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Projected number of children with isolated spina bifida or down syndrome in England and Wales by 2020

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Abbreviations:
NorCAS
Northern Congenital Abnormality Survey
NDSCR
National Down Syndrome Cytogenetic Register
CI
confidence interval
iRR
incidence rate ratio
HR
Hazard ratio

ABSTRACT

Children with major congenital anomalies often require lifelong access to health and social care services. Estimating future numbers of affected individuals can aid health and social care planning. This study aimed to estimate the number of children aged 0–15 years living with spina bifida or Down syndrome in England and Wales by 2020. Cases of spina bifida and Down syndrome born during 1998–2013 were identified from the Northern Congenital Abnormality Survey and the National Down Syndrome Cytogenetic Register, respectively. The number of infants born with spina bifida during 1998–2019 were estimated by applying the average prevalence rate in the North of England to actual and projected births in England and Wales. Poisson regression was performed to estimate the number of infants born with Down syndrome in England and Wales during 1998–2013 and 2004–2019. The numbers of children aged 0–15 living with spina bifida or Down syndrome in 2014 and in 2020 were then estimated by multiplying year- and age-specific survival estimates by the number of affected births. An estimated 956 children with isolated spina bifida, 623 children with spina bifida and hydrocephalus and 11,592 children with Down syndrome aged 0–15 years will be living in England and Wales by 2020, increases of 7.2%, 12.0% and 12.7% since 2014, respectively. Due to improvements in survival, an increase in population size and changes in maternal age distribution at delivery, we anticipate further increases in the number of children living with spina bifida or Down syndrome by 2020.

1. Introduction

Spina bifida occurs in 4 per 10,000 pregnancies in Europe, with approximately 31% of these resulting in live births (EUROCAT, 2016). Infant survival for children born with spina bifida has been reported as 71% in the UK (1985–2003) and 87% in the US (1979–1994) (Tennant et al., 2010; Wong and Paulozzi, 2001). Down syndrome (trisomy 21) affects approximately 22 per 10,000 pregnancies in Europe, with the risk increasing with maternal age (EUROCAT, 2016; Loane et al., 2013). Fifty percent of cases result in a termination of pregnancy or fetal death and, of the live births, infant survival is around 90% (EUROCAT, 2016; Irving et al., 2008). The live birth prevalence of Down syndrome has increased because of the increased proportion of women entering pregnancy at advanced maternal age (Morris and Alberman, 2009). However, terminations of Down's syndrome pregnancies due to an increase and improvements in antenatal screening have caused the number of live births with Down's syndrome to remain constant (Morris and Alberman, 2009, Khoshnood et al., 2015) Survival of affected individuals also improved over time (Wong and Paulozzi, 2001; Rankin et al., 2012; Shin et al., 2012). While several studies worldwide have reported the live birth prevalence and survival of Down syndrome and spina bifida (Rankin et al., 2012; Morris et al., 2002; Savva et al., 2010; Zaganjor et al., 2016; Weijerman et al., 2008; Oakeshott et al., 2010), to our knowledge none have combined these estimates to predict the population size of children with these conditions.

Spina bifida and Down syndrome are examples of severe structural and chromosomal congenital anomalies respectively, where the affected individuals require lifelong specialised health care. This can include: complex surgeries, out-patient follow-up and access to disability equipment and special education, all of which come at substantial financial and emotional cost to society and the family (Dunlap et al., 2011; Radcliff et al., 2012; Geelhoed et al., 2011). For example, a US study reported a 13-fold increase in private care expenditures for children with spina bifida compared to the general population (Ouyang et al., 2007). Therefore, it is important to estimate the number of individuals living with these conditions in order to make some inferences on future costs. Given that the transition from pediatric to adult care occurs around age 16 in the UK, and children can require additional

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support in adaptation to changes in the service provision, it is important to estimate the number of children of this age living with these conditions.

We estimated the number of children aged 0–15 years who will be living with spina bifida or Down syndrome in England and Wales by the beginning of 2020.

2. Patients and methods

2.1. Data sources

The Northern Congenital Abnormality Survey (NorCAS) was a population-based register that collected data on cases of congenital anomalies delivered to women residing in the North of England, covering approximately 29,000 births per year. Cases of congenital anomaly diagnosed before age 12 years (16 prior to 2002) were included on the NorCAS. The survey used multiple sources of case ascertainment, such as antenatal ultrasonography, fetal medicine departments, cytogenetic laboratories, the regional cardiology centre, pathology departments, and paediatric surgery. The register was active between 1985 and 2014, but was superseded by the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) in March 2015. In 2008, there was a one-off data linkage between the Office for National Statistics (ONS) for England death registrations and data for NorCAS cases born between 1985 and 2003. More information regarding the NorCAS and data linkage is available elsewhere (Tennant et al., 2010).

The National Down Syndrome Cytogenetic Register (NDSCR) was a population-based register that collected data on cases of Down syndrome born to mothers resident in England and Wales. The register worked in collaboration with the Association of Clinical Cytogeneticists and their members, meaning that when a case of Down syndrome was diagnosed, either prenatally or postnatally, a form was completed by the corresponding regional cytogenetic laboratory and notified to the NDSCR. More information on the NDSCR can be found elsewhere (Morris and Springett, 2014). For each case, data on year of birth, maternal age and place of residence (Wales, England: North East, North West, Yorkshire and the Humber, East, East Midlands, West Midlands, South East, South West, and London) was recorded (among other variables).

Live births between 1st January 1998 and 31st December 2016 by year, region and maternal age category were available from the ONS for England and Wales. Projected births between 1st January 2017 and 31st December 2019, by region, year of birth and maternal age were available from the ONS for England (ONS, 2014a) and by year of birth and maternal age for Wales (ONS, 2014b).

2.2. Case classification and inclusion

The NorCAS recorded text descriptions and WHO ICD-10 codes for up to six individual congenital anomalies per case (World Health Organization, 2010). These were categorised into group (the organ system affected, e.g. 'nervous system'), subtype (the specific condition, e.g. 'spina bifida'), and syndrome (e.g. 'Di George syndrome') based on EUROCAT guidelines (EUROCAT, 2008; 2014). Cases with more than one ICD code were assigned a primary diagnosis using an hierarchical approach described previously with the highest allocated from: 1) chromosomal syndromes; 2) genetic syndromes; 3) skeletal dysplasias; 4) other genetic anomalies (resulting from microdeletions or mutations); or 5) other syndromes of non-genetic origin (Tennant et al., 2010; EUROCAT, 2008). Isolated cases were allocated to their primary anomaly group and subtype. Cases with two or more structural anomalies were reviewed to identify a primary group or subtype, or to assign a diagnosis of multiple anomalies (two or more unrelated structural anomalies across separate organs). Live born cases of spina bifida (ICD-10: Q05) delivered between 1st January 1998 and 31st December 2013 in the North of England were identified from the NorCAS. Cases of spina bifida with chromosomal or additional structural anomalies were excluded because survival and temporal trends are different in these cases. However, cases with spina bifida and hydrocephalus were included but coded separately, because hydrocephalus occurs as a direct result of spina bifida and is part of the same condition (Yeates et al., 2016).

Data on live born cases of Down syndrome (ICD-10 Q90) delivered between 1st January 1998–31st December 2013 in England and Wales by year, maternal age (< 30, 30–34 and ≥ 35 years) and region were obtained from the NDSCR. Cases of Down syndrome were only included if there was cytogenetic evidence that would lead to a diagnoses of Down syndrome. Cases of Down syndrome with multiple congenital anomalies were included as the additional anomalies are likely to be part of the Down syndrome.

2.3. Statistical analysis

Using Poisson regression models with year of birth as the explanatory variable, we found no evidence of a trend over time in isolated spina bifida ($p = 0.17$) or in spina bifida with hydrocephalus ($p = 0.54$) born in the North of England between 1998 and 2013. Therefore, the number of cases of spina bifida born in England and Wales between 1998 and 2019 was estimated by multiplying the average spina bifida North of England live birth rate during 1998–2013 by the number of actual (1998–2016) and predicted (2017–2019) live births in England and Wales between 2014 and 2019.

Using a multivariable Poisson regression model, we found that year of birth, maternal age, region, and interactions between year of birth and maternal age, and year of birth and region, were all significantly associated with the live birth prevalence of Down syndrome (all $p < 0.001$). Therefore, using the actual and predicted number of live births in England and Wales, the number of live births affected by Down syndrome between 2014 and 2019 were estimated from the Poisson model. In a sensitivity analysis we estimated the number of live births using the average Down syndrome live birth prevalence rate between 1998 and 2013 applied to the number of live births between 2014 and 2019. Maternal age data was missing in 11.5% of Down syndrome cases. Therefore, the proportion of cases within each maternal age category was multiplied by the total number of cases to provide estimated case numbers.

Spina bifida and Down syndrome survival according to birth year (1985–2003) was modelled using Royston-Parmar regression, a type of survival model that uses a flexible parametric approach (with cubic splines) to model baseline hazard (Royston and Parmar, 2002), adjusted for year of birth. The model was extrapolated to estimate survival for children born up to 2020 at various ages e.g. for children born in 2004, 16 year survival (i.e. the age reached by 2020) was estimated specific to this year. Survival was assumed to be equal in all regions of England. These survival estimates were multiplied by the actual and predicted case numbers born each year and summed to estimate the number of children with spina bifida or Down syndrome aged 0–15 years by 2014 and 2020.

3. Results

3.1. Live birth prevalence

There were 78 live born cases of spina bifida notified to the NorCAS between 1998 and 2013, including 33 (42.3%) with hydrocephalus. In the same time period, there were 509,679 live births in the North of England, giving a live birth prevalence of 0.9 (95% CI: 0.6–1.2) per 10,000 live births for isolated spina bifida and 0.6 (95% CI: 0.4–0.9) for spina bifida with hydrocephalus.

There were 10,985 live born cases of Down syndrome notified to the NDSCR between 1998 and 2013. In the same period, there were