SAVING NEWBORN BABIES – THE BENEFITS OF INTERVENTIONS IN NEONATAL CARE IN NORWAY OVER MORE THAN 40 YEARS

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ABSTRACT

The aim of this study was to examine the effect that the introduction of new medical interventions at birth has had on mortality among newborn babies in Norway during the period 1967-2011. During this period there has been a significant decline in mortality, in particular for low birth weight infants. We identified four interventions that together explained about 50% of the decline in early neonatal and infant mortality: ventilators, antenatal steroids, surfactant and insure. The analyses were performed on a large set of data, encompassing more than 1.6 million deliveries (Medical Birth Registry of Norway). The richness of the data allowed us to perform several robustness tests. Our study indicates that the introduction of new medical interventions has been a very important channel through which the decline in mortality among newborn babies occurred during the second half of the last century.

1. INTRODUCTION

In this paper, we examine the effect that the introduction of new medical interventions at birth has had on mortality among newborn babies in Norway over a period of more than 40 years. Medical interventions used in neonatal units are very costly, and they contribute to a substantial part of hospital care expenditure (Richardson *et al*., 2001; Gilbert *et al.*, 2003; Almond *et al*., 2005; Schmitt *et al.*, 2006). Somewhat surprisingly, in the light of the high costs, there are few studies within the economic literature where the benefits of these interventions have been assessed.

The gold standard for determining the effects of medical interventions on any health outcome is randomized controlled trials. Based on the evidence, the general perception is that medical innovation and improvements in medical technology have made a contribution in reducing infant mortality, particularly for low birth weight infants, during the second half of the last century (Saugstad *et al*., 2006; Cutler *et al*., 2012). The introduction of the following interventions is particularly highlighted: ventilators, antenatal steroids, surfactant and insure.

On the other hand, randomized controlled trials have their limitations. In particular, the results may be difficult to generalize to populations that are different from those in the study. Even if interventions have been shown to be effective in clinical studies, the effects may be smaller in real life settings (Steckler and McLeroy, 2008; Gerber and Green, 2012). Several factors influence the effectiveness of the interventions, for example: Are the diagnostic criteria clear, i.e. is it obvious which type of infant should receive the treatment? Do the staff agree on the criteria for when the treatment should be provided? Do the staff have the skills to administer the treatment? Alternatively, are the staff reluctant to change their medical practice to a type of treatment that is new and unknown? Does the neonatal intensive care unit have enough resources to provide the new treatment? What are the effects of the interventions in the months after birth? Also, it is difficult to obtain data over a sufficiently long time span so that long-term effects can be estimated.

We examined our research question using a large and unique set of data, which contains information about early neonatal mortality and infant mortality, and detailed medical information about nearly all births in Norway during the period 1967-2011.

This is a period where there has been a significant decline in infant mortality. To what extent has the use of new medical interventions at birth contributed to this decline?

Below, we first briefly describe the types of intervention that were the focus of our study, and review the most relevant background literature. We then describe the main characteristics of our study population, the data and the empirical model. Finally, the results are presented and discussed.

2. TYPES OF INTERVENTION AND BACKGROUND LITERATURE

We focused on the introduction of the following interventions: ventilators, antenatal steroids, surfactant and insure. Antenatal steroids are usually given to the mothers in the maternity wards in order to speed maturation of foetal lung function for infants with a risk of premature delivery. The three other interventions are used for newborn babies in neonatal units. Ventilators provide breathing support, as premature babies have fragile and tiny lungs. Surfactant helps to keep the lung sacs open, and is used for the treatment of respiratory distress syndrome. Insure, which stands for INtubate – SURfactant – Extubate, is an alternative way to treat infants who need surfactant (Aguilar *et al.*, 2013). With conventional surfactant therapy the infant is intubated, and the surfactant administered through an endotracheal tube. The tube is left in place, and the infant is supported by some kind of assisted mechanical ventilation. With insure, the infant is extubated after the surfactant is administered, and then respiratory support is provided by means of non-invasive positive pressure ventilation, such as CPAP (Courey *et al.*, 2015).

The administration of antenatal steroids and surfactant are fairly simple one-time treatments. Use of ventilators and insure are types of treatment that have longer duration and that require highly qualified staff. Several studies have shown that mortality rates for very low birth weight infants are lower if the infants are treated in large neonatal intensive care units compared to in smaller units (Phibbs *et al.*, 1996, 2007; Hamilton *et al.*, 2007). This is mainly because more highly trained and more experienced staff, and better facilities are available in larger units compared to in smaller units. Therefore, the effect on early neonatal mortality and infant mortality of using ventilators and insure may be related to the size of the neonatal department.

One consistent finding in the literature is that the mortality risk is higher for infants born in hospitals with no or few neonatal resources compared to those born in hospitals with a sufficient level of such resources. This is particularly the case for low birth weight infants. Lasswell *et al.* (2010) reviewed 41 publications, including randomized clinical controlled trials, cohort and case-control studies published between 1979 and 2008. They concluded that: "for VLBW (birth weight < 1500g) and VPT (less than 32 weeks' gestation) infants, birth outside of a level III hospital is significantly associated with increased likelihood of neonatal or predischarge death". There are at least two reasons for this. First, low birth weight infants would receive a sub-optimal level of care if born in hospitals with no or few neonatal resources (for example see: Cordero *et al.*, 1982; Hemminki, 1985; Field *et al*., 1991; Menard *et al.*, 1998; Cifuentes *et al.*, 2002). Second, transporting infants who need neonatal care from one hospital to another can be harmful (Modanlou *et al.*, 1980; Harris *et al.*, 1981; Lamont *et al.*, 1983; Kollée *et al*., 1988; Bowman *et al.*, 1988; Lee *et al.*, 2001; Messner, 2011). This strongly supports the need for appropriate and effective referral routines for high-risk deliveries to hospitals with neonatal departments before delivery.

The most relevant research for our study is that of Almond *et al*. (2010) and Bharadwaj *et al*. (2013). Using a regression discontinuity design, they showed that very low birth weight infants had a higher probability of survival if they were transferred to a neonatal unit compared to if they were not. The authors had no data that could explain which types of intervention or which types of service were important. Our study extends this research, as we were able to identify the exact intervention that was effective. In addition, we were able to quantify the contribution that each of the four interventions has made to the decline in infant mortality over more than 40 years.

With the exception of the work of Almond *et al*. (2010) and Bharadwaj *et al*. (2013), nearly all observational studies within this field have used cross-sectional data. Typically, these studies show no or very little relationship between the supply of neonatal intensive care units and neonatal mortality (Merenstein *et al*., 1985; Goodman *et al*., 2002). On the basis of the results from these studies, several researchers and policymakers have questioned the effectiveness of neonatal care, in particular in the USA (Silverman, 1993; Merenstein, 2001; Goodman *et al*., 2001; Grumbach, 2002). Such doubt may be unjustified, as the results from cross-sectional studies may be biased,

among other things because unobserved heterogeneity is not taken into account in the analyses.

3. MATERIAL AND METHODS

3.1. The institutional setting for neonatal care in Norway

Our study was performed within a standardized institutional health care setting with public funding. In Norway, all health services (neonatal care included) are financed through taxes, and everyone has free health care at the point of delivery and equal access given equal need (Ministry of Health, 2002). All hospitals, where all neonatal care is provided, are publically owned and financed, with doctors who receive a fixed salary. There is no competition between hospitals for infants who need neonatal care. The country is divided into hospital areas in which the capacity of neonatal departments is planned according to the expected number of infants who need neonatal care within the catchment area.

A standardized institutional health care setting has a major advantage compared to other settings. Ideally, neonatal care should be provided according to medical needs. This is not necessarily the case in market-based systems with private health insurance and with incentive-based payment systems for neonatologists and paediatricians (Goodman *et al*., 2002). For example, the type of insurance, and the level of insurance that the parents have, will be correlated with the amount and type of neonatal care provided (McCarthy *et al*., 1979; Braveman *et al*., 1991; McCormick and Richardson, 1995). Further, in market-based health care systems, the type and amount of neonatal care provided may be influenced by the economic incentives that the neonatologists or paediatricians have (Baker and Phibbs, 2002; Profit *et al*., 2007; Shigeoka and Fushimi, 2014). For example, they may provide the treatment that gives the highest income, which, within reasonable limits, may not be highly correlated with health care needs. One strength of the current analyses is that private health insurance or incentive-based payment systems do not bias our results.

3.2. Study population

Postnatal advanced interventions are provided at hospitals with neonatal departments. There are 21 such hospitals. This number was the same throughout the whole study period 1967-2011. Our study population encompassed all infants who were born in these hospitals between 1967 to 2011 - altogether 1 612 789 infants. This represents 70% of all deliveries during that period. The rest of the infants were born in local hospitals, which do not have a neonatal department (Grytten *et al*., 2014a).

The percentage of all newborn infants who have been transferred from a maternity ward to a neonatal department has been much the same during the study period. For example, in the 1970s and early 1980s about 8% of all newborn infants were transferred (Larssen *et al.*, 1981). At the end of the last century it was about 9%, and at the end of the last decade it was about 8% (Medical Birth Registry of Norway, 2015). Nearly all the transfers were from a maternity ward that was located in the same hospital as the neonatal department, i.e. these infants did not need to be transported to another hospital.

Only about 0.5% of all newborn infants were transferred from one neonatal department to another. Most of these were transferred to a neonatal department located at a regional hospital for diagnosis and treatment of congenital abnormalities (Ministry of Social Affairs, 1984; Meberg *et al*., 1993; Meberg and Hansen, 2005). There are 5 regional hospitals in Norway.

Throughout the whole study period, less than 1% of all newborn infants were transferred from local hospitals, which do not have neonatal department, to hospitals with neonatal department (Bjerkedal *et al.*, 1975; Fevang and Finne, 1975; Ministry of Social Affairs, 1984; Medical Birth Registry of Norway, 2015). This low percentage can be explained in two ways:

First, the majority of mothers live in the catchment area of hospitals that have a neonatal department. Second, all mothers are assessed to determine whether their pregnancy is high risk. This is done through a comprehensive antenatal care programme that encompasses all pregnant mothers from gestation week 9 until they give birth (Norwegian Directorate for Health and Social Affairs, 2005a). According to national guidelines, several visits to a midwife and/or a doctor are recommended during that period of the pregnancy. During the 1970s and 1980s 14 visits were recommended

(Blondel *et al.*, 1985). This was reduced to 12 visits during the 1990s, and to 7 at the end of 2000 (Backe, 2001; Norwegian Directorate for Health and Social Affairs, 2005b). Risk assessment is particularly important for mothers who live in the catchment area of a hospital *without* a neonatal department. For these mothers, if their pregnancy is assessed as high risk, they are referred before delivery to hospitals that have a neonatal department. This referral system is effective – virtually all high risk deliveries occur at hospitals with neonatal departments (Grytten *et al*., 2014a).

3.3. The source of the data

We carried out our main analyses on data from the Medical Birth Registry of Norway (MBRN) (www.fhi.no). Maternity units report all births in Norway to MBRN (Irgens, 2000). We collected information about use of advanced interventions using a questionnaire that we sent to all senior neonatologists in every neonatal department. We asked them to provide the following information: "Enter as accurately as possible the five-year interval your hospital introduced the use of ventilators, antenatal steroids, surfactant and insure". The response options were the following: the first interval was 1967-1969, then each 5-year interval from 1970-2004, the last interval was 2005-2011. All the 21 senior neonatologists replied.

3.4. The model specification

In the analyses, we defined four dummy variables for the four interventions. For each of the four variables, the value of the variable was 0 for each 5-year interval before it was introduced, and 1 from the 5-year interval in which it was introduced, and subsequently. Our core regression model is then defined as:

$$Y_{ijtp} = \alpha + \beta_1 Ventilators_{jp} + \beta_2 Antenatal\_steroids_{jp} + \beta_3 Surfactant_{jp} + \beta_4 Insure_{jp} + \sum_c \gamma_c \cdot Control_{ijtp}^c + \sum_j \delta_j \cdot Hospital_j^j + \phi \cdot Year_t^{-1} + \sum_j \eta_j \cdot Hospital_j^j \cdot Year_t^{-1} + u_{ijtp} \quad (1)$$

where Y_{ijt} is a binary variable indicating death of individual *i* born at hospital *j* in year *t* (from 1967 to 2011) in period *p* (five-year interval). For all four interventions, we measured the effects on death by running three separate regressions for each of the following outcomes Y_{ijt}: death during the first week after birth (early neonatal mortality), death during the first year after birth (infant mortality), and death during the period one week to one year after birth.

We expect the sign of the parameters β_1 to β_4 to be negative. Further, based on the evidence from medical research, we expect the effects to be largest for small infants. Therefore, for each of our outcomes Y_{ijt}, separate regressions were run for the following weight groups: ≤1000g, 1001-1500g, 1501-2500g, >2500g.

In order to take account of potentially confounding effects, Equation (1) includes controls for a range of factors. First, the equation includes fixed hospital effects, by way of a set of $Hospital^j$ indicators and associated parameters δ_j. This was done in order to control for all time-invariant heterogeneity between hospitals, for example stable regional differences in neonatal care. Second, the equation includes control for the inverse of the birth year, by way of the $Year^{-1}$ variable and its associated parameter ϕ. This was done to control for common and stabilizing trends that affect mortality, for example better living standards and public health measures such as improved nutrition. To take into account that the time trend ($Year^{-1}$) could have different effects for infants born in the different hospitals, hospital specific trends were also included using a set of interactions terms, $Year^{-1} \cdot Hospital^j$ and its associated parameters η_j. Third, the equation includes controls for several risk factors of the infant and the mother – see the next section for a detailed description.

We clustered the standard errors at the hospital level to account for positive serial correlation and within hospital correlation (Cameron and Miller, 2015). The estimation of Equation (1) is based on a long time series where the intervention variables changed very little within each neonatal department over time: once the department had got the intervention, it remained in use in all subsequent years. This leads to a potential serial correlation problem, which would lead to misleadingly small standard errors unless it is corrected for (Bertrand *et al*., 2004; Donald and Lang, 2007).

3.5. Control variables

Previous research has shown that the prevalence of risk factors of the infant and the mother has changed over time (Grytten *et al.*, 2011). Unless these factors are properly controlled for, our estimates for the effects of the interventions may be biased.

For the infants, we controlled for birth weight, length of gestation and congenital malformations, as these are the main predictors of death during the first weeks after birth (McCormick, 1985; Kramer *et al*., 2000a; Rosano *et al*., 2000). The probability for death also increases if the foetus has an abnormal presentation and if the birth is a multiple birth (Hannah *et al*., 2000; Luke and Keith, 1992; Matthews and MacDorman, 2007).

Risk factors of the mother that reduce the newborn infant's chance of survival are: whether she has one or more chronic diseases, whether preeclampsia is a complication, whether she has bleeding during pregnancy and whether she is well into her thirties when she gives birth (Matthews and MacDorman, 2007; Koblinsky, 1995; Duley, 2009; Williams *et al*., 1991; Ananth and Savitz, 1994; Cleary-Goldman *et al*., 2005). Infants of mothers with a high level of education have better health compared to infants of mothers with a low level of education (Gortmaker and Wise, 1997; Kramer *et al*., 2000b; Grytten *et al*., 2014b). In Europe, newborn infants of non-European immigrant mothers have a higher mortality rate than infants whose mother is from the native population (Gissler *et al*., 2009). This is also the case in Norway (Naimy *et al*., 2013).

At the hospital level we controlled for the number of infants with a birth weight <1500 g delivered per hospital. This is a measure of the size of the neonatal department, and a proxy variable for the quality of the staff and the facilities. Descriptive statistics for the control variables are given in Grytten *et al.*, 2011.

4. RESULTS

4.1. Descriptive statistics - changes from 1967 to 2011

During the period 1967-2011, there has been a marked decline in early neonatal mortality and infant mortality (Figure 1). The decline was particularly large for infants

with a low birth weight: from nearly 100% to 30% for babies with a birth weight 1000g and less, from 50% to 10% for babies with a birth weight 1001-1500g and from 8% to 2% for babies with a birth weight of 1501-2500g.

For all weight groups 2500g and less, the decline in mortality was about the same for both early neonatal mortality and infant mortality. This implies that if the baby survived the first week after birth, he/she was also very likely to survive until the age of 1 year. For babies with a birth weight greater than 2500g, infant mortality was markedly higher than early neonatal mortality at the beginning of the period. This difference was small at the end of the period.

Ventilators were introduced early in the period (Table I). By the first half of the 1980s, 15 of 21 neonatal departments had ventilators. Antenatal steroids were in use in 5 maternity units during the period 1975-1979. By the first half of the 1990s, 19 maternity units used antenatal steroids. Surfactant was introduced during a short time span from the second half of the 1980s to the first half of the 1990s. Use of insure was first in use in one neonatal department during the period 1995-1999. In the second half of the 2000s, 10 departments had introduced the use of insure.

4.2. Effects of interventions on early neonatal mortality and infant mortality

For all birth weight groups, ventilators, antenatal steroids and surfactant had a negative and significant effect on both early neonatal mortality and infant mortality (Table II). The effects were largest for the birth weight groups 1000g and less and 1001-1500g. As expected, the effects were small for babies with a birth weight of more than 2500g.

Ventilators, antenatal steroids and surfactant reduced the probability of early neonatal mortality: from 0.17 (surfactant) to 0.09 (ventilators) for babies with a birth weight 1000g and less, from 0.13 (ventilators) to 0.04 (surfactant) for babies with a birth weight of 1001-1500g, from 0.015 (antenatal steroids) to 0.008 (surfactant) for babies with a birth weight of 1501-2500g, and from 0.0005 (ventilators and surfactant) to 0.0004 (antenatal steroids) for babies with a birth weight greater than 2500g.

For ventilators and antenatal steroids, the sizes of the regression coefficients were fairly similar for both early neonatal mortality and infant mortality. This implies that if babies survived the first week after birth due to treatment with ventilators and

antenatal steroids, they would also survive up to one year of age. This finding is not surprising. It is well known that the majority of deaths occur during the first few days after delivery. For surfactant, the regression coefficients for infant mortality were slightly higher than for early neonatal mortality. This implies that there was a small, but additional gain in survival beyond one week after birth. This is further supported by small, but statistically significant negative regression coefficients for the probability of death during the period one week to one year after birth for surfactant.

Insure had a significant effect for the birth weight groups 1000g and less on both early neonatal mortality and infant mortality. For the other birth weight groups, the regression coefficients had the correct sign (negative), and they were statistically significant at conventional levels for infant mortality, but not for early infant mortality.

In Figure 2, the results from the regression analyses are conveyed visually. We have simulated different infant mortality trajectories during the period 1967-2011 for the hospital with the largest neonatal department in Norway (Rikshospitalet University Hospital). These simulations are based on the parameter estimates obtained in Table II. The control variables have been set at their yearly population mean values.

The blue line illustrates the situation when the trend variable and the four interventions are held constant at their 1967 values. The line is fairly horizontal. This indicates that without adjustments for trend and interventions, infant mortality at the end of the period would have been fairly similar to the mortality at the beginning of the period.

In the green trajectory all the four interventions are kept at their 1967 level throughout, while the trend variable varies according to its yearly observed level. Thus, this represents the predicted mortality where the unobservable factors that influence mortality during the period 1967-2011 have been taken into account. The difference between the blue and green trajectories can be interpreted as the contribution that the unobservable factors make to the decline in infant mortality during the period. Their contributions are in the range 20 to 30 per cent.

The light blue trajectory lets both the trend variable and the four intervention variables vary as they are observed over the time period. In other words, this is the predicted trajectory of the full model. A first impression is that predicted probabilities closely mirror the actual infant mortality rates in Norway 1967-2011 (Figure 1), that is

our model seems to fit the data well. The difference between the light blue and green trajectories can be interpreted as the contribution that the four interventions make to the decline in infant mortality from 1967 to 2011. Broadly speaking, their contributions are about 50 per cent for all weight groups.

4.4. Supplementary analyses

We did several supplementary analyses, mainly to test the robustness of the estimations, but also to test other relevant hypotheses.

4.4.1. Does the effect of ventilators and insure depend on the size of the neonatal department?

This hypothesis was tested by extending Equation (1) with two interaction terms:

$$\begin{aligned} Y_{ijtp} = \alpha + \beta_1 Ventilators_{jp} + \beta_2 Antenatal\_steroids_{jp} + \beta_3 Surfactant_{jp} + \beta_4 Insure_{jp} \\ + \lambda NeoDep\_Size_{jt} + \theta_1 Ventilators \cdot NeoDep\_Size_{jt} + \theta_2 Insure \\ \cdot NeoDep\_Size_{jt} + \sum_c \gamma_c \cdot Control_{ijtp}^c + \sum_j \delta_j \cdot Hospital_j^j + \phi \cdot Year_t^{-1} \\ + \sum_j \eta_j \cdot Hospital_j^j \cdot Year_t^{-1} + u_{ijtp} \end{aligned} \quad (2)$$

The size of the neonatal department (NeoDep_Size) was measured as the number of infants with a birth weight <1500g delivered per hospital.

The sample for the analyses was comprised of infants with a birth weight less than or equal to 2500g. For these infants, the outcome of the use of ventilators and insure may vary according to the volume of care provided; i.e. according to the experience of the staff and the quality of the facilities. Our findings support this result for insure. The regression coefficient θ_2 was negative; i.e. both early neonatal mortality and infant mortality were lower if insure was used in large departments as opposed to in small departments (Table III). For the use of ventilators the regression coefficient θ_1 had the expected negative sign, but was not statistically significant at conventional levels.

4.4.2. Does the effect of the interventions depend on whether the delivery occurred in a hospital without a neonatal department?

Our main analyses were carried out on a sample that encompassed all infants who were born in hospitals with a neonatal department (Table II). We carried out supplementary analyses to take into account that the interventions may also have had an effect on very low birth weight infants who were born at a local hospital. After delivery, these infants would most likely have been transported to a hospital with a neonatal department. Therefore, for these very low birth weight infants we could assign them to the neonatal department they were referred to.

We reanalysed the data with a sample of all infants with a very low birth weight. This included both infants who were born in a hospital with a neonatal department, and those who were born in a local hospital and transported to a hospital with a neonatal department.

In the analyses we included, in Equation (1), interaction terms between each of the interventions, and a dummy variable for whether the infant was born at a local hospital or not. Positive signs for the interaction terms would indicate adverse effects of transporting the infant from one hospital to another. Alternatively, positive signs would indicate sub-optimal initial management of the infant if he or she was born in a setting with an inappropriate level of care. For three of the interaction terms, the signs were positive for early neonatal mortality and infant mortality (Table IV). However, only one of the terms was statistically significant at conventional levels. The lack of statistical significance most likely reflects lack of power due to the small number of very low birth weight infants born in local hospitals. Only 1497 very low birth weight infants were born in the 166 local hospitals that existed during the study period of 44 years.

4.4.3. Data aggregated to the hospital period level

One challenge with our data is that there are few clusters (n=21). In this case, the standard errors might be biased, even with clustering (Bertrand *et al.*, 2004; Cameron and Miller, 2015). In the literature there is no clear rule about how many clusters are needed in order to obtain an unbiased estimate of the standard errors by using standard clustering procedures. Camron and Miller (2015) argue that the number "may range from less than 20 clusters to less than 50 clusters". Our data are in the borderland.

There is no obvious way of how to get unbiased standard errors in the case of few clusters. One solution, as suggested by Bertand *et al.*, (2004), is to aggregate the time series information to the highest unit of measurement. This is both a transparent and a conservative method of estimation. Therefore, we robust-tested our main results as presented in Table II by performing additional analyses at the hospital period level. Our outcome variable was then measured as the proportion of infants who died during each five-year interval per hospital. We ran analyses for each weight group. Hospital fixed effects ($Hospital^{j}$), the inverse of the birth year ($Year^{-1}$) and hospital-specific trends ($Year^{-1} \cdot Hospital^{j}$) were included as additional control variables.

The results from the analyses of the aggregated data (Table V) were fairly similar to the results from our analyses of the individual level data as presented in Table II. For example, for all types of interventions, the signs and the sizes of the regression coefficients were about the same. Further, in the analyses of the aggregated data most of the coefficients were statistically significant at conventional levels. The results, as presented in Table V, indicate that the estimation of the micro data (Table II) with clustering at the hospital level worked fairly well.

4.4.4. Different trend specifications

Equation (1) was specified with an inverse time trend. We carried out two types of analysis to test the robustness of this specification.

First, we re-estimated Equation (1) with hospital specific quadratic and quartic inverse time trends. The results from this estimation (Table VI) were fairly similar to the results from our main analyses as presented in Table II.

Second, we carried out analyses for three 10-year periods (Tables VII). For each of the 10-year periods it was plausible to assume a linear time trend. We studied the introduction of ventilators (1970-1979), antenatal steroids (1980-1989) and surfactant (1985-1994). Each of the three 10-year periods coincides with the period in which *most* neonatal departments introduced ventilators (1970-1979), antenatal steroids (1980-1989) and surfactant (1985-1994) (Table I). For each of the 10-year periods, the analyses were carried out for the whole sample, and for the sample of infants with a birth weight less than or equal to 2500g. The linear trend was made hospital specific. The outcome measures were early infant mortality and infant mortality. For all three types of

intervention, the regression coefficients had the correct sign, and they were statistically significant at conventional levels (Tables VII).

We made comparison groups that covered the whole period 1967-2011 (Table VII). The regression coefficients estimated on the samples that encompassed the periods of 10 years were comparable to the coefficients estimated on the samples that covered the whole period: The coefficients for the comparison groups were slightly larger for antenatal steroids and surfactant, but slightly smaller for the use of ventilators.

4.4.5. Leads and lags

We did an event history analysis, with leads and lags presented in one model. The analyses were carried out for the whole sample, and for those with a birth weight less than or equal to 2500g. The outcome measure was infant mortality.

We redefined Equation (1) to capture pre- and post-intervention effects. For each of the four interventions, we defined the following variables: The contemporaneous effect is defined as 1 only in the five-year period when the intervention was introduced and 0 in all other periods. The first lead dummy variable equals 1 only in the (five-year) period preceding the intervention, and 0 otherwise. The second lead variable equals 0 in all periods up to the period starting 10 years before the intervention, then 1 in the succeeding period, and 0 in all the later periods. The two lagged dummies are defined similarly; the first lag-variable equals 1 only in the first period after the introduction, the second lag-variable equals 1 in all periods starting in the second period (= 10 years after the intervention) and later.

In these regressions, we did not expect the lead variables to have any effect on our outcome. This is supported by our results (Table VIII). The estimates for the lead variables were not statistically significant at conventional levels. This was the case for both samples (for all birth weight groups and for the group with birth weight less than or equal to 2500g). Those results stand in clear contrast to the effects of the lag variables: these coefficients were of a reasonable size, they had the correct sign (negative), and they were statistically significant at conventional levels.

The estimates for the variables measuring the introductory period *p* (five-year interval) were negative and statistically significant at conventional levels. Interestingly,

for all types of intervention the coefficients for the lag variables were larger in absolute values than the coefficients for the variables measuring the introductory period; i.e. there were some delayed effects. This may, for example be because it takes some time for the staff to be familiar with when and how to use the interventions.

5. DISCUSSION

There are few real life studies in which the benefits of the advances in neonatal care have been examined. However, the limited number of studies that exist support the findings of our study (Schwartz *et al*. 1994; Almond *et al*. 2010; Bharadwaj *et al*. 2013). Schwartz *et al*. (1994) found that early neonatal mortality was reduced by 30 per cent after surfactant was introduced. The study encompassed nearly 4000 newborn babies from 14 perinatal centres in the USA during the period 1985 to 1990. The birth weight of these babies was between 500 to 1500g. The effect in the study by Schwartz *et al*. (1994) is slightly larger than the effect we found. We have not been able to identify any real life studies where the effect of the other three interventions on early neonatal or infant mortality has been studied.

Within the field of medicine, there are numerous clinical and experimental studies in which the effects of ventilators, antenatal steroids and surfactant have been examined. In most of the studies, it is the effect of surfactant that has been assessed. Most studies have been carried out on samples with infants with a low birth weight (<2500g). The benefits of surfactant have been summarized in several Cochrane Reviews. A consistent finding is that infant mortality is lowered by the use of surfactant therapy. In several reviews, the size of the effect is measured as the risk difference between the treatment and the control groups. Typically, the size of the risk difference is -0.04 with a confidence interval ranging from -0.14 to -0.01 (Rojas-Reys *et al.*, 2012; Bahadue and Soll, 2012; Soll, 1998; Seger and Soll, 2009). In our study, the regression coefficient for the introduction of surfactant on infant mortality was -0.039 as estimated on the sample of infants with a low birth weight (Table VII, see column with comparison group). Thus, our finding is fairly similar to the main findings from the medical literature about the effect of surfactant.

The overall impression is that our results for antenatal steroids and ventilators are in line with the results from studies that have been carried out within the field of clinical and experimental medicine. For example, several clinical studies have found that infant mortality rate is lowered by the use of antenatal steroids for pregnancies with a risk of preterm delivery (Doyle *et al.*, 1986; Crowley, 1995; Schaap *et al.*, 2001; Carlo *et al.*, 2011; Abbasi *et al.*, 2007). Similar to in our study, previous research has found the largest effects of the use of antenatal steroids for the lowest birth weight groups. This is also the case for the use of ventilators (Williams and Chen, 1982; Horbar *et al.*, 2002). For example, one study from the field of epidemiology has suggested that the marked decline in infant mortality among babies with a low birth weight in the United States in the 1970s was due to the introduction of ventilators in neonatal intensive care units (Horbar *et al.*, 2002).

Our results support the large amount of literature that shows that neonatal mortality is markedly higher for high risk deliveries if babies are born in a hospital with no neonatal resources. Thus, for such deliveries the safest way to give birth is for the mother to be transferred before delivery to a hospital with a neonatal department (Messner, 2011). Even within neonatal departments there are differences in how effective the interventions are. For example, insure has the greatest effect the larger the department is.

Viewed in isolation, our findings are encouraging. On the other hand, what is the quality of life of infants who were saved by the interventions? A general finding in the literature is that low birth weight infants (<2500g) "have higher rates of subnormal growth, illnesses and neurodevelopmental problems" compared to infants with normal birth weights (≥2500g) (Hack *et al*., 1995). The prevalence of medical problems increases as the infant's birth weight decreases (Hack *et al*., 1995; Paneth, 1995). Further, the adverse outcomes of having a low birth weight are apparent in adolescence and even in adults (for a review see: Saigal and Doyle, 2008; Risnes *et al*., 2011). It is reasonable to assume that those who were saved in our study were likely to suffer from much the same medical and cognitive problems that are reported in the literature. Living with and dealing with these problems represents a cost both to the individual and to society (Gilbert *et al.*, 2003; Schmitt *et al.*, 2006; Mangham *et al.*, 2009; Hummer *et al*., 2014). These are costs that should be taken into account when the overall benefits of the interventions are assessed.

In our study design we took advantage of the fact that hospitals introduced advanced medical interventions at different times. One possible limitation of that approach is that the timing for the introduction of the interventions may have accompanied other immediate changes in the neonatal units. For example, new members of staff might have been employed, the skills of the existing staff might have been raised by further training, and the units might have started to use new and more modern facilities. With our study design we cannot be absolutely sure that the effects that these changes could have on mortality are completely disentangled from the effects of the interventions themselves. To some extent this could have been taken into account if data on type and number of staff and facilities had been available for each hospital, preferably for each year, back in time. Unfortunately, such data were not available.

On the other hand, our study had some advantages that strengthen the credibility of the results. First, the analyses were performed within a standardized institutional health care setting. All neonatal units in Norway were publically owned and financed throughout the whole study period. Neither the parents nor the neonatologists had economic incentives that could influence whether the infants received care or not, or which intervention was used. Sample selection is unlikely to be a problem, as nearly all high risk deliveries occurred at hospitals that had a neonatal department. Second, we had extensive controls for risk factors of the mother and the infant. After inclusion of all these control variables, it is unlikely that the results are biased due to unobservable risk factors that are correlated with the timing for when the interventions were introduced. Third, we used hospital fixed effects and hospital specific trends in the estimations. Differences in practice style between neonatal units may be correlated with the timing for when the interventions were introduced. These potential correlations are cancelled out by the use of hospital fixed effects. Further, we included hospital specific trends to pick up non-observable characteristics that could vary within hospitals over time. Additional analyses showed that the results were robust to several different trend specifications. Fourth, we did an event history analysis to test for potential confounders. The results from that analysis did not weaken our main results.

In conclusion, our results highlight an important channel through which the decline in early neonatal mortality and infant mortality occurred during the second half of the last century in Norway. That channel is through the introduction of the following interventions: ventilators, antenatal steroids, surfactant and insure. Altogether, these

interventions explained a decline of about 50 per cent in early neonatal mortality and infant mortality from 1967 to 2011. Most western countries experienced a similar decline in infant mortality as in Norway during the second half of the last century. We believe that our findings can be generalized to these countries, and thus provide an explanation for this decline in infant mortality.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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Table I. Number of neonatal departments and the percentage of deliveries according to type of intervention and time period of implementation

		Type of intervention							
		Ventilator		Antenatal steroids		Surfactant		Insure	
Time period	Total number of deliveries	Number of neonatal departments	Percentage deliveries	Number of neonatal departments	Percentage deliveries	Number of neonatal departments	Percentage deliveries	Number of neonatal departments	Percentage deliveries
Before 1970	77,880	-	-	-	-	-	-	-	-
1970-1974	148,163	6	39	-	-	-	-	-	-
1975-1979	141,213	12	62	5	32	-	-	-	-
1980-1984	144,985	15	78	8	49	-	-	-	-
1985-1989	165,473	20	96	15	77	5	19	-	-
1990-1994	188,384	21	100	19	93	20	97	-	-
1995-1999	192,227	21	100	21	100	21	100	1	7
2000-2004	216,861	21	100	21	100	21	100	6	23
2005-2010	337,603	21	100	21	100	21	100	10	44

Table II. Effects of ventilators, antenatal steroids, surfactant and insure on mortality according to birth weight during the periods: ≤ 1 week, 1 week-1 year, ≤ 1 year.
Standard errors clustered at the hospital level

	Birth weight											
	≤ 1000g			1001 - 1500g			1501-2500g			> 2500g		
Type of intervention	≤ 1 week	≤ 1 year	1 week-1 year	≤ 1 week	≤ 1 year	1 week-1 year	≤ 1 week	≤ 1 year	1 week-1 year	≤ 1 week	≤ 1 year	1 week-1 year
Ventilator	-0.0953 **	-0.0565	0.0388 **	-0.1364 ***	-0.1203 ***	0.0161	-0.0134 **	-0.0144 **	-0.0011	-0.0005 **	-0.0003	0.0002
	(0.0438)	(0.0375)	(0.0195)	(0.0297)	(0.0232)	(0.0111)	(0.0054)	(0.0056)	(0.0014)	(0.0002)	(0.0004)	(0.0002)
Antenatal steroids	-0.1586 ***	-0.1313 ***	0.0273	-0.0932 ***	-0.0893 ***	0.0039	-0.0156 **	-0.0148 **	0.0009	-0.0004 **	-0.0001	0.0003
	(0.0422)	(0.0380)	(0.0185)	(0.0268)	(0.0229)	(0.0113)	(0.0048)	(0.0056)	(0.0017)	(0.0001)	(0.0003)	(0.0003)
Surfactant	-0.1733 ***	-0.2214 ***	-0.0481 ***	-0.0445 **	-0.0770 ***	-0.0325 ***	-0.0085 ***	-0.0165 ***	-0.0080 ***	-0.0005 ***	-0.0027 ***	-0.0022 ***
	(0.0393)	(0.0361)	(0.0121)	(0.0141)	(0.0137)	(0.0066)	(0.0024)	(0.0035)	(0.0018)	(0.0001)	(0.0003)	(0.0002)
Insure	-0.1059 **	-0.1351 **	-0.0292 **	-0.0078	-0.0307 *	-0.0230 ***	-0.0023	-0.0059 **	-0.0036 **	-0.0002	-0.0007 ***	-0.0005 ***
	(0.0402)	(0.0453)	(0.0122)	(0.0181)	(0.0182)	(0.0056)	(0.0019)	(0.0024)	(0.0012)	(0.0001)	(0.0002)	(0.0001)
Number of live born infants	5263	5263	5263	9577	9577	9577	68,832	68,832	68,832	1,467,021	1,467,021	1,467,021
Number of deaths	1673	2189	516	1040	1414	374	1390	2113	723	1632	4645	3013

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10
** p<0.05
*** p<0.001

Table III. The effects of the use of ventilators and insure on early neonatal and infant mortality according to the size of the neonatal department.
Sample: infants with a birth weight ≤ 2500g. Standard errors clustered at the hospital level

	Additive model		Model with interaction terms	
Type of intervention	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year
Main effects:				
Ventilator	-0.0272 ***	-0.0253 ***	-0.0200 **	-0.0188 *
	(0.0083)	(0.0074)	(0.0102)	(0.0103)
Insure	-0.0098 *	-0.0172 **	-0.0076	-0.0138 **
	(0.0056)	(0.0064)	(0.0053)	(0.0060)
Size of neonatal department				
Number of infants with a birth weight < 1500g	-0.0003 ***	-0.0003 ***	0.0001	0.0001
	(0.0000)	(0.0000)	(0.0004)	(0.0004)
Interaction terms:				
Ventilator · Number of infants with a birth weight < 1500g			-0.0002	-0.0002
			(0.0004)	(0.0004)
Insure · Number of infants with a birth weight < 1500g			-0.0001 *	-0.0002 **
			(0.0001)	(0.0001)
Number of live born infants	83,672	83,672	83,672	83,672
Number of deaths	4103	5716	4103	5716

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10
** p<0.05
*** p<0.001

Table IV. The effects of the interventions on early neonatal and infant mortality according to whether the infant was born in a local hospital, or not.
Sample: All live born infants with a birth weight < 1500g. Standard errors clustered at the hospital level

	Additive model		Model with interaction terms	
Type of intervention	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year
Main effects:				
Ventilator	-0.1222 ***	-0.1022 ***	-0.1232 ***	-0.1012 ***
	(0.0264)	(0.0206)	(0.0293)	(0.0225)
Antenatal steroids	-0.0992 ***	-0.0838 **	-0.1022 **	-0.0892 **
	(0.0298)	(0.0258)	(0.0324)	(0.0277)
Surfactant	-0.0919 ***	-0.1268 ***	-0.0944 ***	-0.1317 ***
	(0.0197)	(0.0193)	(0.0204)	(0.0200)
Insure	-0.0400	-0.0667 **	-0.0396	-0.0651 **
	(0.0263)	(0.0282)	(0.0265)	(0.0285)
Infant born in local hospital	1.0865 **	0.9228 **	1.0938 **	0.9625 **
	(0.3988)	(0.4676)	(0.4080)	(0.4723)
Interaction terms:				
Ventilator · Infant born in local hospital			-0.0127	-0.0409
			(0.0634)	(0.0533)
Antenatal steroids · Infant born in local hospital			0.0042	0.0038
			(0.0651)	(0.0524)
Surfactant · Infant born in local hospital			0.0714	0.1407 **
			(0.0858)	(0.0691)
Insure · Infant born in local hospital			0.0403	0.0124
			(0.0608)	(0.0815)
Number of live born infants	16,176	16,176	16,176	16,176
Number of deaths	3401	4372	3401	4372

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10
** p<0.05
*** p<0.001

Table V. Analyses at the hospital period level. Effects of ventilators, antenatal steroids, surfactant and insure on the proportions of infants who died during each five-year interval per hospital according to birth weight. Standard errors clustered at the hospital level

	Birth weight							
	≤ 1000g		1001 - 1500g		1501-2500g		> 2500g	
Type of intervention	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year
Ventilator	-0.1087 **	-0.0852 *	-0.0982 ***	-0.0728 **	-0.0135 **	-0.0138 **	-0.0003	0.0001
	(0.0519)	(0.0441)	(0.0272)	(0.0239)	(0.0050)	(0.0051)	(0.0002)	(0.0004)
Antenatal steroids	-0.0770 *	-0.0542	-0.0801 **	-0.0838 **	-0.0130 ***	-0.0156 ***	-0.0006 ***	-0.0007 **
	(0.0406)	(0.0429)	(0.0275)	(0.0285)	(0.0037)	(0.0047)	(0.0002)	(0.0003)
Surfactant	-0.2307 ***	-0.2817 ***	-0.0360 *	-0.0821 ***	-0.0051 **	-0.0098 **	-0.0002	-0.0021 ***
	(0.0283)	(0.0323)	(0.0191)	(0.0221)	(0.0017)	(0.0028)	(0.0001)	(0.0003)
Insure	-0.1297 **	-0.1292 ***	-0.0226	-0.0360	0.0011	-0.0024	-0.0001	-0.0006 **
	(0.0400)	(0.0339)	(0.0272)	(0.0251)	(0.0014)	(0.0020)	(0.0002)	(0.0003)
Number of hospital five-year intervals	177	177	183	183	185	185	186	186

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10
** p<0.05
*** p<0.001

Table VI. Alternative specifications of hospital-specific time trends. Effects of ventilators, antenatal steroids, surfactant and insure on early neonatal and infant mortality according to birth weight. Standard errors clustered at the hospital level

	Birth weight							
	≤ 1000g		1001 - 1500g		1501-2500g		> 2500g	
Type of intervention	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year
Ventilator								
Quadratic inverse time trends	-0.1274 **	-0.0860 **	0.1621 ***	-0.1470 ***	-0.0194 ***	-0.0202 ***	-0.0007 **	-0.0005
	(0.0414)	(0.0368)	(0.0286)	(0.0229)	(0.0052)	(0.0055)	(0.0002)	(0.0004)
Quartic inverse time trends			-0.1650 ***	-0.1502 ***	-0.0212 ***	-0.0220 ***	-0.0007 **	-0.0005
			(0.0286)	(0.0230)	(0.0052)	(0.0056)	(0.0002)	(0.0004)
Antenatal steroids								
Quadratic inverse time trends	-0.1815 ***	-0.1519 ***	-0.0977 ***	-0.0936 ***	-0.0176 ***	-0.0168 **	-0.0005 **	-0.0002
	(0.0436)	(0.0383)	(0.0283)	(0.0246)	(0.0050)	(0.0059)	(0.0002)	(0.0003)
Quartic inverse time trends			-0.1021 ***	-0.0973 ***	-0.0180 ***	-0.0172 **	-0.0006 ***	-0.0003
			(0.0262)	(0.0225)	(0.0049)	(0.0058)	(0.0002)	(0.0003)
Surfactant								
Quadratic inverse time trends	-0.1771 ***	-0.2242 ***	-0.0501 **	-0.0828 ***	-0.0090 ***	-0.0171 ***	-0.0005 ***	-0.0027 ***
	(0.0393)	(0.0361)	(0.0158)	(0.0154)	(0.0027)	(0.0039)	(0.0001)	(0.0003)
Quartic inverse time trends			-0.0500 **	-0.0829 ***	-0.0090 ***	-0.0171 ***	-0.0005 ***	-0.0026 ***
			(0.0155)	(0.0152)	(0.0027)	(0.0040)	(0.0001)	(0.0003)
Insure								
Quadratic inverse time trends	-0.1145 **	-0.1407 **	-0.0214	-0.0449 **	-0.0028	-0.0068 **	-0.0003	-0.0008 ***
	(0.0429)	(0.0480)	(0.0240)	(0.0240)	(0.0022)	(0.0029)	(0.0002)	(0.0002)
Quartic inverse time trends			-0.0302	-0.0537 *	-0.0031	-0.0073 **	-0.0003 *	-0.0009 ***
			(0.0289)	(0.0287)	(0.0024)	(0.0033)	(0.0002)	(0.0003)
Number of live born infants	5263	5263	9577	9577	68,832	68,832	1,467,021	1,467,021
Number of deaths	1673	2189	1040	1414	1390	2113	1632	4645

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10
** p<0.05
*** p<0.001

Table VII. Effects of the use of ventilators, antenatal steroids and surfactant on early neonatal and infant mortality according to time period for estimation, and birth weight.
Standard errors clustered at the hospital level

	Time period			
	Ten-year period[1]		Comparison group (1967-2011)	
Type of intervention	≤ 1 week	≤ 1 year	≤ 1 week	≤ 1 year
Ventilator				
Whole sample	-0.0022 ***	-0.0033 ***	-0.0016 **	-0.0013 **
	(0.0003)	(0.0003)	(0.0005)	(0.0005)
Number of live born infants	280,814	280,814	1,550,693	1,550,693
Number of deaths	2026	3208	5735	10,361
Birth weight ≤ 2500g	-0.0386 ***	-0.0380 ***	-0.0273 **	-0.0253 ***
	(0.0031)	(0.0036)	(0.0083)	(0.0074)
Number of live born infants	14,093	14,093	83,672	83,672
Number of deaths	1496	1824	4103	5716
Antenatal steroids				
Whole sample	-0.0022 ***	-0.0012 ***	-0.0021 ***	-0.0017 **
	(0.0001)	(0.0002)	(0.0006)	(0.0008)
Number of live born infants	303,743	303,743	1,550,693	1,550,693
Number of deaths	1107	2520	5735	10,361
Birth weight ≤ 2500g	-0.0221 ***	-0.0183 ***	-0.0286 **	-0.0253 **
	(0.0019)	(0.0027)	(0.0086)	(0.0089)
Number of live born infants	15,292	15,292	83,672	83,672
Number of deaths	797	1229	4103	5716
Surfactant				
Whole sample	-0.0006 **	-0.0020 ***	-0.0020 ***	-0.0049 ***
	(0.0003)	(0.0004)	(0.0005)	(0.0007)
Number of live born infants	346,106	346,106	1,550,693	1,550,693
Number of deaths	1053	2408	5735	10,361
Birth weight ≤ 2500g	-0.0109 **	-0.0217 **	-0.0257 ***	-0.0392 ***
	(0.0047)	(0.0081)	(0.0048)	(0.0055)
Number of live born infants	18,448	18,448	83,672	83,672
Number of deaths	759	1250	4103	5716

Control variables, hospital-specific effects and hospital-specific trends are included in all analyses

* p<0.10

** p<0.05

*** p<0.001

[1] Ten-year time periods: Ventilators:1970-1979, Antenatal steroids: 1980-1989, Surfactant: 1985-1994

Table VIII. Lead and lag effects on infant mortality. Estimated on the whole population of infants and on a sample of infants with birth weight ≤ 2500g [1,2]. Separate regressions for each intervention. Standard errors clustered at the hospital level

Type of intervention	Lead two periods (T_0 -10)	Lead one period (T_0 -5)	Introductory period (Contemporaneous effect T_0)	Lag one period (T_0 +5)	Lag two periods (T_0 +10)
Ventilator					
Whole sample	-0.0007	-0.0021	-0.0025 *	-0.0035 **	-0.0048 ***
	(0.0013)	(0.0015)	(0.0015)	(0.0014)	(0.0013)
Birth weight ≤ 2500g	0.0021	-0.0050	-0.0210 **	-0.0355 ***	-0.0487 ***
	(0.0152)	(0.0119)	(0.0089)	(0.0088)	(0.0096)
Antenatal steroids					
Whole sample	-0.0004	-0.0010	-0.0020 **	-0.0021 **	-0.0033 ***
	(0.0006)	(0.0007)	(0.0009)	(0.0008)	(0.0008)
Birth weight ≤ 2500g	-0.0023	-0.0108	-0.0293 **	-0.0324 **	-0.0521 ***
	(0.0076)	(0.0086)	(0.0117)	(0.0107)	(0.0123)
Surfactant					
Whole sample	-0.0009	-0.0008	-0.0030 **	-0.0045 ***	-0.0063 ***
	(0.0006)	(0.0008)	(0.0009)	(0.0010)	(0.0011)
Birth weight ≤ 2500g	-0.0112	-0.0185	-0.0330 **	-0.0447 **	-0.0617 ***
	(0.0098)	(0.0124)	(0.0168)	(0.0161)	(0.0157)
Insure					
Whole sample	0.0001	-0.0007	-0.0030 ***	-0.0042 ***	-0.0069 ***
	(0.0006)	(0.0008)	(0.0006)	(0.0012)	(0.0008)
Birth weight ≤ 2500g	-0.0024	-0.0082	-0.0160 **	-0.0287 *	-0.0333 ***
	(0.0072)	(0.0070)	(0.0057)	(0.0153)	(0.0081)

* p<0.10
** p<0.05
*** p<0.001

[1] Whole sample: Number of live born infants = 1,550,693, number of deaths = 10 361

[2] Infants with birth weight ≤ 2500g: Number of live born infants = 83,672, number of deaths = 5716

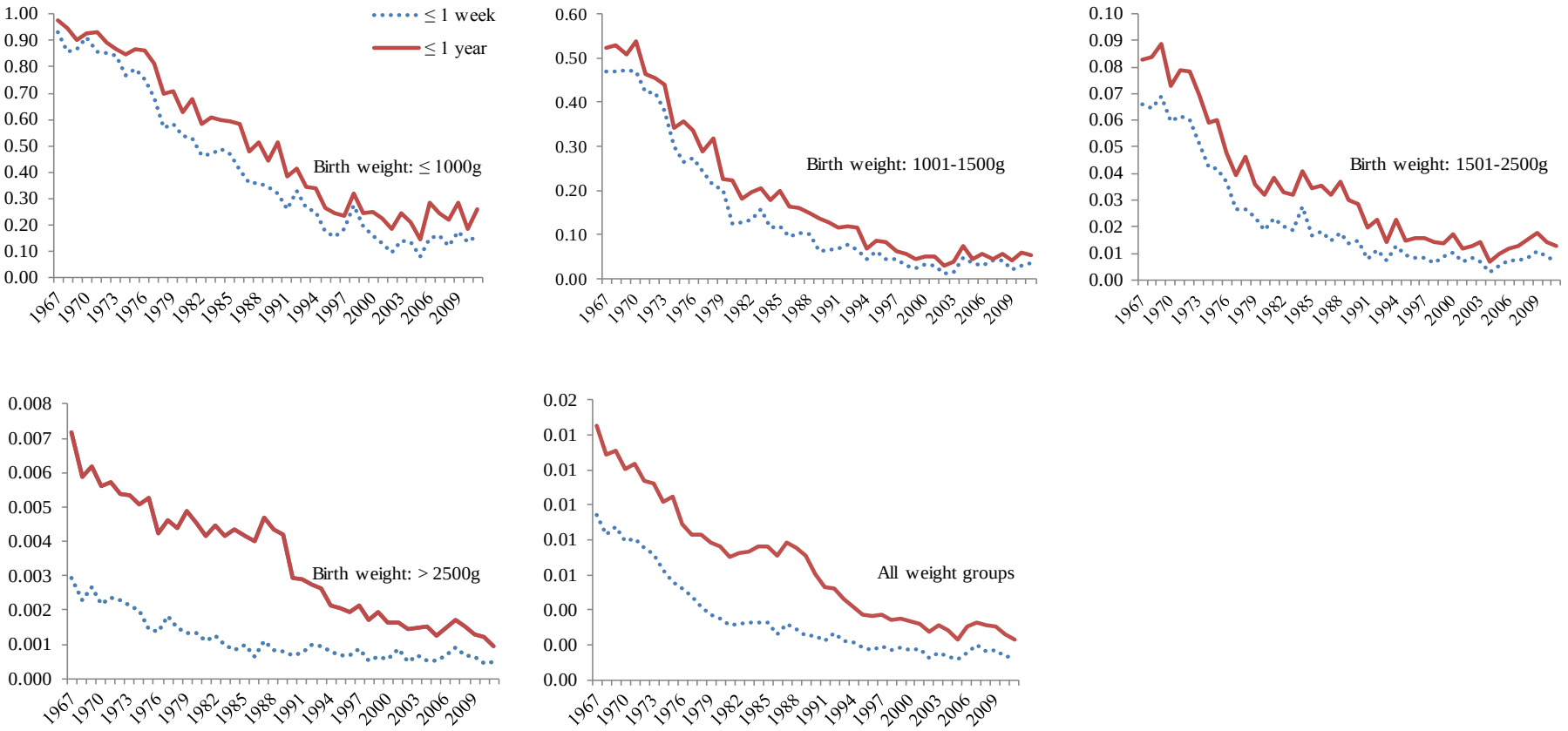

Figure 1. The proportion of infant deaths during the first week and the first year of life, according to year. All births in Norway 1967-2011

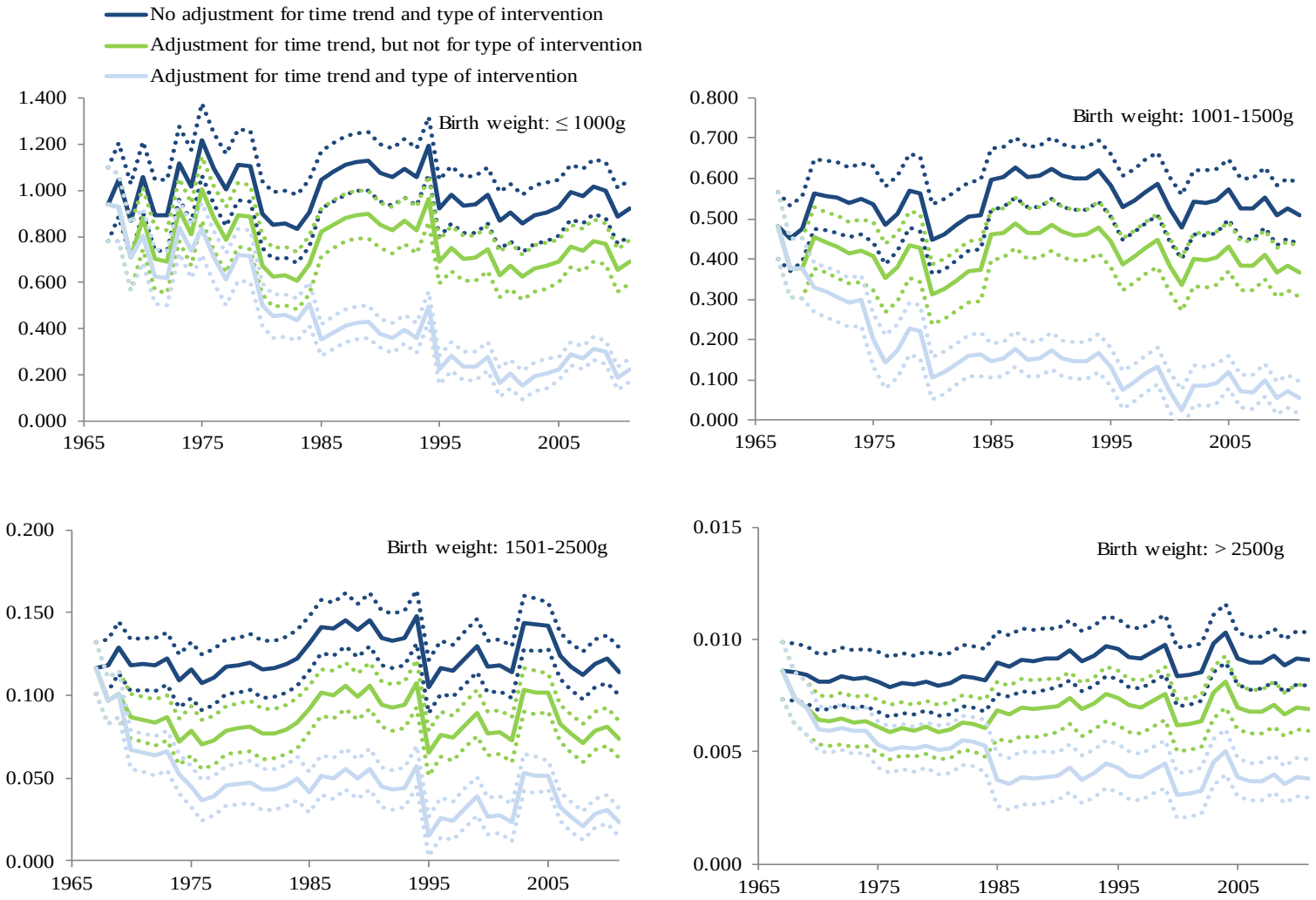

Figure 2. Predicted infant mortality for infants at the largest maternity department in Norway 1967-2011. All predictions are based on regressions where risk factors of the infants, characteristics of the birth, characteristics of the mother, and predisposing factors of the mother have been set at the population mean values. 95% confidence interval given by dotted lines