
The North of England Multiple Pregnancy Register: Five-Year Results of Data Collection

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From 1998 the population-based North of England Multiple Pregnancy Register (MPR) has collected data on all multiple pregnancies in the region from the earliest point of ascertainment in the pregnancy. This article describes the development of the MPR and the findings of the first 5 years of data collection. Mothers now give explicit consent for their inclusion with named data, in accordance with section 60 of the Health and Social Care Act 2001. During 1998 to 2002, 2310 twin pregnancies were registered, with an increasing twinning rate of 13.6 to 16.6 per 1000 maternities. Chorionicity ascertainment in twin maternities with at least one stillbirth or live birth has improved from 81% in 1998 to 91% in 2002. Before 24 weeks of gestation, 8.4% (359/4620) of fetuses were lost either spontaneously or as a result of termination of pregnancy. The perinatal mortality rate was much higher in monochorionic than dichorionic twins, mainly due to differences in stillbirth rates (49.0 vs. 11.5 per 1000 maternities respectively, risk rate = 4.2; 95% confidence intervals 2.7–6.6). The gestational-age-specific neonatal mortality rates were similar in twins and singletons, except in the group of term births (≥ 37 weeks' gestation) when compared by conventional gestational age categories. For stillbirths, the rates were even lower than in singletons in gestational age categories of less than 32 weeks. The register is an important resource of data on multiple pregnancies, which allows monitoring of trends in multiple birth rates and pregnancy losses and provides a unique opportunity for etiological and long-term follow-up studies.

Multiple pregnancy presents increasing challenges to obstetricians and midwives, because the rates of multiple pregnancies have steadily increased in recent years, and such pregnancies continue to carry greater hazards than singleton pregnancies for both the fetus and newborn baby.

The consistent increase in the number of multiple births in England and Wales has been well documented by the Office for National Statistics (ONS; Macfarlane et al., 2000). The main reasons for this are the increasing average age at which women choose to start families, and the use of ovulatory stimulation and other assisted reproductive technologies (ART). In 1998 the Regional Maternity Survey Office (RMSO) established a prospective regional register of all multiple pregnancies, the North of England Multiple Pregnancy Register (MPR). The principal aims of this register were to quantify more precisely the hazards of multiple pregnancy, to determine the changes in the epidemiology of multiple pregnancy over time and to develop a core dataset at the population level for future studies in twin research (Glinianaia et al., 2002).

This article gives an update on the development of the MPR and describes the main findings of the first five years of data collection.

Methods

The MPR aims to capture data on all multiple pregnancies in the former Northern Region (1993 boundaries), comprising five counties: Northumberland, Tyne and Wear, Durham, Cumbria, and Cleveland. The population of this area is around 3 million with approximately 32,000 deliveries per year. The MPR ascertains multiple pregnancies from the earliest antenatal scan on which a multiple pregnancy is determined, and then successively at the time of the 20-week anomaly scan and at delivery. Multiple pregnancy may also be identified following miscarriage, or by the discovery of the remains of a second fetus at the time of an apparently singleton

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Table 1
Multiple Pregnancy, Maternities, and Twinning Rates in the Northern Region, 1998–2002

	1998	1999	2000	2001	2002
Twin pregnancies	478	448	460	432	492
Twin maternities*	432	417	423	414	481
Triplet pregnancies	17	22	15	10	11
Higher order multiple pregnancies	2	1	1	2	0
TWINNING RATE /1000 maternities	13.6	13.6	14.4	14.4	16.6
Total maternities	31,737	30,652	29,340	28,717	28,890

Note: *maternities are pregnancies with at least one live-birth or stillbirth; the definition of the twinning rate is as given in the previous MPR paper (Glinianaia et al., 2002).

birth. Initial ascertainment is provided on a notification card which gives basic identifying information and, where possible, the ultrasound assessment of chorionicity. Full data are then obtained following birth by completion of a data registration form at the delivery hospital (Glinianaia et al., 2002).

Regional Multicentre Research Ethics Committee approval was obtained for the register, but in keeping with recent United Kingdom regulations and guidance, particularly with regard to the *Health and Social Care Act 2001* (Anonymous, 2001) and the *Data Protection Act 1998* (anonymous, 1998), we have introduced a mechanism for obtaining explicit consent from parents to allow us to retain their data on the register. On receipt of the notification card, a letter and appropriate forms are sent to the mother’s obstetrician asking them to discuss consent with the mother at the next hospital visit. If she declines, identifying

data are deleted leaving an anonymized record of basic clinical and epidemiological data.

The records are linked internally to the long standing Perinatal Mortality Survey (PMS; Northern Regional Health Authority Coordinating Group, 1984), the Northern Congenital Abnormality Survey (NorCAS; Northern Regional Survey Steering Group, 1992) and the Northern Diabetic Pregnancy Survey databases, all kept by the RMSO (<http://www.rmso.org.uk>). The RMSO databases were developed by Beaumont Colson Ltd database designers using bespoke software. The external linkage with the ONS birth and death tapes is built into the database automatically to allow cross validation. This system provides accurate data on the incidence of multiple pregnancy as well as the outcome in terms of early fetal loss, selective feticide, stillbirth, all deaths to the age of 1 year, and any congenital abnormality. The RMSO also hosts a population-based register of cerebral palsy, North East

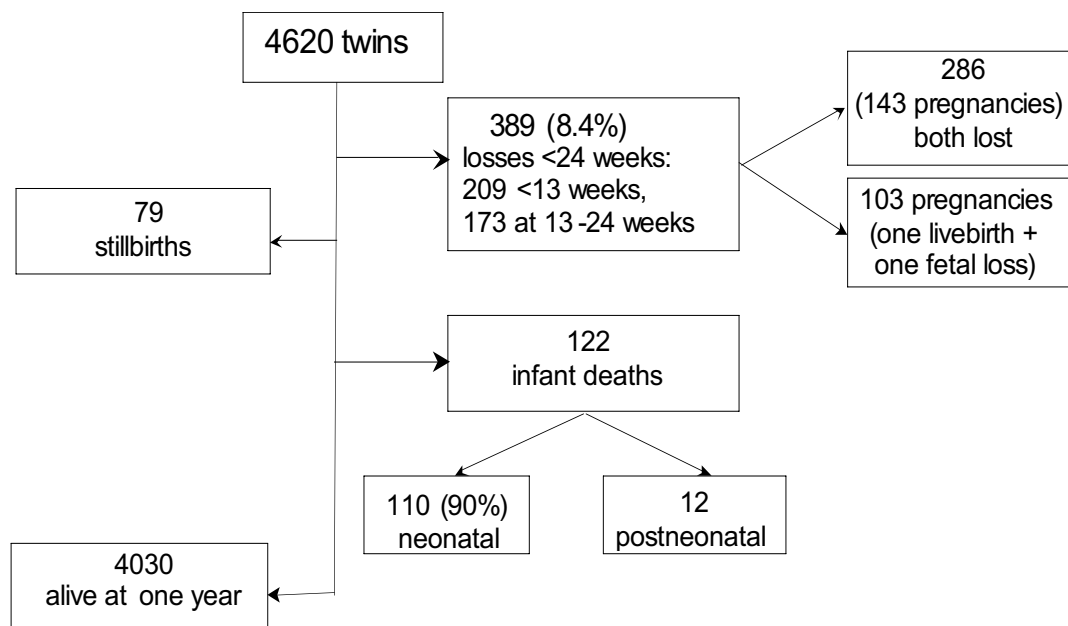


Figure 1
Outcome of twin pregnancies, Northern Region, 1998–2002.

Table 2
Mortality of Twins to the End of the First Postnatal Year

TWIN 1	TWIN 2					Total
	IPSB	ENND	LNND	PNND	Survivor	
IPSB	1		1		2	4
ENND	1	23	3		11	37
LNND		2			9	11
PNND		1			6	7
Survivor		16	6	5	1914	1945
Total	2	42	9	5	1942	2002

Note: IPSB = intrapartum stillbirth; ENND = early neonatal death; LNND = late neonatal death; PNND = postneonatal death.

Collaborative Cerebral Palsy Survey (NECCPS; Anonymous, 1999). NECCPS is not directly linked to the MPR, PMS or NorCAS but if necessary, the records can be linked across by using unique identifiers. In a similar way, the MPR can also link multiple birth data to the Regional Fetal Medicine Unit database at the Royal Victoria Infirmary in Newcastle upon Tyne to obtain information on ultrasound indicators on fetal wellbeing. Finally, by capturing the unique National Health Service number on all live-born babies, we will be able to trace their whereabouts when follow-up studies are carried out.

Chorionicity is ascertained where there is appropriate antenatal ultrasound determination and subsequently by placental examination and histology. Gestational age at birth is automatically calculated in the database using working estimated date of delivery based on obstetric estimates, including ultrasound, and the actual date of delivery. By convention, twins are labeled one or two antenatally according to their proximity to the cervical os. This differs from labeling at delivery, where twin 1 is the twin that is delivered first, irrespective of the antenatal position. The RMSO cannot capture data on the use of artificial reproductive technologies in relation to multiple pregnancies as set out by the Human Fertilisation and Embryology Authority (HFEA).

As the ONS does not collect information on gestational age, and to allow gestation specific mortality rates to be calculated for singletons and compared with those in twins, Scottish data for 1998 to 2002 were used to derive proxy values for the gestational age distribution of singleton births in our population (personal communication, ISD Scotland, NHS National Services Scotland).

Results

While the number of births in the region declined from 32,203 in 1998 to 29,391 in 2002, the twinning rate increased from 13.6 to 16.6 per 1000 maternities. The numbers of triplet and higher order multiple pregnancies declined substantially (Table 1).

Overall mortality for the whole cohort of 4620 twins is shown in Figure 1: 8.4% of fetuses died before 24 weeks, 1.7% were stillbirths, 2.3% died in the first month, and a further 0.3% died before the end of the first year.

Table 2 shows that for babies alive at the onset of labor there was no apparent disadvantage to the second twin at delivery.

Table 3 shows gestational-age-specific stillbirth and neonatal mortality in twins and singletons. Most of the neonatal deaths (83.6%) among twins occurred in babies born at less than 32 weeks of gestation compared to 52.4% in singletons. Notably, gestation specific death rates did not differ between live-born twins and singletons, except at term (≥ 37 weeks' gestation). In stillbirths, the rates were lower in twins than in singletons in gestational age categories of less than 32 weeks. These findings confirm that because of the differences in gestational age distributions in twins and singletons (Figure 2), optimal gestational age does differ in these two different populations (Luke et al., 2005; Minakami & Sato, 1996).

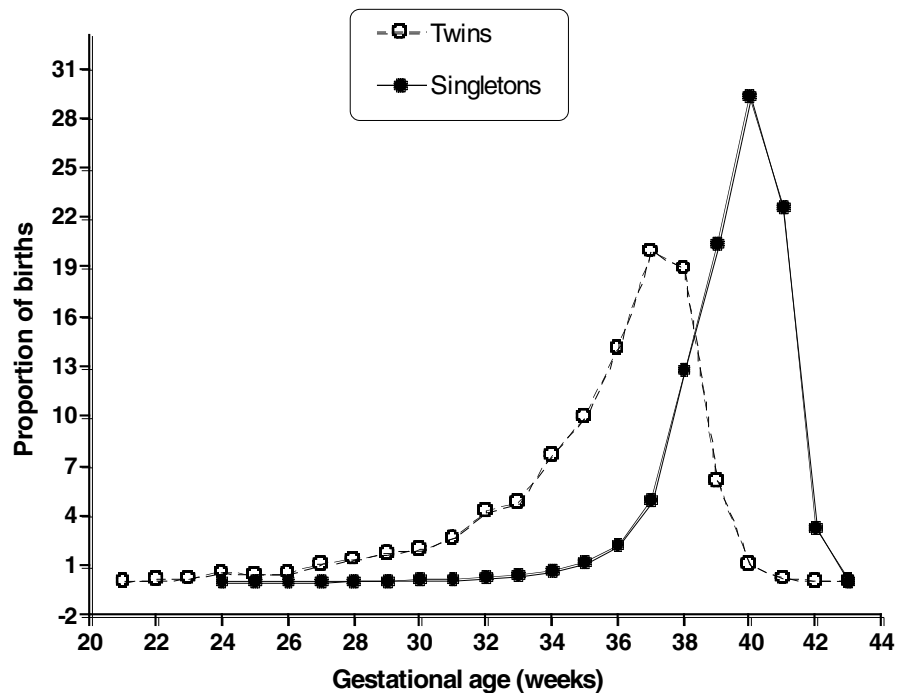
Overall, about 90% of multiple pregnancies were diagnosed by 18 weeks of gestation (65% before 13 weeks), with no significant change over the 5 years. Chorionicity in twin pregnancies was ascertained for 81% of maternities in 1998 but this had improved to 91% in 2002. Over this time the relative proportions of monochorionic and dichorionic twins remained the

Table 3
Gestational-Age-Specific Stillbirth and Neonatal Mortality in Twins and Singletons, 1998–2002

Gestational age (weeks)	SBR in twins N (rate per 1000 births)	NMR in twins N (rate per 1000 live births)	SBR in singletons N (rate per 1000 births)	NMR in singletons N (rate per 1000 live births)	RR SBR (95% CI)	RR NMR (95% CI)
< 28	24 (96.4)	68 (535.4)	199 (330.0)	188 (465.3)	0.29 (0.20–0.43)	1.15 (0.95–1.40)
28–31	10 (29.9)	24 (74.1)	116 (109.3)	55 (58.2)	0.27 (0.15–0.52)	1.27 (0.80–2.02)
32–36	30 (17.6)	11 (6.6)	194 (25.6)	71 (9.6)	0.69 (0.47–1.01)	0.68 (0.36–1.28)
37+	15 (7.4)	7 (3.5)	283 (2.1)	150 (1.1)	3.62 (2.16–6.08)	3.21 (1.51–6.84)

Note: SBR = stillbirth rate; NMR = neonatal mortality rate; RR = rate ratios; CI = confidence intervals

Singleton gestational age distribution is given based on Scottish singleton data for 1998–2002 (personal communication, ISD Scotland, NHS National Services Scotland).

**Figure 2**

Gestational age distribution of twin and singleton births.

same and there was no change in the ratio of like-sex to opposite-sex twins. In contrast, overall perinatal mortality differed substantially between monozygotic twins (70.9/1000 births) and dizygotic twins (including twins with unknown chorionicity; 30.9/1000 births). Figure 3 demonstrates that this is entirely attributable to the stillbirth difference.

From 1998 to 2002 6.7% of twin pregnancies (155/2310) were complicated by a congenital anomaly involving 176 individuals.

Rates of normal, instrumental and cesarean delivery were broadly stable over the 5 years, with about half of all twin pregnancies being delivered by cesarean section.

Discussion

We have shown that in our population in the north of England, rates of twinning continue to increase while rates of triplets have decreased. Our data also show that with current practice the second twin is not at higher risk of perinatal death than the first twin when both are alive at the onset of labour or before elective cesarean section.

We believe that our methods for ascertainment, which underpin the rigor of the register, are robust. We are able to cross check the ascertainment of twin births against the birth data from the ONS, but as the ONS labels a delivery as a singleton even when there is an early loss of a twin fetus, our ascertainment is likely to be more complete. We acknowledge that we cannot be certain of capturing all the early twin preg-

nancies, some of which will later become singletons, because not all women book in time to undergo a first trimester ultrasound scan. We therefore have to regard the early-pregnancy twin ascertainment as a minimum estimate. However, we can be confident that our ascertainment of twin maternities is robust, and that the data demonstrating a year-on-year increase in the twin maternity rate are accurate.

The rates of twinning have to be seen in a historical context; we found that in 1998 the rate in our population was 13.6 per 1000 maternities, but the ONS data for our population show that the rates were 12.0 in 1994 and 9.8 in 1990 (Glinianaia et al., 1998). In this report we have therefore captured a snapshot of a continuing change and it is unclear as to whether the twinning rate will continue to rise further. There are likely to be many reasons for this. The natural twinning rate increases with maternal age, and women who make reproductive choices that delay their first pregnancy thereby increase their risk of twins. A more conservative approach to ART, with only two eggs now being returned, is probably responsible for the welcome decline in triplet pregnancies. However, we cannot determine the balance between those pregnancies conceived with the aid of ovulation enhancing drugs (e.g., clomiphene) and those conceived entirely artificially.

As far as we are aware we remain the only UK register of multiple pregnancy with ascertainment from the first ultrasound scan and with a direct link to our regional registers of congenital abnormality, pregnancy loss and infant mortality and also to the

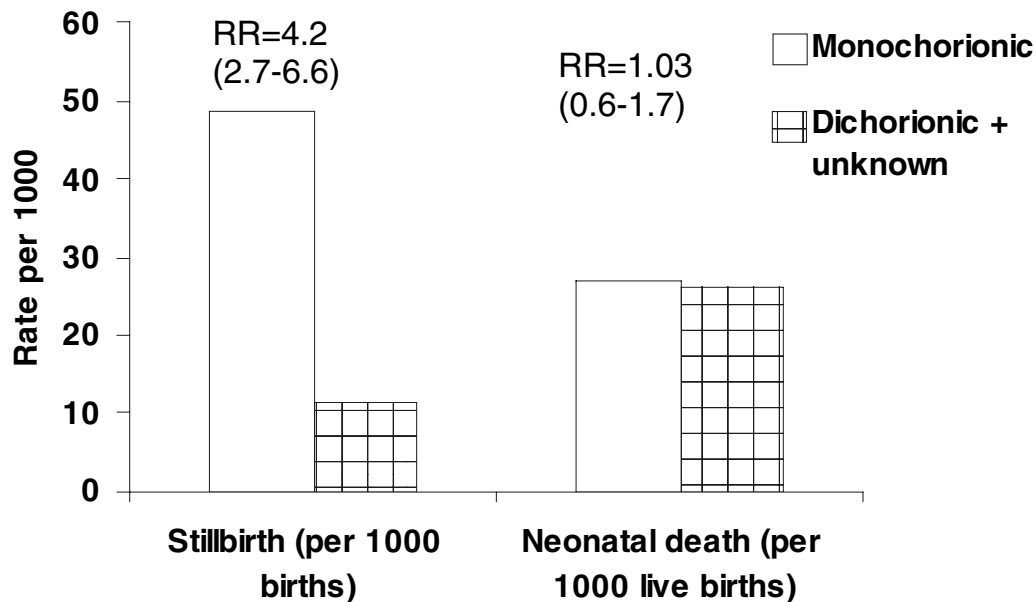


Figure 3

Stillbirth and neonatal mortality rates in twins by chorionicity.

national birth data, and an indirect link to our regional register of cerebral palsy. However, our current inability to identify those pregnancies conceived using ART, because of the legal framework of the HFEA, remains a significant limitation. We hope that the current review of this legislation will allow us to develop this aspect in the future.

The ability to ascertain adverse outcomes such as congenital abnormality and cerebral palsy will assume even greater importance with the changing demographics of pregnancy and, in particular, the modern tendency of mothers to delay pregnancy until after the years of highest fertility. Older mothers have an increased risk both of spontaneous twin pregnancy and fetal abnormality, while the tendency of twin pregnancies to deliver prematurely increases the risk of cerebral palsy as well as being the principal pathway to neonatal and postneonatal death.

The ability to capture data on multiple pregnancies from very early in pregnancy makes the MPR a unique resource for perinatal epidemiology research and provides the basis for etiological and long-term follow up studies. It also allows a far more sophisticated analysis of multiple pregnancies than the broad-brush data provided by the ONS. The continuance and further development of the MPR should be seen as a public health priority and a key component of the drive to improve maternal and child health.

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