
INSIGHT

The Aboriginal Birth Cohort Study: When is a cohort study not a cohort design?

Dorothy E.M. MACKERRAS,^{1,2} Gurmeet R. SINGH¹ and Susan SAYERS¹

¹Menzies School of Health Research, Institute of Advanced Studies, Charles Darwin University, Darwin, Northern Territory, and ²Food Standards Australia New Zealand, Canberra, Australian Capital Territory, Australia

Abstract

Aims: The paper describes how a variety of different epidemiological study designs can be applied to data arising from a single prospective study.

Methods: An overview of the data collection phases of the Aboriginal Birth Cohort Study is given. We illustrate how different research questions that require different analytical designs can be asked of the data collected in the present study.

Results: With reference to five generic questions in health research, we showed how sixteen specific questions could be addressed in the Aboriginal Birth Cohort Study. These referred to a range of analytical designs.

Conclusion: Readers need to take care not to confuse the overall design of a study with the design of a specific analysis. When conducting systematic literature reviews, studies should be classified according to the analytical design used in the specific report included in the review and not according to the design of the overall project.

Key words: aboriginal, cohort, epidemiologic methods, systematic reviews, urban-rural.

Introduction

Epidemiology texts often describe various epidemiological designs as completely separate entities. This may suggest that only one design can be used in a particular research project. However, a large number of papers describing a range of results using different research designs may be generated from one research project. Papers from cohort studies, such as the Aboriginal Birth Cohort Study (ABCS),^{1–3} might describe results that are clearly cross-sectional rather than longitudinal analyses of the data.⁴ Guidelines, including nutrition and dietary guidelines produced by organisations such as the National Health and Medical Research Council (NHMRC)⁵ and the World Health Organisation (WHO)⁶ are now based on systematic literature reviews in which studies are classified according to their design. For example, the NHMRC's criteria class randomised controlled trials, cohort,

case-control and cross-sectional designs as different levels of evidence.^{7,8} Guidelines and recommendations based primarily on well-conducted studies with designs of higher classification are more trusted to guide practice than those that are based on studies with lower design classifications.⁸ Consequently, it is important to identify the analytical design of a study correctly. This paper describes how a variety of different epidemiological study designs can be applied to data arising from a single prospective study.

Methods

In this paper, we describe how a project conducted as a cohort overall can provide data to answer a number of different questions using a range of analytical designs. An overview of the data collection phases of the ABCS is given. We illustrate how different research questions that require different analytical designs can be asked of the data collected in the present study. We discuss the implications of this for readers and conductors of systematic reviews.

Results and discussion**Overview of the ABCS: A case study***Wave 1—Selection and recruitment*

A total of 686 singleton newborns of women recorded as Aboriginal in the Delivery Suite Register in the

D.E.M. Mackerras, PhD, Adjunct Principal Research Fellow, Chief Public Health Nutrition Advisor

G.R. Singh, PhD, Senior Research Fellow

S. Sayers, PhD, Principal Research Fellow

Correspondence: D.E.M. Mackerras, Food Standards Australia New Zealand, PO Box 7186, Canberra BC ACT 2610, Australia. Email: dorothy.mackerras@foodstandards.gov.au

Present address: D. Mackerras, Food Standards Australia New Zealand, 55 Blackall St, Barton, ACT 2606, Australia.

Accepted June 2010

Table 1 Comparison of selected peri-natal characteristics in infants who were routine deliveries from the Darwin Health Region and who were referred prior to birth,¹ Aboriginal Birth Cohort Study

	Darwin Health Region subset (n = 570)	High-risk referred subset (n = 116)	Total cohort (n = 686)
Mean birthweight, g (SD)	3098 (601)	2639 (830)	3020 (668)
Low birthweight, %	13	40	18
Fetal growth restriction, %	25	41	24
Preterm, %	7	26	10

Royal Darwin Hospital (the Hospital) between January 1987 and March 1990 were recruited into the ABCS. Relevant peri-natal data were obtained by a combination of methods, namely examination of the infant to determine gestational age by the Dubowitz score, maternal interview about topics such as smoking and abstraction of medical records.¹

The Hospital was the 'local' (and only) hospital for the Darwin Health Region (the Region) and was also the major tertiary referral centre for a much larger region of northern Australia. The two populations served by the Hospital are reflected in the ABCS participants. Infants from the Region were 83% (570/686) of the total cohort, and 54% (570/1053) of the total birth of the Region. The remainder were 62% (116/185) of referred babies born during the recruitment period. There was no difference in the sex ratio and birthweight frequencies showed minimal differences at all ranges of birthweights between those recruited and not recruited.² Infants recruited from the Region are likely to be representative of all babies born in the Region in that non-recruitment was related to the paediatrician's absence from Darwin at the time they were born. The other participants were high-risk *in utero* referrals from the larger area and would not be representative of all babies in the population from which they were drawn.

Distinguishing between the two types of participants is important for data analysis. Estimates of the prevalence or incidence of health characteristics are more useful if they are generalisable to a definable wider population rather than simply describing the population actually studied. Therefore, we include only those living in the Region (Region subset) when describing the prevalence of diseases and behaviours. Table 1 shows the cross-sectional data for the two groups at birth.¹ Using the total cohort population, rather than the Region subset, would lead to a biased estimate of these characteristics for the Region. Adjusting for one factor, such as low birthweight, would not remove confounding by differences in other factors, such as fetal growth restriction, birth length or other factors. However, all subjects with data can be included when investigating cause–effect relationships and methodological questions because the total study population is a fixed cohort. For example, an analysis of Wave 1 data confirmed that low maternal body size and smoking habit are risk factors for low birthweight in this population, as they are for the general population.⁹

Wave 2—Follow up at mean age 11.4 years

Between December 1998 and March 2001, 572 (83.4%) were followed up and an additional 18 (2.6%) had died.^{1,4} Measurements included anthropometry, blood pressure, kidney ultrasound and respiratory function. Blood and urine specimens were analysed for biomarkers of diabetes (glucose and insulin levels), cardiovascular disease (various lipids) and kidney function, as well as folate levels and a full blood count.^{1,4} A brief questionnaire about social circumstances, such as the number of people living at home, was administered to the child or, occasionally, the carer.^{1,4} A cross-sectional analysis of results from the Region subset in Wave 2 showed that although community-dwelling children were shorter and lighter than urban-dwelling children (as was expected), blood pressure and lipid levels were not consistently lower in community children than urban children.⁴ The prevalence of anaemia was higher in community-dwelling children than urban children but there was no difference in red cell folate levels.⁴

Wave 3—Follow up at mean age 18.4 years

Between December 2006 and January 2008, 591 were traced but only 469 (68.4%) were examined owing to barriers such as isolation and inclement weather. Another 27 (3.9%) had died since birth.³ Many of the parameters measured in Wave 2 were repeated in Wave 3.³ In addition, we administered a 30-item emotional wellbeing questionnaire, a computer-based card game to test reaction time, additional cardiovascular parameters such as carotid intima-media thickness and pulse wave variability, a dental examination and analysed the urine samples for iodine, cotinine and renal health markers.³ The present study focuses on collecting objective measures of health and nutritional status, such as birthweight, height and blood biochemistry in all Waves because of the limitations of assessing dietary intake in this population.¹⁰

Future data collection

Funding permitting, Wave 4 will probably occur in 2012, 25 years after recruitment, and is likely to be similar to Wave 3. Further waves of data collection in adulthood will probably be more widely spaced and interview data will be supplemented with medical record data (with consent). As chronic diseases such as diabetes, heart disease and renal

failure start to develop, it will be possible to perform the more customary analyses for a cohort study and examine factors that are related to disease incidence.

Ethics

Each wave of the study was approved by the Top End Ethics Committee (which has had several name changes since the study started). Its Aboriginal Subcommittee has veto powers. For Wave 3, the Committee agreed that participants were mature minors and could give informed consent for themselves. However, parents of those aged below 18 years were also informed of the study.

Epidemiological study designs and the ABCS

The five generic questions in health research

Despite the many research questions that can be asked in health research, most can be classified into one of five generic types (Box 1). Table 2 shows examples of the possible research questions that could be asked of the data from the ABCS, their generic type^{7,8} and the range of analytical designs that might be used to examine these questions.

Box 1 The five generic questions in health research^{7,8}

- Occurrence—describes the incidence or prevalence of a disease, condition or behaviour
- Aetiology—asks the question ‘does X cause Y?’
- Intervention—asks the question ‘does treatment X prevent or cure Y?’
- Prognosis—describes the natural history of a condition
- Screening accuracy—can be divided into two subcomponents
 - Comparison of a new method of measurement against a standard method
 - Examination of whether introducing the new test into a population reduces the incidence of disease

Data at the individual level

The cohort design can be described as a study in which people without the disease/outcome are selected based on being exposed, or not, to a putative causative agent. All subjects are followed up to compare the incidence of the disease/outcome in the exposed *versus* the unexposed groups. This description implies that the investigator actively seeks out groups with and without the exposure. This is true of some studies—for example, investigators might deliberately identify groups with different types of occupational exposures. In other studies such as the ABCS,

a group of people from a common source are collected and exposure groupings are created later depending on the study question. Because each baby’s weight was measured in the ABCS, participants can be divided into low-birthweight (‘exposed’) and not-low-birthweight (‘unexposed’) groups and differences in various outcomes between the two groups can then be examined. For example, we have examined whether differences exist between the birthweight groups in growth¹¹ respiratory function¹⁴ and biochemical markers related to cardiovascular disease¹⁵ measured at Wave 2 after adjusting for suitable confounders. The advantage of not selecting participants based on a single exposure is that multiple exposures can be examined. For example, we are not limited to examining birthweight; maternal smoking or diabetes during pregnancy could be examined as exposures for future disease. The ‘exposures’ do not have to be measured in the first wave of data collection. For example, the relationship between attained adult height and future mortality could be examined by using height measured at Wave 3 or 4 and then following up from that time.

Although cohort designs are usually carried out to examine the aetiology of an outcome, they can also be used as descriptive studies. An inception cohort is the best design for studying prognosis.^{7,8} A group of people with a condition or exposure who are either not diseased or at a defined point in their condition are followed to determine the natural history of the condition from that point;⁶ there is no comparison with another group. For example, when examining the question ‘what is the incidence of diabetes following diagnosis of impaired glucose intolerance?’, ‘inception’ is the diagnosis of impaired glucose tolerance. The participants in the ABCS were among the first in Australia to receive the Hepatitis B vaccine at birth and presence of antibodies to this vaccination was tested at Wave 3. Consequently, the inception cohort to examine the longevity of the protective antibodies includes only those who were vaccinated at birth.

A case–control design is often described as one in which subjects are selected based on the presence or absence of disease. Then the history of exposure is measured, usually by questionnaire, although medical, occupational or other records might also be available. The purpose of the control (non-diseased) group is to describe the distribution of the exposure in the population from which the cases arose. Case–control studies are often carried out by collecting cases that occur in a defined geographic area and then contrasting these with a random sample derived from the same area as the control group. The case–control design can be incorporated into a project originally set up as a cohort study because cases occur over time and a randomly selected subset of those who do not become a case by a designated end date then become the controls. In the latter approach (usually referred to as a nested case–control or a case–cohort study) one would not use the word ‘select’ about the collection of the cases. Because information about exposures is ascertained without the potential bias of knowing the disease outcomes, a nested case–control/case–cohort study can be

Table 2 Examples of the different types of questions that have been and could be asked as a cohort study progresses, and the design of each question type

Wave (mean age)	Examples of data collected in this Wave	Examples of questions that can be examined using data collected at this Wave and previous Waves ^(a)	Analytical design	Generic question type ^{7,8}
1 (0 year)	Birthweight & length Maternal recall of smoking during pregnancy	What is the prevalence of low birthweight? ¹	Cross-sectional (Region subset) ^(b)	Occurrence
		Is low birthweight associated with maternal smoking habit during pregnancy? ⁹	Case-control	Aetiology
2 (11 years)	Height, weight, skinfolds Waist circumference Blood pressure, lipids Full blood count Kidney ultrasound Location of residence Cause of death in decedents	What is the mean height, weight and height- and weight-for-age z-score of children at mean age 11? ⁴	Cross-sectional (Region subset)	Occurrence
		Were low-birthweight infants more likely to be shorter and lighter at age 11 than non-low-birthweight infants? ¹¹	Cohort	Aetiology
		Is there a difference in mean height, weight and blood pressure between children who live in urban and remote locations? ⁴	Cross-sectional (Region subset)	Occurrence
		Is the prevalence of anaemia at age 11 different if the WHO and US cut-offs for haemoglobin are used? ¹²	Cross-sectional	Methodological comparison
3 (18 years)	Height, weight Waist circumference Blood pressure, lipids Urinary iodine concentration Urinary cotinine CIMT Smoking habit Hepatitis B virus antibody Serum folate Emotional wellbeing Cause of death in decedents	What is the median urinary iodine concentration at mean age 18? ¹³	Cross-sectional (Region subset)	Occurrence
		Were low-birthweight infants more likely to have higher CIMT at age 18 than non-low-birthweight infants?	Cohort	Aetiology
		Do children who had lower blood pressure at age 11 have higher CIMT at age 18 than children who had higher blood pressure at age 11?	Cohort	Aetiology
		Is self-reported smoking a valid indicator of smoking habit, using urinary cotinine as the gold standard?	Cross-sectional	Methodological comparison
		What is the long-term persistence of the hepatitis B virus antibody in those who received the hepatitis B vaccination at birth?	Inception cohort	Prognosis
4 (25 years)	Height, weight, biochemistry etc Urinary iodine concentration Serum folate Cause of death in decedents	What is the median urinary iodine concentration of the population at mean age 25?	Cross-sectional (Region subset)	Occurrence
		Has median urinary iodine concentration and serum folate changed since Wave 3? (Iodine and folic acid fortification introduced between Waves 3 and 4).	Pre-post trend with no control group (Region subset)	Intervention (evaluation)
5 (X years)	Weight, biochemistry etc Cause of death in decedents Diagnosis of various diseases	What is the incidence of diabetes of Region residents to age X?	Cohort (Region subset)	Occurrence
		Were low-birthweight infants more likely to die of heart disease by age X than non-low-birthweight infants?	Cohort	Aetiology
		Is waist circumference measured at age 18 years a better predictor of death by age X than body mass index measured at age 18 years?	Cohort	Methodological comparison

^(a) Appropriate adjustment for confounders assumed in all analyses.^(b) Subset living in the Darwin Health Region.

CIMT, carotid intima-media thickness.

graded as a cohort study, not a case-control study, and provides the same grade of evidence as a cohort study in systematic reviews.

Why would one analyse a project set up as a cohort as a case-control design? There are two reasons. One reason is when there are known losses from the baseline. In the ABCS, liveborn singleton infants, not pregnant women, were recruited. If a research question concerns events before birth (e.g. is maternal smoking related to birthweight?⁹), then the ABCS does not have a complete set of pregnancy outcomes (twins, miscarriages and stillbirths are missing) and so a case-control design is used. (The cohort design to examine a maternal smoking-birthweight relationship would require starting with women who became pregnant and following all of them to ascertain pregnancy outcome). The second reason for doing a nested case-control design is when it is expensive to assess the majority who have not developed the disease, for example, if frozen blood must be analysed to assess exposure status. In this case, a random sample of the non-diseased is taken but the data must be analysed as a case-control design because the prevalence of disease in the whole cohort has been altered.

A cross-sectional design with a representative sample of a definable wider population is the best design for describing the prevalence of diseases and risk factors.⁷ Australian examples of this are the 1995 National Nutrition Survey¹⁶ and the 2007–2008 National Health Survey.¹⁷ Surveys are often analysed according to demographic subgroups such as men *versus* women, children of various ages or area of residence. Cross-sectional studies can be carried out in smaller settings but careful thought is needed to determine exactly who the sample represents. If it is a haphazard sample, then the results might not be generalisable beyond those studied. Although the ABCS was not specifically sampled to be representative, we think that the subgroup who live in the Region are likely to be representative of the Indigenous population of the Region, although this may become less true over time as the population of the Region changes. Indigenous people commonly attend clinics in their preschool years and in later adult life when chronic disease starts to occur. Women also attend for contraception and obstetric care in their teenage years and young adulthood. As there is a relative lack of information about chronic disease and other risk factors in Aboriginal primary and high-school aged children and young men, the prevalence data from Wave 2 and 3 provide a useful insight into these periods of life in these groups in the Region. We have previously compared the prevalence of various factors related to chronic disease in the urban and remote-dwelling participants in the Region at Wave 2⁴ and have described the median urinary iodine concentration (MUI) of those living in the Region at Wave 3.¹³ A cross-sectional analysis that examines an aetiological association would not have to be representative of an external population. However, this type of analysis is a poor design for assessing a cause-effect question^{7,8} because it is often not clear which of the two factors occurred first and therefore should be called the cause.

Data at the population level

Sometimes, data might have been collected on individuals but are reported at the group or population level as percentages or rates, for example, mortality rates. When only aggregate data are available or there is no information about each individual's behaviour, information cannot be linked at the individual level. The ecological design examines linkages at the group level. For an aetiological question, this is generally less strong than individual level data analysis because it compares summary data described at the population level to make inferences about aetiology at the individual level. A commonly seen example of an ecological analysis is the scatterplot of average dietary fat intake and breast cancer incidence across different countries.

Another type of ecological design is the pre-post design. Mandatory fortification of bread with iodine, by replacing salt with iodised salt, occurred in Australia in 2009.¹⁸ We intend to measure urinary iodine concentration again in the ABC participants in Wave 4. At first glance, it might seem that a cohort analysis could be done; however, virtually all participants would be 'exposed' to the intervention to some extent. It is more suitable to compare the MUI of the population in Wave 3 (pre) and Wave 4 (post). Although the description of MUI at each of Waves 3 and 4 is a cross-sectional design with data collected on individuals, the comparison of the two medians is an ecological pre-post study with no control group. The assessment of MUI in this instance is based on prior work that has indicated what change in iodine status this intervention (i.e. a particular level of food fortification) should achieve. The exact question posed is 'has this intervention worked in this population group as it is expected to?' This type of question is often referred to as evaluation rather than 'intervention'. Drawbacks of ecological designs are that it is often not possible to adjust for confounding factors beyond age and sex, and other changes, such as screening practices, may affect the results.

Methodological studies

Another type of analysis examines the methods used in research, for example, the repeatability of a food frequency questionnaire or its validity compared with another dietary intake assessment method. This commonly requires either a cross-sectional design or a cohort design depending on the exact question posed.

A cross-sectional design is used when determining whether two different ways of measuring something give the same result. For example, do two different observers measure the same height on survey participants? Alternatively, the same data could be categorised in different ways to examine the performance of different indicators derived from the information. We have shown that the prevalence of anaemia in the Wave 2 data is different if the WHO or US cutpoints are used and these lead to different age-sex groups being identified for intervention.¹²

A cohort design is used when comparing the ability of different methods to predict future disease. For example, there is debate about what body adiposity indicators are

best. The question is 'best for what?' If 'a better measure of body fat now', then methods such as body mass index and waist circumference should be compared with a gold-standard reference measure, such as dual energy X-ray absorptiometry, performed at the same time (cross-sectionally). However, if 'better predictor of future diabetes incidence' is meant, then a cohort design must be used, body mass index and waist circumference measured at baseline and diabetes incidence collected. It will be some time before we can contribute our results to this debate!

Conclusion

Participants in modern cohort studies are followed for many years and data are often collected in repeated waves. This allows a range of different questions to be answered during the progress of the study, and answering these questions may require different designs or substudies. Using different designs allows investigators to conduct useful analysis during the course of a long-term study such as the ABCS. Different questions can also be addressed at different times; for example, the cross-sectional descriptions can be done immediately whereas the longitudinal element may take decades.

The quality and usefulness of each analysis from a larger study must be assessed in relation to the specific question that it addresses. When using NHMRC^{7,8} or similar criteria, an analysis should be classified according to the design used and not according to the design of the overall study. A single paper might even report two analyses, each using a different design, from the same study and in this case, different classifications would be given to each analysis. The exact design used in a paper may not always be obvious from the title or abstract of the paper, especially if the overall project title is used. This is particularly important when scanning large numbers of abstracts to select a particular type of design into a systematic review. The design of the specific analysis should be described when summarising the result for a specific literature review, although the name of the overall study is useful for identification; for example: 'the cross-sectional median serum folate in 18.4-year-old Aboriginal teenagers participating in the ABCS and living in the former Darwin Health Region in 2007–2008 was 12.6 nmol/L.

Large research projects can answer a range of questions using a range of study designs. It is important to examine the methods of each reported analysis carefully and to distinguish the overall design of the research project from the design of the analysis being described in a specific report.

References

- Sayers SM, Mackerras D, Singh G, Bucens I, Flynn K, Reid A. An Australian Aboriginal birth cohort: a unique resource for a life course study of an Indigenous population. A study protocol. *BMC Int Health Hum Rights* 2003 (Mar 6); **3** (1): 1.
- Singh GR, Sayers SM, Mackerras DEM. The Australian Aboriginal Birth Cohort Study: the lifecourse and much more. *Aust Epidemiol* 2009; **16** (3): 14–16.
- Sayers S, Singh G, Mackerras D *et al.* Australian Aboriginal Birth Cohort study: follow-up processes at 20 years. *BMC Int Health Hum Rights* 2009 (Sep 24); **9**: 23.
- Mackerras DE, Reid A, Sayers SM, Singh GR, Bucens IK, Flynn KA. Growth and morbidity in children in the Aboriginal Birth Cohort Study: the urban-remote differential. *Med J Aust* 2003; **178**: 56–60.
- NHMRC. *How NHMRC develops its guidelines* (Available from: <http://www.nhmrc.gov.au/guidelines/how.htm>, accessed 29 April 2010).
- WHO. *First Meeting of the WHO Nutrition Guidance Expert Advisory Group (NUGAG)*. (Available from: http://www.who.int/nutrition/topics/NUGAG_subgroup_micronutrient_dietandhealth/en/index.html, accessed 29 April 2010).
- NHMRC. *How to review the evidence: Systematic identification and review of the scientific literature*. Endorsed November 1999. (Available from: http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/cp65.pdf, accessed 29 April 2010).
- NHMRC. *Additional levels of evidence and grades for recommendation for developers of guidelines*. 2009 (Available from: http://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/Stage%20%20Consultation%20Levels%20and%20Grades.pdf, accessed 29 April 2010).
- Sayers S, Powers J. Risk factors for Aboriginal low birthweight, intrauterine growth retardation and preterm birth in the Darwin Health Region. *Aust N Z J Public Health* 1997; **21**: 524–30.
- Lee AJ, Smith A, Bryce S, O'Dea K, Rutishauser IH, Mathews JD. Measuring dietary intake in remote Australian Aboriginal communities. *Ecol Food Nutr* 1995; **34**: 19–31.
- Sayers S, Mackerras D, Halpin S, Singh G. Growth outcomes for Australian Aboriginal children aged 11 years who were born with intrauterine growth retardation at term gestation. *Paediatr Perinat Epidemiol* 2007; **21**: 411–17.
- Mackerras D, Singh G. The prevalence of anaemia depends on the definition: an example from the Aboriginal Birth Cohort Study. *Eur J Clin Nutr* 2007; **61**: 135–9.
- Mackerras D, Singh G, Eastman CJ. Iodine status of Aboriginal teenagers in the Top End. *Asia Pac J Clin Nutr* 2008; **17**: S91.
- Bucens IK, Reid A, Sayers SM. Risk factors for reduced lung function in Australian Aboriginal children. *J Paediatr Child Health* 2006; **42**: 452–7.
- Sayers S, Singh G, Mott S, McDonnell J, Hoy W. Relationships between birthweight and biomarkers of chronic disease in childhood: Aboriginal Birth Cohort Study 1987–2001. *Paediatr Perinat Epidemiol* 2009; **23**: 548–56.
- Australian Bureau of Statistics. *4805.0—National Nutrition Survey. Nutrient Intakes and Physical Measurements Australia 1995*. Canberra: Australian Bureau of Statistics, 1998.
- Australian Bureau of Statistics. *4364.0—National Health Survey: Summary of Results, 2007–2008 (Reissue)*. Australian Bureau of Statistics, 28th August, 2009. (Available from: <http://www.abs.gov.au/ausstats/abs@.nsf/mf/4364.0/>, accessed 2 November 2009).
- Food Standards Australia New Zealand. *Approval Report. Proposal P1003. Mandatory iodine fortification for Australia*. 6th August 2008. (Available from: <http://www.foodstandards.gov.au/foodstandards/proposals/proposalp1003mandato3882.cfm>, accessed 6 November 2009).