

Cohort Profile: The Mater-University of Queensland Study of Pregnancy (MUSP)

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How did the study come about?

At the initiative of three hospital-based obstetricians one of the authors (JMN) and another sociologist attended a 1978 meeting to explore the potential for collaborative research. No specific project was proposed by the obstetricians. Two of the obstetricians had been trained in Scotland; one in Aberdeen where he had had some familiarity with the work of obstetrician Dugald Baird and sociologist Raymond Illsely.

The obstetricians argued for an agenda which was clinically oriented. The two sociologists were more focussed on understanding how some social constructs (e.g. social class) might be relevant to explaining health outcomes. The initial year of the study was characterised by frequent (at least weekly) meetings at which the aims and substance of the proposed study were debated vigorously. As an initial decision the team focused on factors associated with adverse pregnancy outcomes. The first major project was to be a 3-5 year longitudinal study of pregnant women which would include a 6-month child post-natal follow-up as the main outcome of interest.

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Funding

After a period of about one year, which included repeated piloting of questionnaires and methods of data collection, an application was submitted to the National Health and Medical Research Council (NHMRC). It was successful. This grant was for a three-year study of women from their first obstetrical clinic visit, with follow-ups 3-5 days and 6 months after the birth. While this initial grant was generous by Australian standards, the data collection took over four years and was also supported by the Mater Hospital and the University of Queensland's Department of Obstetrics and Gynaecology. Separate NHMRC grants were subsequently obtained on three additional occasions – all for three-year funding cycles. There have also been two separate NIH grants to fund two intensive follow-ups of a sub-sample characterised by high rates of maternal depression.

NHMRC funding has been obtained for:

- 1981-83 (recruitment and initial follow-ups),
- 1986-88 (5-year follow-up)
- 1995-97 (14-year follow-up)
- 2002-04 (21-year follow-up)

At all phases of data collection data have been obtained not only in relation to the fetus/child/young adult but also the biological mother of the child. A significant proportion of the principal investigators' time has been allocated to seeking grants from a variety of agencies to continue the study. Funding has also been obtained from a variety of sources (eg. Queensland Health, Criminology Research Council). The project has also been successful in obtaining a share of an NHMRC Capacity Grant (to develop the research methodology and statistical skills specific to longitudinal studies), as well as a post-doctoral fellowship. In addition some five PhD candidates have successfully obtained their degrees, and a further five are currently completing their doctoral dissertations.

While one might reasonably view the continuing need to obtain funding as a time consuming diversion from the preparation of research papers, it has had the effect of forcing the principal investigators to reassess the aims, objectives and methods that MUSP adopts. Every MUSP

NHMRC grant has had to compete in an environment where only about 20-25% of applications are successful.

What does MUSP cover and how has it changed?

Three of the original principal investigators, John Morrison, J. Doug Keeping and Allan Chang, were university-based obstetricians providing medical services at the Mater-Misericordiae Hospital in Brisbane. The Mater has a large obstetrics unit, accounting for about 50% of the births in Brisbane, the capital city of the state of Queensland. Of about 6000 deliveries (1981-1983) a year at this large tertiary facility, about 3500 were of public patients while the remainder were patients of private obstetricians. The Mater Hospital is owned and managed by a Catholic order, the Sisters of Mercy. Despite this, the demographic characteristics of patients attending the Mater Hospital are broadly similar to those of the relevant Brisbane population¹. It is the only major obstetrical unit on the south side of the Brisbane River.

Recruitment began in January 2001 with a sampling frame that involved all consecutive pregnant women attending a booking in clinic, usually in the first trimester of pregnancy. Emergency transfers and admissions referred from other hospitals were excluded from the sampling frame. In total 8556 consecutive public patients were approached at their first obstetrical clinic visit and invited to participate in the study. Some 8458 agreed to complete the recruitment questionnaire. The MUSP is unusual insofar as detailed psychological, social, pregnancy outcome, and health data is available for almost 99% of the sample initially selected¹.

Of the 8458 women who agreed to participate in the study, 7631 mothers gave birth to a live singleton baby at the study hospital, of whom 7223 constitute our birth cohort (Table 1). The major losses were women who had their child at another hospital (usually due to change of residence) and miscarriages. Also, some 59 women had multiple births. The latter are followed-up but excluded from most analyses. Further, of the 7223 successful pregnancies in the cohort, some 516 women gave birth to a second child, during the three years pregnant women were recruited. These women were asked to complete a separate recruitment questionnaire for each pregnancy.

The resulting sample appears to be representative of public obstetrical patients but differs from private obstetrical patients in a number of characteristics. Public patients are predominantly from middle to lower SES groups (lower family income and education levels), they are much more likely to be tobacco smokers, to be unmarried at the time they were recruited and more frequently exhibited a range of risk characteristics generally associated with poorer health outcomes. Initial attempts to recruit a sub-sample of private patients were of limited success and a decision was therefore made to obtain as complete a sample of public patients as possible.

Table 1: Cohort outcomes (8556 women approached)

Lost to Sample	Reasons for Loss	Remaining in Cohort
98	Refusals at first approach	8458
710	No delivery at study hospital	7748
59	Multiple births	7689
58	Deaths during delivery	7631
312	Lost at post-natal stage	7319
41	Deaths post-delivery (hospital)	7278
55	Adopted out	7223

How often have participants been followed-up?

To date there have been seven stages of data collection (Table 2) with a number of the stages involving the collection of data from multiple sources. In practice the MUSP comprises two parallel cohorts – one addressing the health and development of children from the pre-natal period until 21 years of age; the other of pregnant women followed until middle-age. There is a unique opportunity here to relate changes over the mother's life course to the developmental health of her child.

What has been measured?

In the early stages of the study obstetricians, sociologists and a statistician developed the main research questions, and the measurements relating to these. As the children matured, the interest of the obstetricians waned and a paediatrician (WB) and a pediatric psychiatrist (MO) joined the team as principal investigators. The MUSP is characterised by a diversity of measurements, but with a persistent interest in the health, growth, development, learning and behaviour of children and young adults. These reflect the disciplinary interests and the varied backgrounds of the principal investigators. There are over 2000 items of data in the MUSP

spanning many topic areas (see Table 2). In general the MUSP has used short, multiple-item scales with good reliability and adequate validity. In some instances scales have been reduced in length (e.g. The Achenbach Child Behaviour Check List² was shortened to 31 items at the five-year follow-up) to enable more topic areas to be addressed at each phase of data collection. Where practicable the shortened versions of a scale have been compared against the results obtained from the complete set of items, for a small sample.

Another important element of MUSP has been the use of repeated measurements, and readministration of the same items, over an extended period of time. For example, the Delusions-Symptoms-States-Inventory³ has been completed by mothers at every stage they were administered a questionnaire. Similarly it is possible to track patterns of substance use by both the mother and adolescent/young adult over an extensive part of the life course.

Attrition in the MUSP

The study has raised questions about how one defines and characterizes a cohort and its losses to follow-up, or attrition. This has led to the development of a variety of strategies for examining and statistically adjusting for attrition.

Of the 8556 women invited to participate in the study, 8458 accepted the invitation and 7223 gave birth to a live, singleton baby at the study hospital. Thus, for the analysis of later outcomes, 7223 constitutes the baseline sample and attrition estimation uses this denominator. At the 6-month follow-up, 6720 women (93%) responded to the questionnaire. Numbers at the 5-year follow-up varied by proforma used: 5259 mothers (73%) provided data for their child, 5234 mothers (72%) provided data on their own health, but only 4010 (56%) child physical assessments were completed, due largely to resource constraints. A similar pattern is evident at the 14-year follow-up with 5185 mothers (72%) and 5172 children (72%) responding. Child assessments were only completed for 3799 children (53%). At the 21-year follow-up (being finalized) about 4000 mothers and 3800 children have provided useable data.

Table 2: Content of Measurements

<i>Stage</i>	<i>Socio-demographics</i>	<i>Lifestyle</i>	<i>Mental health well being</i>	<i>Physical health and anthropometry</i>
1 (1981-83) First clinic visit	Age at visit, marital status, income, religiosity, dwelling type, employment	Smoking, alcohol, cannabis, medication use, TV watching	Anxiety, depression, stress, child attachment, quality of marital relationship	Health, height, weight
2 (1981-84) After birth 3-5 days	Marital status, employment during pregnancy, obtaining government benefits	Smoking, alcohol, first attendance antenatal care, cannabis	Anxiety, depression, size (adequacy) of social networks, quality of marital relationship	Health during pregnancy, problems during labor (birth, health of baby after birth)
3 (1981-84) Medical record				Past obstetrical history, height and weight of mother and father, detailed current birth obstetrical record
4 (1981-84) F/U 6 mths Mother	Employment status, partners employment status, income, marital status changes	Breastfeeding duration, smoking, alcohol, cannabis, use of child care services	Anxiety, depression, post-natal depression, satisfaction with caring for baby, quality of marital relationship	Baby health at 6 months, child development, immunisation status
5 (1986-88) F/U 5 yrs	Children in household, family income, marital status, employment history	Patterns of child care, and smoking, alcohol, cannabis use	Anxiety, CBCL, depression, stress and life events inventory, quality of marital relationship	Mother's report on her own health and her child's health, health problem inventory
6(a) (1995-97) F/U 14 yrs Adolescent	Age	TV watching, smoking, alcohol, relationship, attachment to parents, exercise	YSR - school performance	Weight, height, eyesight, BP, pulse, pubertal stage, Raven's SPM and WRAT
6(b) (1995-97) F/U 14 yrs Mother	Family income, marital status, type of family, employment	Smoking, alcohol, pattern of food consumption	CBCL, health problem inventory, maternal anxiety, depression, quality of marital relationship, violence in marital relationship	
7(a) (2001-04) F/U 21 yrs Young adult	Employment, income, education, housing, marital status, number of children, religious beliefs and practices	Smoking, alcohol, food frequency questionnaire, physical activity, sexual activity, TV watching, driving behaviour, delinquency scale	CES-D, YASR, CIDI, auto anxiety, depression, illicit substance use	Height, weight, BP, respiratory function, waist and hip circumference, PPVT
7(b) (2001-04) F/U 21 yrs Mother	Employment, income, education, housing, marital status, number of children	Smoking, alcohol, food frequency questionnaire	Medical service use, , anxiety, depression, quality of marital relationship	Height, weight, BP, respiratory function, waist and hip circumference, PPVT, health problem inventory

While attrition has been high at later follow-ups, a great deal is known about the characteristics of those lost; complete data are available for the stage 2 questionnaire and birth records at stage 3, as well as the stage 1 questionnaire on the baseline cohort of 7223 women as well as antenatal and perinatal factors relevant to the child. Those children lost to follow-up are disproportionately of low birthweight, their mothers are less likely to have completed high school, be in their teenage years at first clinic visit, be single at first clinic visit, be smokers and to have poorer mental health.

MUSP has used a variety of statistical modelling approaches to assess the predictors of attrition and the likely impact of attrition on substantive findings. The first approach to this has involved developing a mathematical model which assesses the predicted bias in a relative risk estimate, given known exposure-specific attrition, and examines the sensitivity of this to assumptions about the risk of a health outcome in those lost-to-follow up compared to those not lost. Several qualitative results emerge from this:

- If loss-to-follow-up (LTFU) is unrelated to exposure or unrelated to the health outcome, there is no bias in the observed association
- If LTFU is *greater* in the exposed and those lost are *less* likely to experience the adverse health outcome, the observed association *overestimates* the true association
- If LTFU is *less* in the exposed and those lost are *more* likely to experience the adverse health outcome, the observed association *overestimates* the true association
- If LTFU is *greater* in the exposed and those lost are *more* likely to experience the adverse health outcome, the observed association *underestimates* the true association
- If LTFU is *less* in the exposed and those lost are *less* likely to experience the adverse health outcome, the observed association *underestimates* the true association

In the MUSP, it is generally the case that those lost to follow-up are disproportionately from the lower socioeconomic groups and thus would be expected

to have a worse health profile. Based on the above modeling, estimates of association are most commonly a conservative estimate of the real strength of a relationship.

Quantitatively, the modeling also demonstrates that the predicted bias is only a major concern when attrition is very high, and when the relationships between LTFU and exposure, and LTFU and the health outcome, are reasonably strong (RR of 2 or more).

More recently, we have used approaches which involve developing a predictive model for attrition, using baseline covariates. This allows the predicted probability of attrition, conditional on an individual's baseline covariate values to be calculated, for an individual. The relationship between an exposure and a health outcome is then based upon an analysis, such as multivariate logistic regression, which weights observations according to the inverse probability of attrition, effectively reconstructing a complete sample, under an assumption of missing at random within strata defined by the predictors of attrition. We have also begun to explore the impact of multiple imputation in the MUSP setting. Multiple imputation involves estimating relationships among variables using known data, using these to impute values which are missing among those variables, and incorporating sampling variability for the imputed values.

The analytic problems which are a consequence of missing data are particularly evident when data are taken from a number of the stages of data collection. Because not all respondents participating in later stages of data collection participated in all the previous stages, the usual procedure of listwise deletion, or using a 'complete' dataset for multivariate analysis excludes a large number of observations, perhaps resulting in a highly select sub-group. Multiple imputation allows for a complete set to be constructed, with benefits to the generalisability of findings.

Key Findings

Reflecting the diversity of the interests of the principal investigators, the findings are in three broad categories; those which assess the impact of the social and psychological world on the health of the respondents; those that examine the association between the physical/biological characteristics of mothers and children

and how these impact on developmental health of the child; and finally, there are a series of papers which discuss a range of methodological issues.

Social and psychological impacts on child developmental health

The health consequences of socioeconomic disadvantage have been documented at different stages of the life course of the child. Socioeconomically disadvantaged mothers have the highest rate of unplanned pregnancies and contraceptive failure^{4,5}. By late pregnancy they have received the least information about their pregnancy⁶ and they are the most likely to relinquish their baby for adoption once it is born⁷.

After birth the developmental health of children from socioeconomically disadvantaged backgrounds is substantially worse in a number of ways which suggests that these children are likely to have less opportunity to attain good health outcomes in adulthood. Children of socioeconomically disadvantaged mothers have the highest rates of developmental delay by 5 years of age⁸ and by this age they already have the highest rates of health care use, chronic health problems and poor dental health⁹. Children from these disadvantaged backgrounds not only more often manifest cognitive development problems by age five¹⁰ but they also have higher rates of impaired mental health and behaviour problems^{11, 12, 13}. We have found that maternal smoking, breastfeeding, and child obesity are predictors of elevated blood pressure in 5 year old children¹⁴. Because early childhood blood pressure is one of the better predictors of high blood pressure in later life, these findings have implications for efforts to prevent what have previously been considered adult onset diseases.

Factors impacting on the mental health of the mother and her child are discussed in a number of papers. We have found little evidence that post-natal depression constitutes a widespread health problem. Levels of maternal depression are lowest in the postnatal period and appear to increase as the child grows up¹⁵. Maternal mental health, including maternal depression, is influenced by marital breakdown and marital conflict¹⁶ and poor maternal mental health, as well as marital problems, have independent effects on subsequent child mental health and child behaviour^{17, 18}.

We have also found that, consistent with other Australian and international studies, immigrants to Australia have children with good child developmental health outcomes despite their sometimes disadvantaged economic status^{19,20}.

Physical/biological findings

The birthweight of children and their physical development have been considered in a number of papers. We have confirmed that low birthweight (for gestational age) is primarily determined by the parent's BMI and maternal tobacco consumption²¹ but that low to moderate levels of maternal alcohol consumption appears to have little measurable impact on the physical development of the fetus²². Severity, not type of growth restriction in term infants, is predictive of mild cognitive and learning problems in adolescence²³. Maternal tobacco consumption in the first trimester of pregnancy, but not pre-pregnancy or late in pregnancy, predicts aggressive/delinquent behaviour when the child reaches five years of age²⁴. There is also a dose-response association between the period of time the mother breastfeeds her child and the child's cognitive (IQ) development²⁵. A series of papers have examined the origins of obesity²⁶ and the factors influencing continuity and discontinuity of obesity in childhood²⁷ and its relationship to blood pressure²⁸ and behaviour²⁹. We have also found little evidence of maternal social/environmental factors impacting on childhood obesity, with the main effects being attributable to parental BMI^{26,27}.

Methodological findings

MUSP's capacity to contribute to the methodology of longitudinal studies is derived from four features of the study. Firstly, there is almost complete enumeration of all women in the sample from the time they were recruited. A great deal is known about those women who have subsequently been lost to follow-up. Secondly, we have siblings separately recruited into the study, enabling us to study the impact of family characteristics on developmental health outcomes. We have found evidence of consistent and strong family effects on child mental health³⁰, child aggressive/delinquent behaviour³¹, and child substance use³². There has also been an opportunity to creatively test the birthweight and child IQ association, by comparing the IQ scores for siblings of different birthweight reared in the same family³³. Thirdly, we have used the availability of repeated measures of the same factor (e.g. tobacco smoking, anxiety, depression) to determine whether there are sensitive periods when

the timing of an exposure is more important – even though this exposure may recur throughout the life course³⁴. The availability of repeated measurements enables MUSP to time both exposures and outcomes in such a way as to assess what may be reciprocal associations and to track changes in mental health and health behaviour over the life course³⁵. Finally, MUSP has obtained identical measures from different informants (e.g. mother, child, teacher). With these multiple measurements it has been possible to validate the quality of surrogate reports (against later outcomes) and estimate the extent to which the characteristics of a respondent influence the validity of the data they provide³⁶.

Strengths and weaknesses

While most of the strengths of MUSP have already been described (e.g. recruitment, the large sample, the repeated measurements using the same measures, the diverse topic areas incorporated in the measurements) the weaknesses become more evident over time.

While the sample is not representative of the total population of women giving birth, it is likely to be a good sample of lower to middle SES women giving birth. Loss to follow-up and the difficulty of retaining contact with the sample is our major concern. The resources required to interview the most willing/available respondents represent a small fraction of the resources required for the least willing/available respondents. Almost invariably we have spent our grant before we have completed our follow-ups. Australian funding agencies are not equipped to fund longitudinal studies at the level that is necessary. It is also a consequence of this pattern of funding that resources have not been available to provide for the extensive data management and research support that is important. The PIs have all worked on the MUSP in a part-time capacity. There have been no full-time staff with dedicated responsibility for managing the study or contributing to the publications.

The size of the sample is also a disadvantage – particularly when the research objectives are to track the progress of a group with a less than common outcome over time. More frequent follow-up would also have been very helpful. The gaps between follow-ups are too long in some instances, making it more difficult to determine the

timing of change. Of course, there would have been substantial benefits to obtaining more physical and biological measurements, but again this is a resource issue.

Accessing the data

Applications to access the data should, in the first instance, be made to Jake M. Najman PhD. The MUSP welcomes interest and offers of collaboration from colleagues, subject to guidelines which can be obtained via the MUSP website. Generally approval of a proposal depends upon the topic of interest, and the degree of access being sought. If topics are already the subject of research in progress then access may be refused or subject to constraints. The website also contains a Memorandum of Understanding which stipulates the conditions under which access is available.

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