of maternal and fetal symptoms and laboratory values. [2,16] The antenatal charts did not systematically include symptoms such as nausea, headache, or results from blood tests (liver enzymes and platelet counts). As we could not include these factors into our gold standard definition, our definition of "true severe preeclampsia" underestimates the true prevalence.

The present study examined validity of preeclampsia registration in the MBRN for women participating in MoBa and giving birth during 1999-2010. More than 90% of the eligible delivery units in the country were covered, and we believe that although the women included were all participants in MoBa, the results are likely true also for the general registration of preeclampsia during these years. MoBa women constitute a small proportion of women giving birth every day, and it is unlikely that clinicians change their notification practice when a MoBa mother comes to deliver.

As a conclusion, the validity of preeclampsia registration in the MBRN has now been studied for most MoBa women, and the results show that in 83%-87% of cases, the registered preeclampsia is true. For the false positive cases, around 80% have components of the syndrome, and the false negative cases are presumably mild forms of the syndrome.

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Table 1

Regional distribution of data from the Medical Birth Registry of Norway (MBRN) and the received gold standard sources. Data for women participating in the Norwegian Mother and Child Cohort Study and giving birth in Norway, 1999-2010.

Region	MBRN		Gold standard sources					
	MBRN data		Received antenatal charts and ICD10		Only received antenatal charts		Only received ICD10 codes	
	Number	Column %	Number	Row %	Number	Row %	Number	Row %
East	926	17.3	556	60.0	352	38.0	13	1.4
South	1,380	25.8	1,099	79.6	229	16.6	49	3.6
West	1,821	34.1	1,672	91.8	37	2.0	108	5.9
Middle	871	16.3	738	84.7	97	11.1	33	3.8
North	342	6.4	283	82.7	41	12.0	15	4.4
Total	*5,340*	*100*	*4,348*	*81.4*	*756*	*14.2*	*218* [b]	*4.1*

Abbreviations: ICD10, International Classification of Diseases, 10th revision; MBRN, Medical Birth Registry of Norway

[b] For an additional 18 women we only received hospital summaries/notes with insufficient information.

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Table 2

Some characteristics of the women and their infants, by Medical Birth Registry (MBRN) preeclampsia status, and, for gold standard preeclampsia, by what source the diagnosis was based upon. Data for women and infants participating in the Norwegian Mother and Child Cohort Study and giving birth/ being born in Norway from 1999 to 2010.

	MBRN data				Gold standard preeclampsia					
	Preeclampsia no N=1,840		Preeclampsia yes N=3,500		Received antenatal charts and ICD10; N=1,551		Received only antenatal charts; N=776		Received only ICD10; N=704	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
35+ years	296	16.1	598	17.1	246	15.9	144	18.6	116	16.5
Primipara	797	43.3	2,195	62.7	1,028	66.3	466	60.1	424	60.2
< 2500 gr	55	3.0	711	20.3	391	25.2	79	10.2	201	28.6
< 37 weeks	87	4.8	851	24.5	475	30.6	96	12.4	227	32.2
Pregestational diabetes	10	0.5	57	1.6	29	1.9	18	2.3	5	0.7

Abbreviations: ICD10, International Classification of Diseases, 10th revision; MBRN, Medical Birth Registry of Norway

Table 3

Positive predictive value (PPV) of preeclampsia (PE) registration in the Medical Birth Registry of Norway (MBRN), overall (A) and in five regions of Norway (B). The gold standard (GS) for true preeclampsia was based on blood pressure and proteinuria recordings on antenatal charts and/or ICD-10 codes from hospital discharge diagnoses. Results are shown for 5340 women participating in the Norwegian Mother and Child Cohort Study and giving birth in Norway, 1999-2010.

A Overall PPV	PE in MBRN and GS	PE in MBRN only	PE in GS only	PPV	95% CI		
Overall results A[a]	2,936	564	95	83.9	[82.7, 85.1]		
Overall results B[b]	3,055	445	112	87.3	[86.2, 88.4]		
B Regional results	PE in MBRN and GS	PE in MBRN only	PE in GS only	PPV	95% CI	Difference in PPV	95% CI around difference
East	467	115	23	80.2	[77.0, 83.4]	−8.2	[−11.9, −4.5]
South	676	162	31	80.7	[78.0, 83.4]	−7.7	[−10.9, −4.5]
West	1,109	145	20	88.4	[86.6, 90.2]	0	Reference
Middle	492	103	14	82.7	[79.7, 85.7]	−5.7	[−9.2, −2.2]
North	192	39	7	83.1	[78.3, 87.9]	−5.3	[−10,4 −0.2]

Abbreviations: CI, confidence interval; GS, gold standard; ICD10, International Classification of Diseases, 10th revision; MBRN, Medical Birth Registry of Norway; PE, preeclampsia; PPV, positive predictive value

[a] True preeclampsia was based on blood pressure increase (from antenatal charts) to at least 140 mmHg systolic and/or 90 mmHg diastolic after the 20th week of gestation together with proteinuria of at least 0.3 g per 24 hours or ≥1 + on dip-stick; or one or more ICD 10 codes indicating preeclampsia (O14 or O15) on the hospital discharge codes.

[b] As above, but in addition the hospital discharge code O13 (ICD-10) was included as sufficient for defining a true preeclampsia case.

Table 4

Positive predictive value (PPV) of preeclampsia (PE) registration in the Medical Birth Registry of Norway (MBRN) by maternal age, parity, maternal diabetes, gestational age and birth weight. The gold standard (GS) for true preeclampsia was based on blood pressure and proteinuria recordings on antenatal charts and/or ICD-10 codes from hospital discharge diagnoses. Results are shown for 5340 women participating in the Norwegian Mother and Child Cohort Study and giving birth in Norway, 1999-2010.

PPV by maternal and infant factors	PE in MBRN and GS[a]	PE in MBRN only	PPV	95% CI	Difference in PPV	95% CI around difference
Maternal age						
35+ years	490	108	81.9	78.8, 85.0	−2.4	−5.8, 1.0
< 35 years	2446	456	84.3	83.0, 85.6	0.0	Reference
Parity						
Primipara	1874	321	85.4	83.9, 86.9	4.0	1.4, 6.6
Para 1+	1062	243	81.4	79.3, 83.5	0.0	Reference
Diabetes						
Yes	48	9	84.2	74.7, 93.7	−0.3	−9.8, 9.2
No	2888	555	83.9	82.7, 85.1	0.0	Reference
Preterm						
< 37 weeks	796	55	93.5	91.8, 95.2	12.8	10.6, 15.0
37+ weeks	2119	507	80.7	79.2, 82.2	0.0	Reference
Birth weight						
< 2,500 gr	667	44	93.8	92.0, 95.6	12.4	10.1, 14.7
2,500+ gr	2,267	519	81.4	80.0, 82.8	0.0	Reference

Abbreviations: CI, confidence interval; GS, gold standard; ICD10, International Classification of Diseases, 10th revision; MBRN, Medical Birth Registry of Norway; PE, preeclampsia; PPV, positive predictive value

[a]True preeclampsia was based on blood pressure increase (from antenatal charts) to at least 140 mmHg systolic and/or 90 mmHg diastolic after the 20th week of gestation together with proteinuria of at least 0.3 g per 24 hours or ≥1 + on dip-stick; or one or more ICD 10 codes indicating preeclampsia (O14 or O15) on the hospital discharge codes.

Table 5

Estimated sensitivity and specificity of preeclampsia (PE) registration in the Medical Birth Registry of Norway (MBRN) for women in the Norwegian Mother and Child Birth Cohort (MoBa). Results are based on data from 5340 MoBa women giving birth in Norway, 1999-2010, and up weighted to account for the total of 78,811 MoBa women who delivered a singleton pregnancy from 22 weeks in the delivery units participating in the validation study.

	Gold standard[a]:		
	PE yes	**PE no**	**Total**
Observed MBRN: PE yes	2,936	564	3,500
Observed MBRN: PE no	*95*	*1,745*	*1,840*
Estimated MBRN[b]: PE no	3,888	71,423	75,311
Totals	6,824	71,987	78,811
Validity (95% CI) [c]	Sensitivity (95% CI)	Specificity (95% CI)	
	43.0 (38.7, 48.2)	99.2 (99.2, 99.3)	

Abbreviations: CI, confidence interval; MBRN, Medical Birth Registry of Norway; PE, preeclampsia;

[a] Gold standard preeclampsia was based on hypertension (at least 140 mmHg systolic and/or 90 mmHg diastolic after the 20th week of gestation) together with proteinuria (at least 0.3 g per 24 hours or ≥1 + on dip-stick) from antenatal charts; or one or more ICD 10 codes indicating preeclampsia (O14 or O15) on hospital discharge codes.

[b] Based on 1,840 randomly chosen women without a preeclampsia registration in which antenatal charts and discharge codes were reviewed for evidence of preeclampsia, and generalized to the total of 78,811 MoBa women who delivered a singleton pregnancy from 22 weeks in one of the delivery units participating in the validation study. Estimated values calculated as follows: False Negatives = (95/1840)*(78,811-3500) = 3,888. True Negatives = (1745/1840)*(78,811-3500) = 71,423

[c] Confidence intervals based on 2.5th and 97.5th bootstrap percentiles from 5,000 bootstrap samples conditional on MBRN PE status. The “Estimated MBRN: PE no” value was re-calculated for each replicate.