

REF: Wong K, Glasson EJ, Jacoby P, Srasuebkul P, Forbes D, Ravikumara M, Wilson A, Bourke J, Trollor J, Leonard H, Nagarajan L, Downs J. Survival of children and adolescents with intellectual disability following gastrostomy insertion. *Journal of Intellectual Disability Research*. 2020 Jul;64(7):497-511. doi: 10.1111/jir.12729. Epub 2020 Apr 21.

Type of Manuscript

Original Research Article

Manuscript Title

Survival of children and adolescents with intellectual disability following gastrostomy insertion.

Authors and Affiliations

Kingsley Wong¹, Emma J Glasson¹, Peter Jacoby¹, Preeyaporn Srasuebkul², David Forbes³, Madhur Ravikumara⁴, Andrew Wilson^{1,5,6,7}, Jenny Bourke¹, Julian Trollor², Helen Leonard¹, Lakshmi Nagarajan^{1,8}, Jenny Downs^{1,7}.

¹ Telethon Kids Institute, Centre for Child Health Research, The University of Western Australia, Perth, Australia; ² Department of Developmental Disability Neuropsychiatry, School of Psychiatry, UNSW Sydney, Sydney, Australia; ³ Medical School, The University of Western Australia, Perth, Australia; ⁴ Department of Gastroenterology, Perth Children's Hospital, Perth, Australia; ⁵ Department of Respiratory Medicine, Perth Children's Hospital, Perth, Australia; ⁶ School of Paediatrics, The University of Western Australia, Perth, Australia; ⁷ School of Physiotherapy and Exercise Science, Curtin University, Perth, Australia; ⁸ Children's Neuroscience Service, Department of Neurology, Perth Children's Hospital, Perth, Australia.

Corresponding Author

A/Professor Jenny Downs, Telethon Kids Institute, The University of Western Australia, PO Box 855, West Perth, Western Australia 6872, Australia. Email: Jenny.Downs@telethonkids.org.au, Phone: +61411161138

Suggested Running Head

Survival following gastrostomy insertion

Conflicts of Interest

The authors have no conflict of interest to disclose.

Sources of Funding Support

The results reported herein correspond to specific aims of project grant APP1103746 to investigator A/Professor Jenny Downs from the National Health & Medical Research Council. A/Professor Helen Leonard is supported by an Australian National Health & Medical Research Council Senior Research Fellowship (#1117105).

Data and Code Disclosure

The data are not publicly available as per the requirements of the Information Access, Use and Disclosure Policy and other relevant health policies adopted by the Department of Health, Western Australia. Computing code used for this study are available upon request.

Acknowledgements

We gratefully acknowledge staff at the WA Data Linkage Branch (Department of Health, Western Australia) and the data custodians for their assistance in obtaining the linked data used in this project and for manuscript review, and we would specifically like to thank the State and Territory Registries of Births, Deaths and Marriages, the State and Territory Coroners, the National Coronial Information System and the Victorian Department of Justice and Community Safety for enabling the use of cause of death unit record file. We acknowledge the Department of Communities (previously the Disability Services Commission), the WA Department of Education, the Catholic Education Office, and the Association of Independent Schools of WA for their assistance with data collection for the IDEA database. We wish to thank the members of the Kulunga Aboriginal Research Project Forum for their input into our analyses of our Aboriginal data.

Survival of children and adolescents with intellectual disability following gastrostomy insertion

Abstract

Objective: Positive health outcomes have been observed following gastrostomy insertion in children with intellectual disability, which is being increasingly used at younger ages to improve nutritional intake. This study investigated the effect of gastrostomy insertion on survival of children with severe intellectual disability.

Methods: We used linked disability and health data of children and adolescents who were born in Western Australia between 1983-2009 to compare survival of individuals with severe intellectual disability by exposure to gastrostomy status. For those born in 2000-2009, we employed propensity score matching to adjust for confounding by indication. Effect of gastrostomy insertion on survival was compared by pertinent health and sociodemographic risk factors.

Results: Compared with children born in the 1980s-90s, probability of survival following first gastrostomy insertion for those born in 2000-2009 was higher (2-year: 94% v 83%). Mortality risk was higher in cases than that in their matched controls (hazard ratio 2.9, 95% confidence interval 1.1,7.3). The relative risk of mortality (gastrostomy vs. non-gastrostomy) may have differed by sex, birthweight and time at first gastrostomy insertion. Respiratory conditions were a common immediate or underlying cause of death among all children, particularly among those undergoing gastrostomy insertion.

Conclusions: Whilst gastrostomy insertion was associated with lower survival rates than children without gastrostomy, survival improved with time, and gastrostomy afforded some protection for the more vulnerable groups and earlier use appears beneficial to survival. Specific clinical data that may be used to prioritize the need for gastrostomy insertion may be responsible for the survival differences observed.

Key Words: enteral feeding, paediatric, mortality, survival, nutrition.

Introduction

Intellectual disability (ID) affects 1-2% of children.(Bourke *et al.* 2016, Maulik *et al.* 2011) For children with severe ID, physical health issues that need hospitalisation are more prominent (Bebbington *et al.* 2013) and the probability of survival to 20 years in a population cohort study was 79%.(Bourke *et al.* 2017) More recently, gastrostomy insertion has been performed increasingly to address feeding and nutritional concerns in medically compromised children with ID, particularly very young children.(Fox *et al.* 2014, Glasson *et al.* 2018, Hatch *et al.* 2018). We recently reported that use of gastrostomy insertion among children with ID who were younger than 3 years increased 5.4% per annum (95% CI 3.4,7.3) over the period 1983-2014.(Glasson *et al.* 2018) Most children will gain weight following gastrostomy (Viktorsdottir *et al.* 2015, Downs *et al.* 2014b, Martinez-Costa *et al.* 2011) and may have fewer all-cause hospital admissions including those related to epilepsy,(Jacoby *et al.* 2020, Nelson *et al.* 2019) but for some children there are risks. In a population-based study of Rett syndrome, a small proportion of children experienced complications ranging from minor wound problems such as granulation to a more serious adverse effect of catheter migration.(Downs *et al.* 2014a) Furthermore, some reports have suggested gastrostomy feeding can exacerbate gastro-oesophageal reflux(Gantasala *et al.* 2013) and in a clinical study of 138 patients with neurological or other diagnoses, the cumulative incidence of a major complication was 15% (95%CI 8.9-24.5) by 5.4 years.(McSweeney *et al.* 2013). Whilst not a panacea, qualitative studies suggest that gastrostomy insertion, which can allow a mix of oral and enteral feeding or full enteral feeding, generally contributes positively to health in children.(Nelson *et al.* 2015)

The relation between improvements in health status post gastrostomy insertion and survival is unclear. Studies have estimated that approximately two thirds of children with severe neurological disability are alive three to four years following gastrostomy insertion.(Catto-Smith and Jimenez 2006, McGrath *et al.* 1992, Smith *et al.* 1999) However, these estimates were generally derived from clinical rather than population samples and have lacked a procedure-free comparison group with similar health status or risk factors. This study described the effect of gastrostomy insertion on survival in children with

severe ID by comparing survival among children who underwent gastrostomy insertion to a matched control sample and analysing variation in survival by pertinent health and sociodemographic risk factors.

Materials and Methods

We conducted a retrospective propensity score-matched cohort study using linked databases available in the state of Western Australia (WA) (2014 population: 2.5 million (Australian Bureau of Statistics 2017)). The observation period was from 1 January 1983 to 31 December 2014, which was determined by the maximum data available at the time of data request.

Cohort selection

The WA population is centralized with approximately 80% living in the greater area of its capital city Perth (Australian Bureau of Statistics 2016b) and all paediatric gastrostomy insertions are performed at the only tertiary children's hospital. We analysed linked population-based health, disability and administrative data sets.(Holman *et al.* 2008, Holman *et al.* 1999, Leonard *et al.* 2013) The state Midwives Notification System (MNS)(Leonard et al. 2013) was used to identify all individuals born alive in WA between 1 January 1983 and 31 December 2009. Cases with ID were defined as those individuals diagnosed between 1 January 1983 and 31 December 2014, based on identification of ID from either the Intellectual Disability Exploring Answers (IDEA) database (Petterson *et al.* 2005) or 2) the WA Register of Developmental Anomalies (WARDA)(Leonard et al. 2013). Births since 2010 were not included to account for the lag between birth and identification of ID and to ensure that most eligible individuals were diagnosed.

For the current study, we selected 1,011 individuals with severe ID (individuals with IQ<40 and those with any level of ID who have had gastrostomy insertion prior to their 18th birthday), and extracted demographic, disability, hospitalisation and mortality data from the IDEA database, WARDA, MNS, the Hospital Morbidity Data Collection (HMDC), and death registrations.(Leonard et al. 2013, Petterson et al. 2005)

Exposure

Individuals were considered exposed if gastrostomy insertion was performed during childhood (0-17 years). The exposure variable was time-varying, and we defined the date of index event as the admission date of the hospitalisation at which the procedure was first performed. Once exposed, the effect was considered to last till the end of follow-up. For hospitalisations that occurred between January 1983 and December 1987, we used the International Classification of Procedures in Medicine codes to identify the procedure (Open gastrostomy: 5-431, 5-432; Percutaneous endoscopic gastrostomy: no code) in the HMDC. Thereafter, the International Classification of Disease, ninth revision (ICD-9-CM) (January 1988 – June 1999) and the Australian Classification of Health Intervention (ACHI) (July 1999 – December 2014) codes were used (ICD-9-CM - Open gastrostomy 43.19; Percutaneous endoscopic gastrostomy 43.11, and ACHI - Open gastrostomy 30375-07, 90302-00; Percutaneous endoscopic gastrostomy 30481-00, 30482-00).

Outcomes

Time to death was the outcome variable in survival analyses. We considered both underlying (i.e. disease or injury that initiated the train of events leading directly to death, or the circumstances of the accident or violence that resulted in the fatal injury) and immediate (i.e. disease or condition directly leading to death as appeared on the medical certificate, coded since 1997) causes of death.

Covariates

Covariates that are potential confounding factors related to both risk of gastrostomy insertion and the outcome included time-invariant baseline (i.e. birth) variables such as child's sex, indigenous status, gestational age, infant weight, birth year, Apgar score at 5 mins after birth, maternal age, residential socioeconomic status and residential remoteness.(Bourke et al. 2017, Wong *et al.* 2019) We categorized gestational age into five groups: very preterm (24-31 weeks); moderate and late preterm (32-36 weeks); early term (37-38 weeks); full term (39-40 weeks) and post term (≥ 41 weeks) based on dating

ultrasound and last menstrual period where dating ultrasound was not available.(American College of Obstetricians and Gynecologists 2013) We grouped infant weight into two categories: <2500 and >=2500 grams. Other covariates, including birth year (1983-1989, 1990-1999, 2000-2009), maternal age (<21, 21-34, >=35 years) and Apgar score (<7 and >=7), were also categorised for descriptive purposes. We measured socioeconomic status with the Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) centile (<=20%, 21-40%, 41-60%, 61-80%, >80%),(Australian Bureau of Statistics 2016a) and ascertained remoteness of residence using the Accessibility and Remoteness Index for Australia score remoteness area categories (major cities, regional or remote).(Hugo Centre for Migration and Population Research) Both indicators were based on mother's home address at child's birth at the Census Collection District level (1996, 2001, 2006) or the Statistical Area 1 level calculated by the Australian Bureau of Statistics.(Australian Bureau of Statistics 2016a) We defined indigenous status as being a person identified as being of Aboriginal and/or Torres Strait Islander (TSI) origin coded as either Aboriginal or non-Aboriginal using a validated algorithm.(Christensen *et al.* 2014)

Potential confounding variables that were time-varying and included (1) total number of hospitalisations, during a 12-month rolling window and with a discharge diagnoses of acute lower respiratory tract infection (including influenza and pneumonia, acute bronchitis, acute bronchiolitis, pneumonitis due to solids and liquids, and other acute lower respiratory tract infection) and epilepsy, and (2) associated average length of stay (ICD codes are shown in eTable1).

Ethics approval

We obtained ethics approval from the Department of Health WA (#2016/32) and the Western Australian Aboriginal Health Ethics Committee (#747).

Statistical analysis

We first estimated the survival functions for those who ever received and never received gastrostomy insertion in the overall cohort (n=1,011) using the Simon and Makuch method (Simon and Makuch 1984) which accounts for a time varying exposure. Time at risk was measured from date of birth until date of

death, or 31st Dec 2014, whichever came first. Individual survival functions were generated for individuals born in the periods 1983-1999 and 2000-2009 to separate the effects of changes in clinical practices since 2000, involving changes in indications and post-operative care in young patients. Our principal analysis involved children born after the year 2000. We generated an original cohort of 252 individuals after excluding children with missing data on baseline covariates (n=19, 7.0%). The distributions of covariates in this cohort between children who ever received (n=120) or never received (n=132) gastrostomy insertion (hereafter referred as the gastrostomy and non-gastrostomy groups, respectively) were compared using the standardised percentage difference.²⁶ A threshold of 10% indicated between group imbalance of potential concern.(Austin 2014b)

We used propensity score matching to reduce the covariate imbalance between the gastrostomy and non-gastrostomy groups. Risk set matching was used, in which a child receiving the procedure at a particular age is matched to another child with similar demographics and medical history who has yet to undergo the procedure at that age.(Li *et al.* 2001) We developed a risk set propensity score model using a time-dependent Cox proportional hazards regression model in which gastrostomy status was regressed on baseline and time-varying covariates, (Lu 2005) and we modelled the associations between continuous baseline variables and the log hazard of gastrostomy insertion using restricted cubic splines with 4 knots.(Harrell 2001) An individual's risk set propensity score at any given time was the linear predictor from the Cox regression model. We then performed a 1:1 nearest-neighbour calliper (0.2 SD) matching without replacement(Austin 2014a) giving rise to matched pairs of cases (i.e. those who received the procedure) and controls (i.e. who had not received the procedure) with similar risk set propensity scores at the age when the procedure took place. The order of individuals in the two groups was randomised before matching.

We examined the matched cohort data for 212 individuals, as with the original cohort, for covariate imbalance between cases and controls. Adjustment was then made for the fact that gastrostomy insertion was carried out on some individuals later in the observation period after they had been matched as controls. It has been shown that exclusion or censoring of such individuals can lead to bias.(Wong *et*

al. 2018) A rank preserving structural failure time model was used, whereby g-estimation is used to generate counterfactual survival times for controls who switched gastrostomy status. These are the survival times which would have been expected had these individuals not undergone gastrostomy insertion. The matched cohort data was amended to include the counterfactual survival times where indicated.

We carried out comparison of survival between the case and control groups within the amended matched cohort in two ways. Firstly, Kaplan-Meier survival functions consisting of probability of survival with time since matching for gastrostomy insertion for the two groups were generated, absolute differences in survival probability at specific follow-up times reported and the log-rank test used to compare overall survival between the groups. To investigate differential effects of gastrostomy insertion on survival, we repeated these analyses with the cohort stratified by sex, indigenous status, residential socioeconomic status, residential remoteness, infant weight and age at first gastrostomy insertion. Secondly, we used Cox proportional hazards regression to estimate the survival hazard ratios associated with gastrostomy insertion using a robust variance estimator to account for the matched pairs.(Austin 2014b) In order to adjust for residual confounding after propensity score matching, we obtained double-robust estimators by including unbalanced baseline and time-varying covariates in the regression models.(Nguyen *et al.* 2017) Interaction terms involving the covariates listed above were subsequently included to investigate differential survival by subgroup.

Sensitivity analyses

We performed sensitivity analyses in the matched cohort to assess the robustness of the adjusted association to unmeasured confounding using the Rosenbaum bounds test.(Rosenbaum 2002) For all Cox regression analyses, the proportional hazards assumption was tested and confirmed using Schoenfeld residuals. Statistical analyses were performed using Stata 15.1 (StataCorp LLC, College Station, Texas).

Results

Development of the original and matched cohorts is illustrated in eFigure 1, and the baseline characteristics of the overall group and the cohorts are shown in eTable 2 and Table 1, respectively. Within the overall group (n=1,011), the estimated probability of survival for individuals with severe ID and gastrostomy born in 2000-2009 was higher than those born in 1983-1999 (2-year: 2000-2009 93.9% [95% confidence interval [CI] 77.0,98.5], 1983-1999 83.4% [95% CI 59.9,93.8]; 5-year: 2000-2009 82.2% [95% CI 68.9,90.2], 1983-1999 68.5% [95% CI 51.2,80.8]) (Figure 1).

Analysis then included 252 WA children and adolescents born between 2000 and 2009 with severe ID. Compared with individuals who never received gastrostomy insertion (n=132), those who underwent the procedure (n=120) were more likely to be female (48.3% v 40.9%), Aboriginal/TSI (21.7% v 9.9%), born preterm (<37 weeks: 35.8% v 15.9%) and born to a young mother (<21 years: 14.2% v 7.6%) (Table 1). In addition, they tended to have lower birthweight (<2500 grams: 31.7% v 18.2%), lower Apgar score (<7: 19.2% v 3.0%), and their mothers were more likely to be residing at their birth in areas that were classified as regional or remote (36.7% v 21.2%). Characteristics of the excluded cohort were similar to that in the original cohort except for infant weight and Apgar score (eTable 3).

Among the 120 children and adolescents who had a gastrostomy insertion in the original cohort, 106 remained in the analysis after matching using the propensity score method. The 14 unmatched individuals were lighter at birth (<2500 grams: 57.1% v. 28.3%), had lower Apgar score at 5 minutes (<7: 50.0% vs. 15.1%), and were more likely to be preterm (<37 weeks: 64.3% vs. 32.1%), when compared with those in the matched cohort (eTable 4). The 106 matched controls comprised 73 unique individuals of whom 33 (45%) were matched prior to gastrostomy insertion and the rest (n=40, 55%) never received the procedure. The proportions of controls that were matched multiple times were 33% (n=11) and 38% (n=15) in the former and latter groups, respectively. Baseline and time-varying characteristics of the matched cohort are reported in Table 1. On average, propensity score matching balanced most covariates except sex, infant weight, maternal age, residential socioeconomic status, residential remoteness, and total number of admissions for acute lower respiratory tract infection and average length of stay of acute lower respiratory tract infection admissions in the 12-month period prior to matching.

The median time of follow-up from matching for first gastrostomy insertion was 6 years 3 months (inter-quartile range 3 years 7 months – 8 years 9 month), during which time 27 individuals died (20.6 deaths per 1,000 person-years). Close to half (52%, 14/27) of the underlying causes of death were related to diseases of the nervous system, in particular cerebral palsy and other neurological conditions (ICD-10 codes G80-G83, n=10). Many immediate causes of death were related to the respiratory system (26%, 7/27) or were ill-defined (30%, 8/27). Among the 19 children and adolescents who received gastrostomy insertion and died within the observation period, diseases of the respiratory system were mentioned at least once in 58% (n=11) of the individuals when multiple causes of death were listed. These conditions appeared in 50% (n=4) of the 8 deceased controls.

The probability of survival among cases was 90.1% (95% CI 82.4,94.6) at 2 years and 85.8% (95% CI 77.1,91.3) at 5 years after matching for first gastrostomy insertion (Table 2). The survival functions differed between the control and case groups (log-rank test: $P = 0.01$) (Table 2, eFigure 2). There was higher risk of mortality in children and adolescents who had received gastrostomy insertion compared with controls, after accounting for the influences of unbalanced covariates (hazard ratio 2.87, 95% CI 1.13,7.26) (Table 3). Females, low birthweight and first gastrostomy insertion before 3 years of age appeared to have lower risk of mortality associated with gastrostomy insertion than their comparison groups, but the evidences were inconclusive. The effects of gastrostomy insertion on survival were similar by indigenous status (Table 3).

Sensitivity analyses

Using Rosenbaum's method of sensitivity analysis for matched data, a gamma value of 1.26 was required before the upper bound on the Wilcoxon signed-rank test P -value reached 0.05. This implies that to attribute a higher risk of mortality due to an unobserved covariate rather than the measured confounding factors, such an unobserved covariate would need to produce a nearly a third increase in the odds of receiving gastrostomy insertion. Thus, it is likely that clinical features (e.g. ability to swallow and

nutritional status) that may influence clinicians when considering gastrostomy insertion but were not available in the linked datasets could have explained the higher mortality risk.

Discussion

Our two-year survival estimate (94%) following gastrostomy for children born 2000 to 2009 was higher than for those born 1983 to 1999. In other studies, two-year survival was 87% in 948 Canadian children with neurological impairment and gastrostomy insertion 1993-2015(Nelson et al. 2019); 83% in 61 children with cerebral palsy and gastrostomy insertion 1990-1998(Catto-Smith and Jimenez 2006); and 74% in an earlier US clinical study of 61 cases with severe cerebral palsy and gastrostomy performed 1984-1989(McGrath et al. 1992). These time trends appear to indicate that survival for children with gastrostomy is improving with time, consistent with changing and more proactive clinical care models including greater use of intensive care services.(Wong et al. 2019) Nevertheless, compared to matched controls, our findings have shown that the procedure remained associated with lower survival in WA born children and adolescents diagnosed with severe ID.

Gastrostomy insertion within the severe ID group could be a marker of even greater clinical severity. For example, within Rett syndrome, a severe neurodevelopmental disability, variability in phenotype including variation in the ability to walk and severity of comorbidities has been observed.(Leonard *et al.* 2017) These individuals would be classified as severe ID, yet greater severity within this group would likely accompany poorer health and survival. In the current study of children with severe ID, those who underwent gastrostomy insertion could have represented a subgroup with greater impairments.

We found little evidence of increased relative mortality risk associated with gastrostomy insertion by indigenous status, which is usually marker of disadvantage. Aboriginal Australians commonly experience health and social disadvantage,(Australian Health Ministers' Advisory Council 2015) however in our study we found that such disadvantages did not confer a major increase in relative mortality risk although we must be mindful of the limited sample size and representativeness of the subgroup. We noted

that females with gastrostomy insertion probably had lower relative risk of mortality than their male counterparts, in contrast to the poorer survival overall in females with ID.(Bourke et al. 2017) Infants with lower birthweight are prone to substantial physical health disadvantages(Saigal and Doyle 2008) but their relative mortality risk appeared to be higher than that of the normal birthweight group, probably due to better care and surveillance but bias due to small sample size cannot be overlooked. Children who received their gastrostomy insertion when older than three years had more than six times the relative risk of death compared with the lower risk for those younger than three years at gastrostomy insertion. This could be explained by earlier support for growth, including lung growth or earlier stabilization of physical health, in response to consistently delivered nutrition and medications.

Vulnerability to poor respiratory health including aspiration is common because of musculoskeletal deformity and gastrointestinal comorbidities.(Santoro *et al.* 2012) We have previously observed that hospitalizations for lower respiratory tract infections continued at a similar rate following gastrostomy(Jacoby et al. 2020) and in the current study, respiratory conditions were listed commonly as immediate or contributory causes of death. Gastrostomy insertion may aggravate the presence or degree of reflux in some children,(Aumar *et al.* 2018) suggesting that personalized feeding regimens in reducing respiratory ill-health is an important future goal.

Strengths and limitations

This study was strengthened by using longitudinal linked datasets for the entire WA population,(Balogh *et al.* 2019) providing a sample size rarely feasible in a clinical population. We used propensity score matching to adjust for confounding by indication and improve the comparability of the gastrostomy and non-gastrostomy groups. Thus, we were better able to interpret the effect of gastrostomy from a causal perspective and reduce the influence of confounding due to peri-natal and socioeconomic risk factors. Some limitations included group characteristics being unbalanced, which occurred due to the relatively low prevalence of severe ID. In addition, as mentioned previously, administrative data were used and the lack of other relevant medical information in the datasets limited our ability to match gastrostomy and non-gastrostomy groups according to clinical attributes. For example, there could be differences in

aetiology of the underlying disorder, functional abilities such as efficiency of swallow and ability to walk, even if with assistance,(MacKay *et al.* 2018) and the presence and/or extent of some comorbidities such as the degree of nutritional compromise or epilepsy control. As well, we could not identify other environmental factors such as extended family supports that could have influenced the care of the child with complex and high needs and possibly survival. Future research would benefit from the use of a more comprehensive dataset from which survival patterns for disadvantaged and minority groups could be more confidently assessed.

Conclusions

Children with severe ID who undergo gastrostomy insertion experience poorer survival than children who do not, but survival rates have improved with time. Specific clinical data that may be used to prioritize the need for gastrostomy insertion may be responsible for the survival differences observed. Additional research evaluating the value of gastrostomy insertion on the quality of life for children and families is needed.

References

- American College of Obstetricians and Gynecologists (2013) ACOG Committee Opinion No 579: Definition of term pregnancy. *Obstet Gynecol*, **122**, 1139-40.
- Aumar, M., Lalanne, A., Guimber, D., Coopman, S., Turck, D., Michaud, L. & Gottrand, F. (2018) Influence of Percutaneous Endoscopic Gastrostomy on Gastroesophageal Reflux Disease in Children. *J Pediatr*, **197**, 116-120.
- Austin, P. C. (2014a) A comparison of 12 algorithms for matching on the propensity score. *Statistics in Medicine*, **33**, 1057-1069.
- Austin, P. C. (2014b) The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. *Stat Med*, **33**, 1242-58.
- Australian Bureau of Statistics (2016a) 2033.0.55.001 - Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA). Government of Australia, Canberra, Australia.
- Australian Bureau of Statistics (2016b) Regional Population Growth, Australia, Cat. No. 3218.0. Australian Bureau of Statistics, Canberra, Australia.
- Australian Bureau of Statistics (2017) Australian Demographic Statistics, Cat. No. 3101.0. Australian Bureau of Statistics, Canberra, Australia.
- Australian Health Ministers' Advisory Council (2015) Aboriginal and Torres Strait Islander Health Performance Framework 2014 Report. AHMAC, Canberra, Australia.
- Balogh, R., Leonard, H., Bourke, J., Brameld, K., Downs, J., Hansen, M., Glasson, E., Lin, E., Lloyd, M., Lunsy, Y., O'Donnell, M., Shooshtari, S., Wong, K. & Krahn, G. (2019) Data Linkage: Canadian and Australian Perspectives on a Valuable Methodology for Intellectual and Developmental Disability Research. *Intellect Dev Disabil*, **57**, 439-462.
- Bebbington, A., Glasson, E., Bourke, J., de Klerk, N. & Leonard, H. (2013) Hospitalisation rates for children with intellectual disability or autism born in Western Australia 1983-1999: a population-based cohort study. *BMJ Open*, **3**.

- Bourke, J., de Klerk, N., Smith, T. & Leonard, H. (2016) Population-based prevalence of intellectual disability and autism spectrum disorders in Western Australia: A comparison with previous estimates. *Medicine*, **95**, e3737.
- Bourke, J., Nembhard, W. N., Wong, K. & Leonard, H. (2017) Twenty-Five Year Survival of Children with Intellectual Disability in Western Australia. *J Pediatr*, **188**, 232-239.e2.
- Catto-Smith, A. G. & Jimenez, S. (2006) Morbidity and mortality after percutaneous endoscopic gastrostomy in children with neurological disability. *J Gastroenterol Hepatol*, **21**, 734-8.
- Christensen, D., Davis, G., Draper, G., Mitrou, F., McKeown, S., Lawrence, D., McAullay, D., Pearson, G., Ridders, W. & Zubrick, S. R. (2014) Evidence for the use of an algorithm in resolving inconsistent and missing Indigenous status in administrative data collections. *Aust J Soc Issues*, **49**, 423-443.
- Downs, J., Wong, K., Ravikumara, M., Ellaway, C., Elliott, E. J., Christodoulou, J., Jacoby, P. & Leonard, H. (2014a) Experience of gastrostomy using a quality care framework: the example of rett syndrome. *Medicine (Baltimore)*, **93**, e328.
- Downs, J., Wong, K., Ravikumara, M., Ellaway, C., Elliott, E. J., Christodoulou, J., Jacoby, P. & Leonard, H. (2014b) Experience of gastrostomy using a quality care framework: the example of rett syndrome. *Medicine*, **93**, e328.
- Fox, D., Campagna, E. J., Friedlander, J., Partrick, D. A., Rees, D. I. & Kempe, A. (2014) National trends and outcomes of pediatric gastrostomy tube placement. *J Pediatr Gastroenterol Nutr*, **59**, 582-8.
- Gantasala, S., Sullivan, P. B. & Thomas, A. G. (2013) Gastrostomy feeding versus oral feeding alone for children with cerebral palsy. *Cochrane Database Syst Rev*, **7**, Cd003943.
- Glasson, E. J., Wong, K., Leonard, H., Forbes, D., Ravikumara, M., Mews, C., Jacoby, P., Bourke, J., Trollor, J., Srasuebku, P., Wilson, A., Nagarajan, L. & Downs, J. (2018) Evolving Trends of Gastrostomy Insertion Within a Pediatric Population. *J Pediatr Gastroenterol Nutr*, **67**, e89-e94.
- Harrell, F. E. (2001) *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*, (Trans. Springer, New York).

- Hatch, L. D., Scott, T. A., Walsh, W. F., Goldin, A. B., Blakely, M. L. & Patrick, S. W. (2018) National and regional trends in gastrostomy in very low birth weight infants in the USA: 2000-2012. *J Perinatol*, **38**, 1270-1276.
- Holman, C. D. J., Bass, A. J., Rosman, D. L., Smith, M. B., Semmens, J. B., Glasson, E. J., Brook, E. L., Trutwein, B., Rouse, I. L., Watson, C. R., de Klerk, N. H. & Stanley, F. J. (2008) A decade of data linkage in Western Australia: strategic design, applications and benefits of the WA data linkage system. *Aust Health Rev*, **32**, 766-777.
- Holman, C. D. J., Bass, A. J., Rouse, I. R. & Hobbs, M. S. T. (1999) Population-based linkage of health records in Western Australia: development of a health services research linked database. *Australia and New Zealand Journal of Public Health*, **23**, 453-459.
- Hugo Centre for Migration and Population Research Accessibility/Remoteness Index of Australia (ARIA).
- Jacoby, P., Wong, K., Srasuebkul, P., Glasson, E. J., Forbes, D., Ravikumara, M., Wilson, A., Nagarajan, L., Bourke, J., Trollor, J., Leonard, H. & Downs, J. (2020) Risk of hospitalizations following gastrostomy in children with intellectual disability. *The Journal of Pediatrics*, **217**, 131-138.
- Leonard, H., Cobb, S. & Downs, J. (2017) Clinical and biological progress over 50 years in Rett syndrome. *Nat Rev Neurol*, **13**, 37-51.
- Leonard, H., Glasson, E., Bebbington, A., Hammond, G., Croft, D., Pikora, T., Fairthorne, J., O'Donnell, M., O'Leary, C., Hansen, M., Watson, L., Francis, R. W., Carter, K. W., McKenzie, A., Bower, C., Bourke, J. & Glauert, R. (2013) Application of Population-Based Linked Data to the Study of Intellectual Disability and Autism. In: *International Review of Research in Developmental Disabilities* (ed R. C. Urbano). pp. 281-327. Academic Press, Burlington.
- Li, Y. P., Propert, K. J. & Rosenbaum, P. R. (2001) Balanced Risk Set Matching. *Journal of the American Statistical Association*, **96**, 870-882.
- Lu, B. (2005) Propensity score matching with time-dependent covariates. *Biometrics*, **61**, 721-728.

- MacKay, J., Leonard, H., Wong, K., Wilson, A. & Downs, J. (2018) Respiratory morbidity in Rett syndrome: an observational study. *Dev Med Child Neurol*, **60**, 951-957.
- Martinez-Costa, C., Borraz, S., Benlloch, C., Lopez-Saiz, A., Sanchiz, V. & Brines, J. (2011) Early decision of gastrostomy tube insertion in children with severe developmental disability: a current dilemma. *J Hum Nutr Diet*, **24**, 115-21.
- Maulik, P. K., Mascarenhas, M. N., Mathers, C. D., Dua, T. & Saxena, S. (2011) Prevalence of intellectual disability: a meta-analysis of population-based studies. *Research in Developmental Disabilities*, **32**, 419-36.
- McGrath, S. J., Splaingard, M. L., Alba, H. M., Kaufman, B. H. & Glicklick, M. (1992) Survival and functional outcome of children with severe cerebral palsy following gastrostomy. *Arch Phys Med Rehabil*, **73**, 133-7.
- McSweeney, M. E., Jiang, H., Deutsch, A. J., Atmadja, M. & Lightdale, J. R. (2013) Long-term outcomes of infants and children undergoing percutaneous endoscopy gastrostomy tube placement. *J Pediatr Gastroenterol Nutr*, **57**, 663-7.
- Nelson, K. E., Lacombe-Duncan, A., Cohen, E., Nicholas, D. B., Rosella, L. C., Guttmann, A. & Mahant, S. (2015) Family Experiences With Feeding Tubes in Neurologic Impairment: A Systematic Review. *Pediatrics*, **136**, e140-51.
- Nelson, K. E., Rosella, L. C., Mahant, S., Cohen, E. & Guttmann, A. (2019) Survival and Health Care Use After Feeding Tube Placement in Children With Neurologic Impairment. *Pediatrics*, **143**.
- Nguyen, T. L., Collins, G. S., Spence, J., Devereaux, P. J., Daures, J. P., Landais, P. & Le Manach, Y. (2017) Comparison of the ability of double-robust estimators to correct bias in propensity score matching analysis. A Monte Carlo simulation study. *Pharmacoepidemiol Drug Saf*, **26**, 1513-1519.
- Petterson, B., Leonard, H., Bourke, J., Sanders, R., Chalmers, R., Jacoby, P. & Bower, C. (2005) IDEA (Intellectual Disability Exploring Answers): a population-based database for intellectual disability in Western Australia. *Annals of Human Biology*, **32**, 237-243.

- Rosenbaum, P. R. (2002) *Observational Studies*, (Trans. Springer, New York.
- Saigal, S. & Doyle, L. W. (2008) An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet*, **371**, 261-9.
- Santoro, A., Lang, M. B., Moretti, E., Sellari-Franceschini, S., Orazini, L., Cipriani, P., Cioni, G. & Battini, R. (2012) A proposed multidisciplinary approach for identifying feeding abnormalities in children with cerebral palsy. *J Child Neurol*, **27**, 708-12.
- Simon, R. & Makuch, R. W. (1984) A non-parametric graphical representation of the relationship between survival and the occurrence of an event: application to responder versus non-responder bias. *Stat Med*, **3**, 35-44.
- Smith, S. W., Camfield, C. & Camfield, P. (1999) Living with cerebral palsy and tube feeding: A population-based follow-up study. *J Pediatr*, **135**, 307-10.
- Viktorsdottir, M. B., Oskarsson, K., Gunnarsdottir, A. & Sigurdsson, L. (2015) Percutaneous endoscopic gastrostomy in children: a population-based study from Iceland, 1999-2010. *J Laparoendosc Adv Surg Tech A*, **25**, 248-51.
- Wong, K., Downs, J., Ellaway, C., Baikie, G., Ravikumara, M., Jacoby, P., Christodoulou, J., Elliott, E. J. & Leonard, H. (2018) Impact of gastrostomy placement on nutritional status, physical health, and parental well-being of females with Rett Syndrome: A longitudinal study of an Australian population. *J of Pediatrics*, **200**, 188-195.e1.
- Wong, K., Leonard, H., Pearson, G., Glasson, E. J., Forbes, D., Ravikumara, M., Jacoby, P., Bourke, J., Srasuebku, P., Trollor, J., Wilson, A., Nagarajan, L. & Downs, J. (2019) Epidemiology of gastrostomy insertion for children and adolescents with intellectual disability. *Eur J Pediatr*, **178**, 351-361.

Table 1. Characteristics of WA-born (2000-2009) children and adolescents with severe intellectual disability in the original cohort and in the propensity score matched cohort, by gastrostomy insertion status

Characteristic	Original cohort (n=252)		Matched cohort (n=212)			
	Gastrostomy ^a (n=120)	Non-gastrostomy ^a (n=132)	Standardized percentage difference ^c	Case group ^b (n individuals=106)	Control group ^b (n strata=106) ^d	Standardized percentage difference ^c
Sex, n (%)						
Female	58 (48.3)	54 (40.9)	14.9	51 (48.1)	45 (42.5)	11.3
Indigenous status, n (%)						
Aboriginal/TSI	26 (21.7)	13 (9.9)	32.7	21 (19.8)	22 (20.8)	-2.3
Residential socioeconomic status [IRSAD], n (row, col%)						
<=20%	33 (51.6, 27.5)	31 (48.4, 23.5)	9.2	28 (51.9, 26.4)	26 (48.2, 24.5)	4.3
21-40%	29 (47.5, 24.2)	32 (52.5, 24.2)	-0.2	27 (51.9, 25.5)	25 (48.1, 23.6)	4.4
41-60%	19 (42.2, 15.8)	26 (57.8, 19.7)	-10.1	18 (48.7, 17.0)	19 (51.4, 17.9)	-2.5
61-80%	27 (51.9, 22.5)	25 (48.1, 18.9)	8.8	24 (44.4, 22.6)	30 (55.6, 28.3)	-13.0
>80%	12 (40.0, 10.0)	18 (60.0, 13.6)	-11.2	9 (60.0, 8.5)	6 (40.0, 5.7)	11.0
Residential remoteness, n (row, col%)						
Major cities	76 (42.2, 63.3)	104 (57.8, 78.8)	-34.4	69 (49.3, 65.1)	71 (50.7, 67.0)	-4.0
Inner regional	13 (52.0, 10.8)	12 (48.0, 9.1)	5.8	12 (63.2, 11.3)	7 (36.8, 6.6)	16.5
Outer regional	13 (61.9, 10.8)	8 (38.1, 6.1)	17.2	12 (46.2, 11.3)	14 (53.9, 13.2)	-5.7
Remote	11 (64.7, 9.2)	6 (35.3, 4.6)	18.3	7 (41.2, 6.6)	10 (58.8, 9.4)	-10.4
Very remote	7 (77.8, 5.8)	<5 ^e	23.0	6 (60.0, 5.7)	<5 ^e	8.9
Birth year						
Mean (SD)	2004 (2.7)	2004 (2.9)	24.7	2004 (2.6)	2004 (2.7)	-6.1
Gestational age, n (row, col%)						
<28 weeks	10 (100, 8.3)	0 (0, 0)	42.5	6 (50.0, 5.7)	6 (50.0, 5.7)	0.0
28-31 weeks	8 (80.0, 6.7)	<5 ^e	26.1	5 (45.5, 4.7)	6 (54.6, 5.7)	-4.2

32-36 weeks	25 (56.8, 20.8)	19 (43.2, 14.4)	16.9	23 (51.1, 21.7)	22 (48.9, 20.8)	2.3
37-38 weeks	30 (39.0, 25.0)	47 (61.0, 35.6)	-23.1	30 (51.7, 28.3)	28 (48.3, 26.4)	4.2
39-40 weeks	39 (42.9, 32.5)	52 (57.1, 39.4)	-14.3	34 (49.3, 32.1)	35 (50.7, 33.0)	-2.0
>=41 weeks	8 (40.0, 6.7)	12 (60.0, 9.1)	-9.0	8 (47.1, 7.6)	9 (52.9, 8.5)	-3.5
Mean (SD)	36.1 (4.7)	38.1 (2.2)	-54.2	36.6 (4.2)	36.8 (4.2)	-3.1
Infant weight, n (row, col%)						
>=2500 grams	82 (43.2, 68.3)	108 (56.8, 81.8)	-31.4	76 (51.7, 71.7)	71 (48.3, 67.0)	10.2
Mean (SD)	2,682 (970)	3,052 (634)	-45.2	2,762 (893)	2,697 (894)	7.3
Apgar score at 5 mins after birth, n (row, col%)						
>=7	97 (43.1, 80.8)	128 (56.9, 97.0)	-52.9	90 (49.2, 84.9)	93 (50.8, 87.7)	-8.2
Mean (SD)	7.8 (2.1)	8.9 (0.9)	-66.4	8.0 (1.9)	7.9 (2.0)	4.8
Maternal age, n (row, col%)						
<21 years	17 (63.0, 14.2)	10 (37.0, 7.6)	21.2	13 (43.3, 12.3)	17 (56.7, 16.0)	-10.8
21-34 years	88 (48.9, 73.3)	92 (51.1, 69.7)	8.0	79 (49.7, 74.5)	80 (50.3, 75.5)	-2.2
>=35 years	15 (33.3, 12.5)	30 (66.7, 22.7)	-27.0	14 (60.9, 13.2)	9 (39.1, 8.5)	15.1
Mean (SD)	28.1 (6.0)	29.8 (6.0)	-28.8	28.2 (6.0)	27.7 (6.2)	8.2
Hospitalization (in the 12 months preceding matching)						
Acute lower respiratory tract infection						
Total number of admissions, mean (SD)	n/a	n/a		0.6 (1.0)	0.5 (1.0)	13.0
Average length of stay (days), mean (SD)	n/a	n/a		3.1 (6.3)	2.1 (4.9)	18.7
Epilepsy						
Total number of admissions, mean (SD)	n/a	n/a		0.5 (1.5)	0.4 (1.3)	4.0
Average length of stay (days), mean (SD)	n/a	n/a		1.4 (4.1)	1.4 (3.4)	0.3

SD, standard deviation; N, number of individuals; TSI, Torres Strait Islanders; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage; n/a not applicable

^a Gastrostomy group included children who ever received gastrostomy insertion, whilst non-gastrostomy group include individuals who never received gastrostomy insertion

^b Cases include children and adolescents who received gastrostomy insertion at time of matching, whilst controls include individuals who had not yet received the procedure at time of matching. A rank preserving structural failure time model was used to generate counterfactual survival times for controls who switched gastrostomy status.

^c Standardized percentage difference is the percentage difference of the sample means in the gastrostomy and non-gastrostomy subgroup as a percentage of the square root of the average of the sample variances in the two groups. Values that are above the 10% threshold used to define imbalance of potential concern are highlighted with grey background.

^d One control individuals per stratum for a total of 73 distinct individuals (40 who never received gastrostomy insertion and 33 who had yet received gastrostomy when risk-set matched but eventually underwent the procedure); note that individuals could contribute to more than one stratum, hence the lesser number of distinct individuals.

^e Data not presented for cell counts less than five cases

Table 2. Estimated probability of survival in children and adolescents with severe intellectual disability in the matched cohort (n=212)

	Matched group	Number of deaths/Time at risk (years)	Incidence rate per 1,000 person-years (95% CI)	Time since matching for first gastrostomy insertion			
				1 year	2 years	5 years	10 years
				Survival probability, % (95% CI)			
Overall		27/1,312	20.6 (13.6,30.0)	97.2 (93.8,98.7)	94.6 (90.4,97.0)	90.0 (84.8,93.5)	80.1 (70.3,87.0)
				Log-rank test statistic ^a χ^2 (df = 1): 6.4, <i>P</i> = 0.01			
	Case ^b	19/636	29.9 (18.0,46.6)	95.3 (89.0,98.0)	90.1 (82.4,94.6)	85.8 (77.1,91.3)	73.5 (58.4,83.8)
	Control ^b	8/675	11.8 (5.1,23.3)	99.1 (93.4,99.9)	99.1 (93.4,99.9)	94.3 (86.8,97.6)	87.8 (76.1,94.0)
	Difference ^c	-	18.0 (2.3,33.7)	-3.8 (-9.9,2.3)	-8.9 (-16.1,-1.7)	-8.5 (-22,5.0)	-14.4 (-22.8,-5.9)
Subgroup analysis							
Sex							
	Male			Log-rank test statistic χ^2 (df = 1): 1.3, <i>P</i> = 0.27			
	Case	7/334	21.0 (8.4,43.2)	94.6 (84.0,98.2)	92.6 (81.5,97.2)	90.5 (78.6,96.0)	74.7 (45.9,89.7)
	Control	<5 ^e	7.8 (4.1,13.3)	100 (-)	100 (-)	95.7 (83.9, 98.9)	92.7 (78.7,97.6)
	Difference	-	13.4 (-4.3,31.1)	-5.5 (-11.4,0.5)	-7.4 (-14.4,-0.4)	-5.2 (-15.0,4.7)	-18.0 (-40.9,4.9)
	Female			Log-rank test statistic χ^2 (df = 1): 2.7, <i>P</i> = 0.10			
	Case	12/302	39.7 (20.5,69.3)	96.0 (85.1,99.0)	87.7 (74.6,94.3)	81.1 (66.8,89.7)	71.5 (54.6,83.1)

	Control	5/278	18.0 (5.8,41.9)	97.8 (85.3,99.7)	97.8 (85.3,99.7)	92.6 (78.8,97.6)	81.7 (59.0,92.6)
	Difference	-	21.7 (-5.7,49.1)	-1.7 (-8.6,5.2)	-10.1 (-20.3,0.1)	-11.5 (-25.2,2.3)	-10.2 (-31.5,11.1)
Indigenous status							
Non-Aboriginal/TSI	Log-rank test statistic χ^2 (df = 1): 5.3, $P = 0.02$						
	Case	15/491	30.5 (17.1,50.4)	95.3 (87.8,98.2)	91.4 (82.7,95.8)	87.3 (77.6,93.0)	69.5 (48.7,83.3)
	Control	7/516	13.6 (5.5,28.0)	98.9 (91.8,99.8)	98.8 (91.8,99.8)	94.1 (84.9,97.8)	85.6 (70.9,93.2)
	Difference	-	17.0 (-1.5,35.4)	-3.6 (-8.7,1.6)	-7.5 (-14.0,-0.9)	-6.8 (-16.1,2.5)	-16.1 (-36.3,4.2)
Aboriginal/TSI	Log-rank test statistic χ^2 (df = 1): 1.0, $P = 0.32$						
	Case	<5 ^e	27.6 (7.5,70.5)	95.2 (70.7,99.3)	85.7 (62.0,95.2)	80.7 (56.3,92.3)	80.7 (56.3,92.3)
	Control	<5 ^e	6.3 (0.2,34.9)	100 (-)	100 (-)	95.0 (69.5,99.3)	95.0 (69.5,99.3)
	Difference	-	21.3 (-8.3,50.9)	-4.8 (-13.9,4.4)	-14.3 (-29.3,0.7)	-14.3 (-33.9,5.2)	-14.3 (-33.9,5.2)
Residential socioeconomic status (IRSAD)							
>20%	Log-rank test statistic χ^2 (df = 1): 4.6, $P = 0.03$						
	Case	15/456	32.9 (18.4,54.2)	94.8 (86.7,98.0)	89.1 (79.4,94.4)	86.2 (75.7,92.3)	69.1 (49.4,82.4)
	Control	8/506	15.8 (6.8,31.2)	98.7 (91.4,99.8)	98.7 (91.4,99.8)	92.2 (82.2,96.7)	83.7 (68.9,91.9)
	Difference	-	17.1 (-2.9,37.0)	-3.9 (-9.5,1.6)	-9.6 (-17.2,-2.1)	-6.1 (-16.4,4.3)	-14.6 (-34.5,5.2)
<=20%	Log-rank test statistic χ^2 (df = 1): 2.0, $P = 0.16$						
	Case	<5 ^e	22.2 (6.0,56.8)	96.4 (77.2,99.5)	92.9 (74.4,98.2)	85.1 (64.9,94.2)	85.1 (64.9,94.2)
	Control	0/170	0 (0,21.7) ^d	100 (-)	100 (-)	100 (-)	100 (-)
	Difference	-	22.2 (0.4,43.9)	-3.6 (-10.4,3.3)	-7.1 (-16.7,2.4)	-14.9 (-28.4,-1.4)	-14.9 (-28.4,-1.4)
Residential remoteness							
Major cities	Log-rank test statistic χ^2 (df = 1): 4.5, $P = 0.03$						

	Case	9/404	22.3 (10.2,42.3)	97.1 (88.8,99.3)	93.9 (84.5,97.7)	90.5 (80.0,95.6)	79.2 (59.7,90.0)
	Control	5/435	11.5 (3.7,26.8)	98.6 (90.4,99.8)	98.6 (90.4,99.8)	96.8 (87.8,99.2)	86.3 (68.3,94.5)
	Difference	-	10.8 (-6.9,28.5)	-1.5 (-6.3,3.3)	-4.7 (-11.1,1.7)	-6.4 (-14.8,2.1)	-7.1 (-26.1,11.9)
Regional/remote	Log-rank test statistic χ^2 (df = 1): 1.0, $P = 0.32$						
	Case	10/232	43.1 (20.7,79.2)	91.9 (76.9,97.3)	83.5 (67.0,92.3)	77.8 (60.4,88.2)	64.3 (39.0,81.3)
	Control	<5 ^e	12.5 (2.6,36.4)	100 (-)	100 (-)	89.9 (71.8,96.6)	89.9 (71.8,96.6)
	Difference	-	30.6 (0.4,60.8)	-8.1 (-16.9,0.7)	-16.5 (-28.5,-4.4)	-12.1 (-29.5,5.3)	-25.6 (-49.7,-1.6)
Infant weight							
>=2500 grams	Log-rank test statistic χ^2 (df = 1): 3.8, $P = 0.05$						
	Case	17/391	43.5 (25.3,69.6)	93.4 (84.8,97.2)	86.0 (75.5,92.2)	81.1 (69.6,88.6)	64.8 (43.3,79.9)
	Control	6/436	13.8 (5.1,30.0)	100 (-)	100 (-)	92.6 (81.5,97.2)	86.2 (70.7,93.9)
	Difference	-	29.7 (6.3,53.1)	-6.7 (-12.3,-1.0)	-14.0 (-22.1,-5.9)	-11.5 (-23.1,0.2)	-21.4 (-42.8,0)
<2500 grams	Log-rank test statistic χ^2 (df = 1): 0.0, $P = 1.00$						
	Case	<5 ^e	8.2 (1.0,29.5)	100 (-)	100 (-)	96.6 (78.0,99.5)	90.1 (63.9,97.6)
	Control	<5 ^e	8.4 (1.0,30.2)	97.1 (81.4,99.6)	97.1 (81.4,99.6)	97.1 (81.4,99.6)	90.7 (64.5,97.8)
	Difference	-	-0.2 (-16.4,16.0)	2.9 (-2.7,8.4)	2.9 (-2.7,8.4)	-0.6 (-9.2,8.1)	-0.6 (-19.6,18.5)
Age at first gastrostomy insertion							
>=3 years	Log-rank test statistic χ^2 (df = 1): 5.0, $P = 0.03$						
	Case	9/174	51.8 (23.7,98.3)	95.5 (83.2,98.9)	90.0 (75.3,96.1)	77.0 (58.6,88.0)	68.4 (43.6,84.1)
	Control	<5 ^e	9.2 (1.1,33.1)	100 (-)	100 (-)	96.6 (78.0,99.5)	84.5 (43.2,96.7)
	Difference	-	42.7 (6.5,78.8)	-4.5 (-10.6,1.6)	-10.0 (-19.4,-0.6)	-19.6 (-35.4,-3.7)	-16.0 (-46.7,14.6)
<3 years	Log-rank test statistic χ^2 (df = 1): 2.6, $P = 0.11$						

Case	10/463	21.6 (10.4,39.7)	95.1 (85.5,98.4)	90.2 (79.4,95.5)	90.2 (79.4,95.5)	77.4 (59.5,88.2)
Control	6/457	13.1 (4.8,28.6)	98.4 (88.9,99.8)	98.4 (88.9,99.8)	93.1 (82.5,97.3)	87.8 (74.3,94.5)
Difference	-	8.5 (-8.5,25.5)	-3.3 (-9.6,3.0)	-8.2 (-16.3,-0.1)	-2.9 (-12.8,7.0)	-10.4 (-27.3,6.6)

χ^2 , chi-squared; df, degree of freedom; CI, confidence interval; TSI, Torres Strait Islanders; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage

^a stratified by matched pair

^b Cases include children and adolescents who received gastrostomy insertion at time of matching, whilst controls include individuals who had not yet received the procedure at time of matching. A rank preserving structural failure time model was used to generate counterfactual survival times for controls who switched gastrostomy status.

^c Absolute difference, comparing case group to control group

^d one-sided, 97.5% confidence interval

^e Data not presented for cell counts less than five cases.

Table 3. Hazard ratios (and 95% confidence intervals) for all-cause mortality, comparing children and adolescents with severe intellectual disability who received gastrostomy insertion with controls in the matched cohort ^a of 212 individuals.

	Hazard ratio (95% CI)
Unadjusted	2.53 (1.10,5.78)
Adjusted ^b	2.87 (1.13,7.26)
Subgroup analysis ^b	
Sex	
Male	4.22 (0.99,18.07)
Female	2.29 (0.77,6.80)
Relative difference	0.54 (0.10,3.06)
Indigenous status	
Non-Aboriginal/TSI	2.88 (1.10,7.54)
Aboriginal/TSI	3.19 (0.35,29.06)
Relative difference	1.11 (0.11,11.18)
Residential socioeconomic status (IRSAD)	
>20%	1.94 (0.79,4.82)
<=20%	IND ^c
Relative difference	IND ^c
Residential remoteness	
Major cities	2.39 (0.74,7.72)
Regional/remote	3.13 (0.82,11.96)
Relative difference	1.31 (0.22,7.93)
Infant weight	
>=2500 grams	3.61 (1.35,9.63)
<2500 grams	1.18 (0.11,12.38)
Relative difference	0.33 (0.03,4.11)

Age at first gastrostomy insertion

>=3 years	6.16 (1.18,32.23)
<3 years	1.87 (0.57,6.06)
Relative difference	0.30 (0.04,2.25)

CI, confidence interval; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage

^a adjusted for matched pair clustering

^b adjusted for unbalanced baseline and time-varying covariates including sex, residential socioeconomic status, residential remoteness, maternal age, infant weight, total of admissions for acute lower respiratory tract infection and average length of stay for acute lower respiratory tract infection in the 12 months prior to propensity score matching

^c No deaths in the control group hence the hazard ratio was indeterminable.

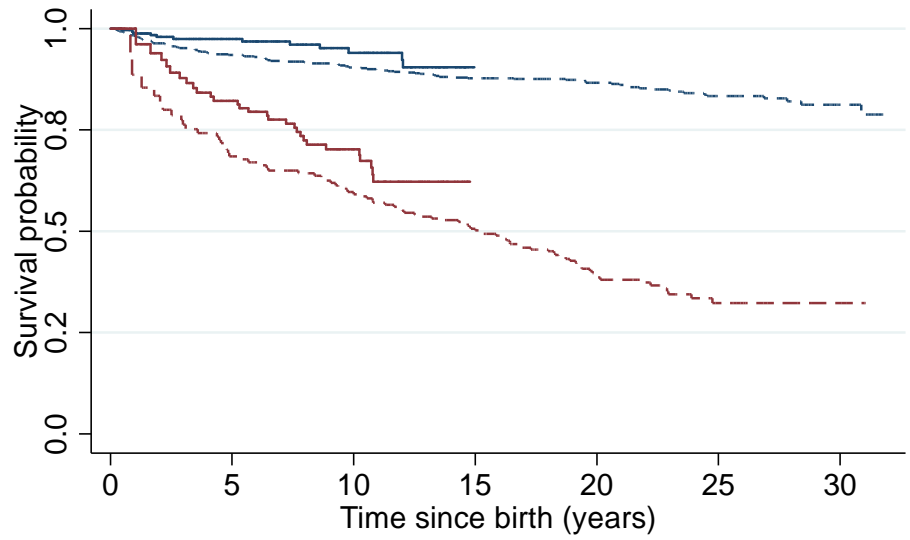
Figure legends

Figure 1: Survival functions by birth period and gastrostomy status (n=1,011)

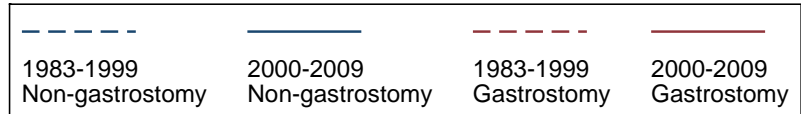
eFigure 1. Flow chart illustrating study inclusion and exclusion criteria

eFigure 2. Survival functions by gastrostomy status and selected subgroups (matched cohort n=212)

Figure 1. Survival functions by birth period and gastrostomy status (n=1,011)

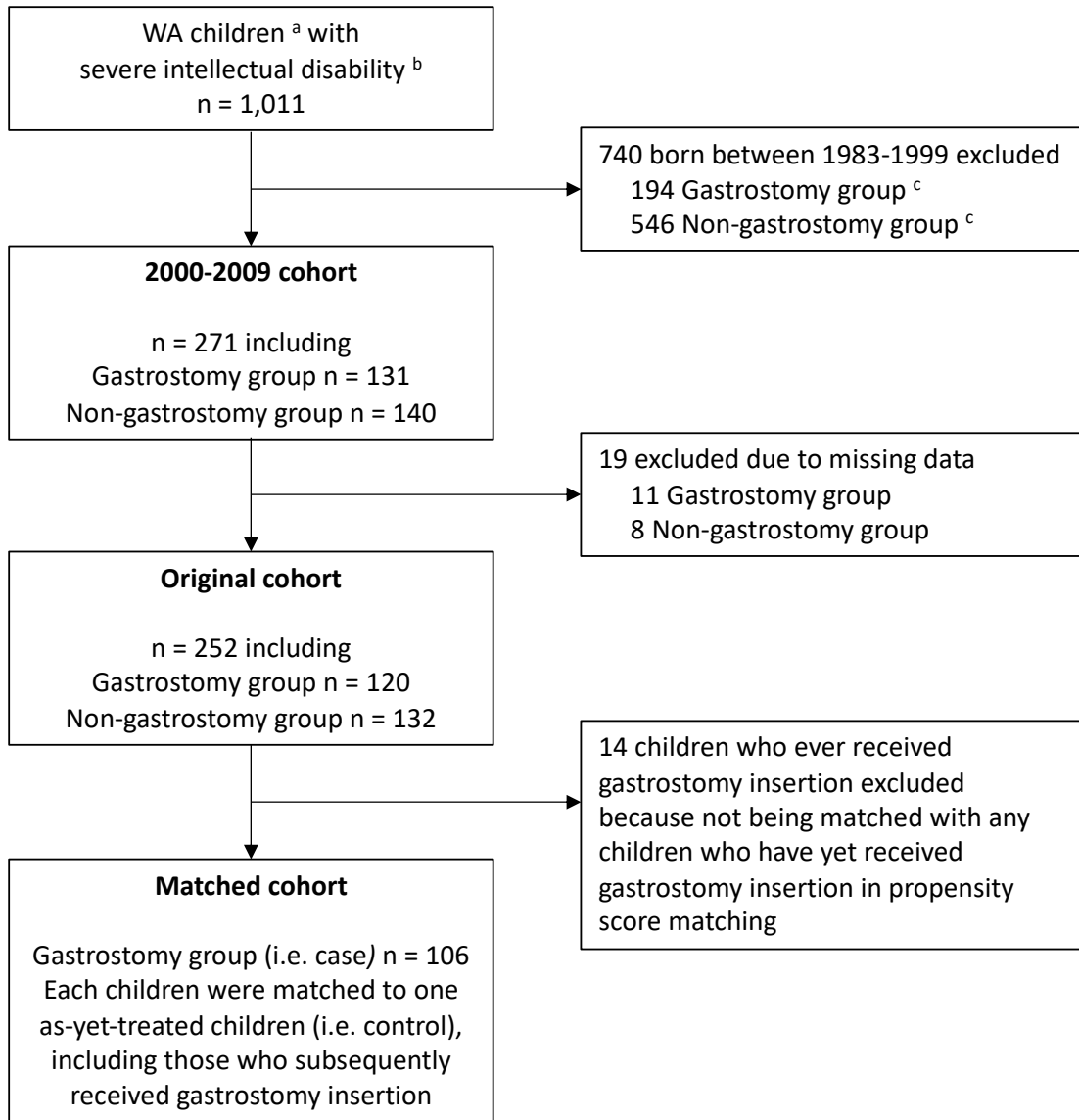


	No. at risk (deaths)												
1983-1999 non-gastrostomy	740	(45)	591	(19)	533	(15)	489	(5)	354	(11)	208	(3)	54
2000-2009 non-gastrostomy	271	(6)	163	(4)	77	(2)	0	(0)	0	(0)	0	(0)	0
1983-1999 gastrostomy	0	(18)	86	(14)	111	(20)	120	(25)	72	(8)	26	(0)	6
2000-2009 gastrostomy	0	(11)	91	(12)	53	(5)	0	(0)	0	(0)	0	(0)	0



SUPPLEMENTARY CONTENT

eFigure 1. Flow chart illustrating study inclusion and exclusion criteria



^a Born alive in WA between 1 January 1983 and 31 December 2009

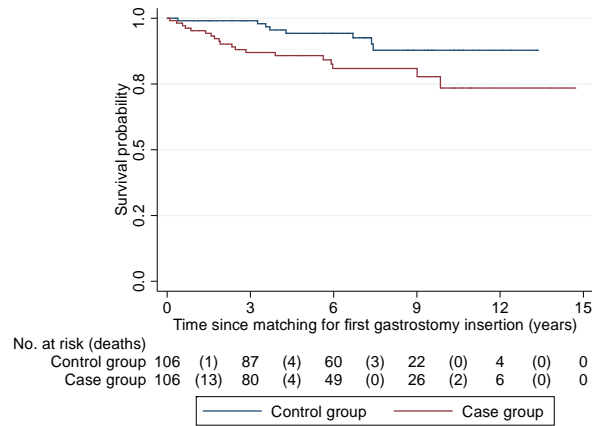
^b Cases with intellectual disability (ID) were defined as those Individuals diagnosed between 1 January 1983 and 31 December 2014, based on identification of ID from the Intellectual Disability Exploring Answers (IDEA) and the WA Register of Developmental Anomalies (WARDA). Individuals with severe ID includes individuals with IQ<40 and those with any level of ID who have had gastrostomy insertion prior to their 18th birthday.

^c Gastrostomy group included children who ever received gastrostomy insertion, whilst non-gastrostomy group include individuals who never received gastrostomy insertion

Note: Children were considered having had gastrostomy insertion if the procedure was performed during childhood (0-17 years)

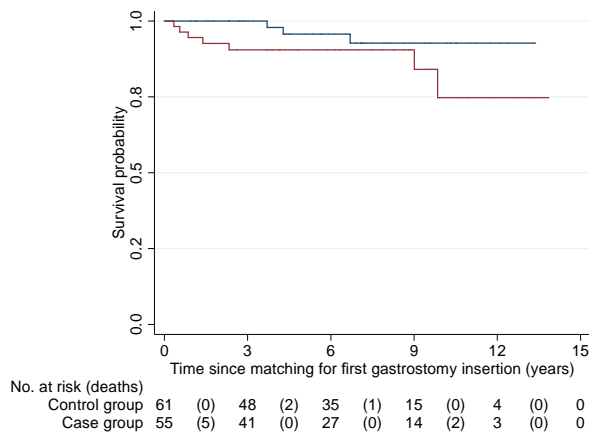
eFigure 2. Survival functions by gastrostomy status and selected subgroups (matched cohort n=212)

A. By gastrostomy status

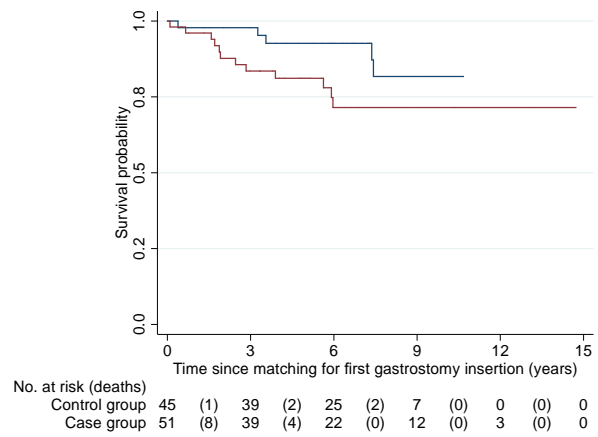


B. Child's sex

Male

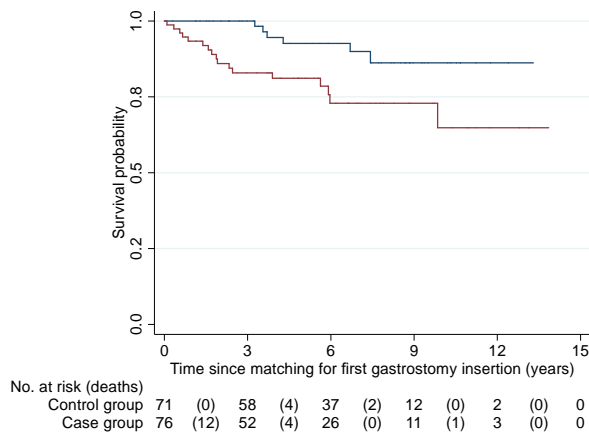


Female

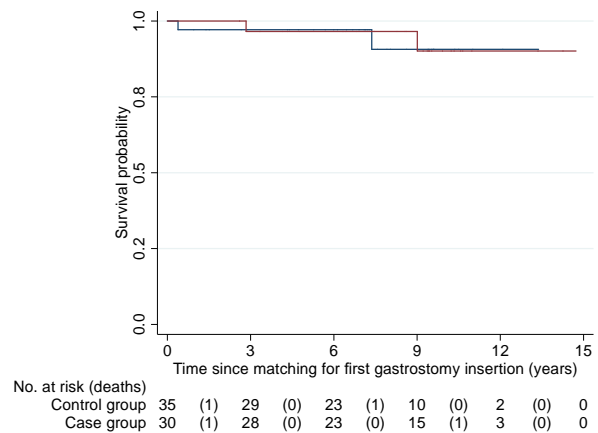


C. Infant weight at birth

>=2500 grams

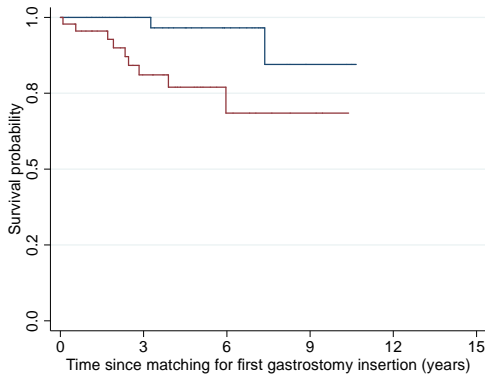


<2500 grams



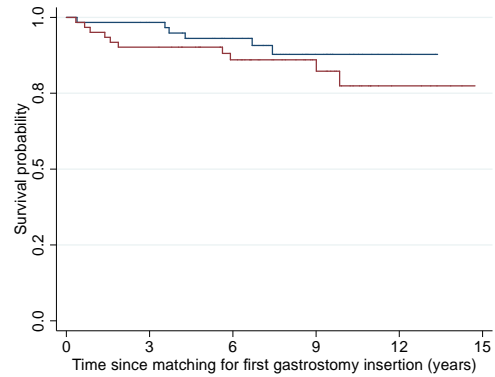
D. Age at first gastrostomy insertion

≥ 3 years



No. at risk (deaths)		0	3	6	9	12	15
Control group	45 (0)	30 (1)	17 (1)	3 (0)	0 (0)	0 (0)	0
Case group	45 (7)	25 (2)	8 (0)	3 (0)	0 (0)	0 (0)	0

< 3 years



No. at risk (deaths)		0	3	6	9	12	15
Control group	61 (1)	57 (3)	43 (2)	19 (0)	4 (0)	0	0
Case group	61 (6)	55 (2)	41 (0)	23 (2)	6 (0)	0	0

Note: Case group include children who received gastrostomy insertion at time of matching, whilst control group includes individuals who had not yet received the procedure at time of matching. A rank preserving structural failure time model was used to generate counterfactual survival times for controls who switched gastrostomy status.

eTable 1. ICD-9-CM and ICD-10-AM diagnostic codes for specific conditions.

Condition	ICD-9-CM	ICD-10-AM
Acute lower respiratory tract infection		
Influenza and pneumonia	480·x 481·x 482·x 483·x 484·x 485·x 486·x 487·x 488·x 514·x	J09·x J10·x J11·x J12·x J13·x J14·x J15·x J16·x J17·x J18·x
Acute bronchitis, acute bronchiolitis and unspecified acute lower respiratory tract infection	466·x 519·8	J20·x J21·x J22·x
Pneumonitis due to solids and liquids	507·x	J69·x
Epilepsy	345·x	G40·x G41·x

x: single or double-digit numbers

eTable 2. Baseline (birth) characteristics of WA-born (1983-2009) individuals with severe intellectual disability (n=1,011): 1983-1999, 2000-2009 and overall cohorts

Characteristic	1983-1999	2000-2009	Overall
n (%)	740 (73.2)	271 (26.8)	1,011 (100)
Sex, n (%)			
Male	454 (61.4)	151 (55.7)	605 (59.8)
Female	286 (38.7)	120 (44.3)	406 (40.2)
Indigenous status, n (%)			
Non-Aboriginal/TSI	657 (88.8)	228 (84.1)	885 (87.5)
Aboriginal/TSI	83 (11.2)	43 (15.9)	126 (12.5)
Residential socioeconomic status [IRSAD], n (%)			
<=20%	185 (25.0)	64 (23.6)	249 (24.6)
21-40%	141 (19.1)	61 (22.5)	202 (20.0)
41-60%	129 (17.4)	45 (16.6)	174 (17.2)
61-80%	114 (15.4)	53 (19.6)	167 (16.5)
>80%	79 (10.7)	30 (11.1)	100 (10.8)
Missing	92 (12.4)	18 (6.6)	110 (10.9)
Residential remoteness, n (%)			
Major cities	473 (63.9)	181 (66.8)	654 (64.7)
Inner regional	52 (7.0)	25 (9.2)	77 (7.6)
Outer regional	69 (9.3)	21 (7.8)	90 (8.9)
Remote	32 (4.3)	17 (6.3)	49 (4.8)
Very remote	21 (2.8)	9 (3.3)	30 (3.0)
Missing	93 (12.6)	18 (6.6)	111 (11.0)
Birth year, n (%)			
Mean (SD)	1991 (4.8)	2004 (2.8)	1994 (7.4)
Gestational age, n (%)			
<28 weeks	11 (1.5)	11 (4.1)	22 (2.2)
28-31 weeks	26 (3.5)	10 (3.7)	36 (3.6)
32-36 weeks	87 (11.8)	48 (17.7)	135 (13.3)
37-38 weeks	218 (29.5)	83 (30.6)	301 (29.8)
39-40 weeks	293 (39.6)	97 (35.8)	390 (38.6)
>=41 weeks	105 (14.2)	22 (8.1)	127 (12.6)
Mean (SD)	38.0 (3.0)	37.2 (3.7)	37.8 (3.2)
Infant weight, n (%)			
<2500 grams	158 (21.4)	71 (26.2)	229 (22.7)
>=2500 grams	582 (78.7)	200 (73.8)	782 (77.3)
Mean (SD)	3,007 (753)	2,858 (831)	2,968 (777)
Apgar score at 5 mins after birth, n (%)			
<7	81 (11.0)	28 (10.3)	109 (10.8)
>=7	655 (88.5)	242 (89.3)	897 (88.7)
Missing	4 (0.5)	1 (0.4)	5 (0.5)
Mean (SD)	8.3 (1.7)	8.4 (1.6)	8.3 (1.7)
Maternal age, n (%)			
<21 years	93 (12.6)	27 (10.0)	120 (11.9)
21-34 years	552 (74.6)	194 (71.6)	746 (73.8)
>=35 years	95 (12.8)	50 (18.5)	145 (14.3)
Mean (SD)	27.4 (6.0)	29.2 (6.0)	27.9 (6.0)

SD, standard deviation; N, number of individuals; TSI, Torres Strait Islanders; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage

eTable 3. Baseline (birth) characteristics of WA-born (2000-2009) children and adolescents with severe intellectual disability (n=271): excluded and included cohorts.

Characteristic	Excluded	Included
n (%)	19 (7.0)	252 (93.0)
Sex, n (%)		
Male	11 (57.9)	140 (55.6)
Female	8 (42.1)	112 (44.4)
Indigenous status, n (%)		
Non-Aboriginal/TSI	15 (79.0)	213 (84.5)
Aboriginal/TSI	<5 ^a	39 (15.5)
Residential socioeconomic status [IRSAD], n (%)		
<=20%	0	64 (25.4)
21-40%	0	61 (24.2)
41-60%	0	45 (17.9)
61-80%	<5 ^a	52 (20.6)
>80%	0	30 (11.9)
Missing	18 (94.7)	0
Residential remoteness, n (%)		
Major cities	<5 ^a	180 (71.4)
Inner regional	0	25 (9.9)
Outer regional	0	21 (8.3)
Remote	0	17 (6.8)
Very remote	0	9 (3.6)
Missing	18 (94.7)	0
Birth year		
Mean (SD)	2003 (3.2)	2004 (2.8)
Gestational age, n (%)		
<28 weeks	<5 ^a	10 (4.0)
28-31 weeks	0	10 (4.0)
32-36 weeks	<5 ^a	44 (17.5)
37-38 weeks	6 (31.6)	77 (30.6)
39-40 weeks	6 (31.6)	91 (36.1)
>=41 weeks	<5 ^a	20 (7.9)
Mean (SD)	37.4 (3.5)	37.2 (3.7)
Infant weight, n (%)		
<2500 grams	9 (47.4)	62 (24.6)
>=2500 grams	10 (52.6)	190 (75.4)
Mean (SD)	2,626 (837)	2,876 (831)
Apgar score at 5 mins after birth, n (%)		
<7	<5 ^a	27 (10.7)
>=7	17 (89.5)	225 (89.3)
Missing	<5 ^a	0
Mean (SD)	8.3 (1.3)	8.4 (1.6)
Maternal age, n (%)		
<21 years	0	27 (10.7)
21-34 years	14 (73.7)	180 (71.4)
>=35 years	5 (26.3)	45 (17.9)
Mean (SD)	31.6 (5.1)	29.0 (6.0)

SD, standard deviation; N, number of individuals; TSI, Torres Strait Islanders; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage

^a Data not presented for cell counts less than five cases.

eTable 4. Baseline (birth) characteristics of WA-born (2000-2009) children and adolescents with severe intellectual disability and ever received gastrostomy (n=120): matched and unmatched cohorts

Characteristic	Unmatched	Matched
n (%)	14 (11.7)	106 (88.3)
Sex, n (%)		
Male	7 (50.0)	55 (51.9)
Female	7 (50.0)	51 (48.1)
Indigenous status, n (%)		
Non-Aboriginal/TSI	9 (64.3)	85 (80.2)
Aboriginal/TSI	5 (35.7)	21 (19.8)
Residential socioeconomic status [IRSAD], n (%)		
<=20%	5 (35.7)	28 (26.4)
21-40%	<5 ^a	27 (25.5)
41-60%	<5 ^a	18 (17.0)
61-80%	<5 ^a	24 (22.6)
>80%	<5 ^a	9 (8.5)
Residential remoteness, n (%)		
Major cities	7 (50.0)	69 (65.1)
Inner regional	<5 ^a	12 (11.3)
Outer regional	<5 ^a	12 (11.3)
Remote	<5 ^a	7 (6.6)
Very remote	<5 ^a	6 (5.7)
Birth year		
Mean (SD)	2006 (2.5)	2004 (2.6)
Gestational age, n (%)		
<28 weeks	<5 ^a	6 (5.7)
28-31 weeks	<5 ^a	5 (4.7)
32-36 weeks	<5 ^a	23 (21.7)
37-38 weeks	0	30 (28.3)
39-40 weeks	5 (35.7)	34 (32.1)
>=41 weeks	0	8 (7.6)
Mean (SD)	32.4 (6.2)	36.6 (4.2)
Infant weight, n (%)		
<2500 grams	8 (57.1)	30 (28.3)
>=2500 grams	6 (42.9)	76 (71.7)
Mean (SD)	2,070 (1,304)	2,762 (893)
Apgar score at 5 mins after birth, n (%)		
<7	7 (50.0)	16 (15.1)
>=7	7 (50.0)	90 (84.9)
Mean (SD)	6.2 (2.5)	8.0 (1.9)
Maternal age, n (%)		
<21 years	<5 ^a	13 (12.3)
21-34 years	9 (64.3)	79 (74.5)
>=35 years	<5 ^a	14 (13.2)
Mean (SD)	26.7 (6.2)	28.2 (6.0)

SD, standard deviation; N, number of individuals; TSI, Torres Strait Islanders; IRSAD, The Index of Relative Socio-Economic Advantage and Disadvantage

^a Data not presented for cell counts less than five cases.