Population Data, Ethics and Paediatric Care:
How we can use population data to guide ethical decision making

PAEDIATRIC GRAND ROUNDS
Riley Hospital for Children

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13 June 2007
Population of Western Australia: 2 Million

Population of Australia: 20.2 Million

Western Australia

Largely Unexplored

- Broome
- Port Hedland
- Carnarvon
- Kalgoorlie
- Perth
- Esperance
Our Mission

‘To improve and promote the health and well being of all children through the unique application of multi disciplinary research’

Aims:

• To conduct high quality research

• To apply research findings to improve the health of children, adolescents and families

• To teach the next generation of health researchers

• To be an advocate for research and for children
ICHR Philosophy

- **Basic Sciences**
  - Data bases
  - Bioinformatics
  - Research support
  - Training
  - Consumer participation
  - Kulunga
  - Commercialisation

- **Clinical Sciences**
  - Hospital & Community care

- **Population Sciences**
  - Public health/Child health policy

**Local, National & International Collaborations**
Research Themes

• Aboriginal child health
• Asthma, allergies & respiratory diseases
• Cancer & leukaemia
• Developmental disorders (BD, CP, ID)
• Infectious diseases
• Mental health
• Developmental origins of health & disease
Australian Research Alliance for Children and Youth

A national collaboration established to facilitate, coordinate and support the development of knowledge and its effective use to enhance the well-being and life chances of children and young people.
Outline

1. Population data and record linkage in WA
   A) Development/ methods/ advantages
   B) Examples for child health services
2. The special case of pharmacovigilance
3. Ethical issues
4. Modernity’s paradox and the imperative for good data
1. Population Data & Record Linkage in WA

A) Development/ methods/ advantages
B) Examples for child health/ services
1970’s
• Public concerns re thalidomide and adverse effects of perinatal care

1980/81
• Establish 1st Australian linkage of births, deaths and midwives (perinatal) records (total population)
• Establish registers of cerebral palsies and birth defects to link to data base

1982/83
• Link computerised hospitalisations

1990 onwards
• Ongoing MCHRDB

2004
• WA data linkage system
Maternal and Child Health Research Database
1980-2003

- Midwives
- Birth Registrations
- Death Registrations
- Birth Linkage
Maternal and Child Health Research Database
1980-2003

- Midwives
- Census GIS code
- Sibships
- Mental health Register
- Birth Registrations
- Death Registrations
- Birth Defects Registry
- Cerebral Palsy Register
- All Hospitalisations 0 - 18 years
- Cohort Studies Twins Register Child Health Surveys
Population databases which can provide data for research

Core Data Sets
- Birth Registrations 1974+
- Death Registrations 1969+
- Hospital Separations 1970+
- Midwives' Notifications 1980+
- Birth Defects 1980+
- Geocoding, socio-economic indices 1986+

Master Links File
- ~600,000 births

Commonwealth Data Systems
- MBS/PBS
- Proposed linkage: Australian Childhood Immunisation Register

Research Databases
- Institute for Child Health Research
  - Snapshot of Maternal & Child Health Research Data Base
  - WA Pregnancy Cohort 1989-92
  - WA Child Health Survey WA Aboriginal Child Health Survey 2001-2
  - WA Twin Register 1980+
  - RASCALS 1995-6
  - Sibships 1980+1993
  - Invasive Pneumococcal Disease 1996+
  - Intellectual Disability 1980+
  - Cerebral Palsy 1956+
  - Autism 1999+
  - Newborn Encephalopathy 1995-7
  - Other

Other State Data Systems
- Proposed linkages: WA justice education, Department of Community Development, Pathology database

Based on and consistent with the WA DATA LINKAGE SYSTEM, February 2004
Advantages of WA Population Data & Record Linkage
e.g. MCHRDB

- 100% sample: unbiased, no one excluded
- Cheap cf. seeking consent/ surveys
- Valid & reliable data on sensitive issues
- Reduces survey burden on populations
- Fast, effective linkage technology
- Privacy protected
- Better data for policy, planning, evaluation
- Improve administrative data
Limitations of WA Population Data & Record Linkage

- Information only available on items and outcomes recorded in data bases (breadth > depth)
- Privacy issues still need to be addressed eg ethics committees, understanding of public good by the community
- Need better, complete denominators
- Changes in diagnostic classifications present challenges for temporal analyses
- (In)accuracy of recorded information
- Incomplete ascertainment
- Sample size for rare disorders (APSU)
Antenatal Factors in Later Disease/ Disability

- Trends in diseases & disability (complete)
- Environmental exposures & later diseases
- Birth outcomes in psychiatric patients
- Intra-uterine growth & later development (DOHaD)
- Pregnancy problems & later childhood diseases
- Reproduction and subsequent maternal health
Evaluation of Medical Care

- Increased very preterm survival - problems in survivors
- IVF & cerebral palsy, disabilities
- IVF & birth defects
- Reasons for and impact of, increasing caesarean sections
- Effects of increased obstetric intervention
- Adverse drug effects (pharmacovigilance)
- Clinical audit
Evaluation of Health Promotion

• Prevention of cot deaths
• Folate campaign for spina bifida
• Childhood vaccination coverage
• Anti-smoking programs
• Don’t Shake Your Baby
• STD, drug and alcohol programs
Trends in Overall CP Western Australia, 1956-1999

Trends in cerebral palsy, stillbirths, and neonatal deaths, Western Australia, 1970-1998

- Stillbirths
- Neonatal deaths
- Cerebral palsy

SB rates per 1000 total births
NND and CP rates per 1000 live births

Year of birth

Total Cerebral Palsy\(^1\) rates by Mode of Delivery, Western Australia, 1980-1999

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1. Excludes cerebral palsy due to postneonatal causes

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Mode of delivery

- Normal/Instrumental
- Elective C/S
- Non-elective C/S

Rate per 1000 live births

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1980-89

1990-99
Cerebral Palsy Numbers and Rates by Gestational age in Western Australia, 1980-1999

1 Excluding cerebral palsy due to postneonatal causes
Proportion of Cases of Cerebral Palsy* from Multiple Gestations, Western Australia, 1960-1999

* Excludes cerebral palsy due to postneonatal causes
Trend in Prevalence of Hypospadias by Associated Congenital Anomalies

- Isolated cases of hypospadias
  - Average rate: 28.5 per 10,000 births, trend: 1.9% p.a., P<0.01

- Cases with associated non-genital congenital anomalies
  - Average rate: 4.3 per 10,000 births, trend: 2.7% p.a., P=0.02

- Cases with associated genital anomalies
  - Average rate: 2.0 per 10,000 births, trend: 1.2% p.a., P=0.48

Source: Nassar, Bower & Barker. Accepted for pub. Am Journal Epi
Association of Hypospadias with other Congenital Anomalies and Degree-of-severity

Isolated cases of hypospadias

- Mild: 87%
- Moderate-severe: 9%
- Unspecified: 5%

Cases with non-genital anomalies

- Mild: 80%
- Moderate-severe: 13%
- Unspecified: 10%

Cases with genital anomalies

- Mild: 51%
- Moderate-severe: 39%
- Unspecified: 0%

Source: Nassar, Bower & Barker. Accepted for pub. Am Journal Epi
Population Based Record Linkage Study
Juvenile Diabetes

• Increase in both Type 1 and Type 2
• Type 1: 11.3/100,000 1985 - 23.2/ in 2002
  All ages 0-14 years
• Type 2: 27% annual increase
• Risk factors
  – Increased maternal age
  – Birthweight (↑) / gestational age (↓)
  – Birth order (protective)
  – Urban > rural
  – Socioeconomic status (↑)

### Prevalence of intellectual disability by source of ascertainment and gender

<table>
<thead>
<tr>
<th>Source of Ascertainment</th>
<th>Male Prevalence Ratio</th>
<th>Female Prevalence Ratio</th>
<th>95% CI Male</th>
<th>95% CI Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1.6</td>
<td>1.5</td>
<td>(1.5-1.7)</td>
<td>(1.4-1.7)</td>
</tr>
<tr>
<td>DSC</td>
<td>1.5</td>
<td>1.5</td>
<td>(1.4-1.7)</td>
<td>(1.5-1.8)</td>
</tr>
<tr>
<td>Education</td>
<td>1.7</td>
<td>1.7</td>
<td>(1.5-1.8)</td>
<td>(1.5-1.8)</td>
</tr>
</tbody>
</table>
Mother <20 years compared with 25-29 years by ID category
Index of relative social disadvantage
<10% compared with >90% by ID category

Mild-moderate ID  Severe ID  ASD

Odds Ratio

10
1
0.1
Mild-moderate ID by index of education and occupation
Odds ratio of fetal growth and intellectual disability in Caucasian children born in WA

Source: Nassar et al unpublished data
OR* for CP in Singletons by Growth and Gestation of Delivery.

*relative pobw z score = 0 in gestational age stratum
Trends in NTD in WA

Source: Bower et al, Birth Defects Registry
NTD in Indigenous and Non-Indigenous infants by Grouped Years of Birth

![Graph showing NTD/1000 births by year of birth for Aboriginal and non-Aboriginal infants.]

- **PR 1.42** in 80-92 year of birth
- **PR 1.69** in 93-95 year of birth
- **PR 1.98** in 96-00 year of birth

Source: C Bower 2005
Cumulative Prevalence of Birth Defects after ICSI & IVF

Source: Hansen, Kurinczuk, Bower & Webb 2002
2. The special case of pharmacovigilance
Urgency for Paediatric Pharmacovigilance

- Many drugs prescribed in pregnancy and childhood no RCT
- Many RCT too small or too short to evaluate harm
- Many RCT exclude co-morbidities, ages, others
- Some drugs (eg folate, antiepileptics, Vit A analogues) need post marketing surveillance
Data Linkage for Pharmacovigilance: Pregnancy

PBS: Commonwealth Dataset

PBS prescriptions 2002-2005

total exposure period:
6 months before conception
to date of pregnancy event
min~28,000 p.a. (70% exposed)

HMDS, MNS, RG Births: State Datasets

pregnancy event, 2002-2005
key = woman

births registered in WA and/or hospital admissions
that indicate a pregnancy occurred,
ICD10 O00-O99 ~40,000 p.a.

Source: Lyn Colvin TICHR Unpublished Data
Pharmacovigilance Initiative
Possible Uses

• Product safety
• Therapeutic effect of drugs - how effective and if effective in all groups
• Drug interactions and their safety/adverse effects
• Therapeutic use of a drug - whether a drug is being prescribed properly and whether it is working
• Drug utilisation/uptake - who is getting it and where
• New drugs replacing old ones - why, how, costs and consequences
• Trends and patterns in prescribing drugs
3. Ethical issues
Consent

• Consent is essential for all research involving participation of individuals
  – Questionnaires, interviews
  – Donate blood, tissues
  – Drug trials etc

• Not all research requires consent
WA Data Linkage Unit
MCHRDB 2004 Onwards

Family links
- Marriage registrations
- Electoral roll
- Birth/death registrations

CORE
(1980-current)
- Midwives notifications*
- Birth registrations
- Hospital Morbidity*
- Death registrations*

National registers
- National Death Index
- National Cancer Registry

Registries
- Cerebral Palsy
- Birth Defects
- Intellectual Disability
- Cancer
- Mental Health

Commonwealth Data
- PBS (Prescription Drug Use)
- MBS (Medicare)
- Australian Childhood Immunisation Register

ICHRS Studies
- Raine Study
- WATCH
- RASCALS
- Child Health Survey
- Aboriginal Child Health Survey

* geocoded
Bias

• Bias is the distortion of the true relationship between exposure and outcome due to flaws in either study design or analysis

• Can give wrong answers
Bias from Non-Participation

- Inability to trace/contact (most common)
- Refusal (rare)

Both of these groups very different from participants

- Magnitude and direction not predictable
- Not quantifiable
- Explain differences in risks between studies
- Poor information for health services and epidemiological research
Consent Rate for Health Research

<table>
<thead>
<tr>
<th>Population</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester Clinic</td>
<td>100%</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>80%</td>
</tr>
<tr>
<td>Australia In Person</td>
<td>60%</td>
</tr>
<tr>
<td>Australia GP Clinic</td>
<td>50%</td>
</tr>
<tr>
<td>USA mailed survey</td>
<td>40%</td>
</tr>
<tr>
<td>UK mailed survey</td>
<td>30%</td>
</tr>
<tr>
<td>Finland mailed survey</td>
<td>20%</td>
</tr>
<tr>
<td>Australia mailed survey</td>
<td>10%</td>
</tr>
</tbody>
</table>
Does TOP Increase the Risk of Later Breast Cancer?

- Recent meta analysis (53 studies)
- Retrospective studies with variable reporting & response rates $RR=1.14(1.09-1.19)$
- Record linking of abortion data to cancer register data $RR=0.93(0.89-0.96)$
- Comparisons of abortion registry & self report data
  - 24% women with breast cancer and
  - 27% women without breast cancer reported incorrectly that they had never had an induced abortion
  - 27% of women reporting a spontaneous abortion did not report it 20 years later

Source: Beral V et al. 2004
Impact of Informed Consent on Participation Bias

- Tu et al (2004) analysed the impact of informed consent on characteristics of participation in the Canadian Stroke Registry
- Overall participation rate of eligible patients was 39%
- Bias - lower in-hospital mortality rate among participants
- Expensive ($500,000 over 2 years for consent alone)
- Scientifically useless
Consent for Population Data & Record Linkage

Seeking consent is:

A) Not practical/feasible
   - Unable to contact 100% of the population (death, mobility)
   - Hugely expensive to contact and get consent

B) Poor science
   - Variable participation - significant bias
   - Poor data on exposures - e.g. recall bias
USA - HIPAA

“As in Europe, any potential social benefits of epidemiological research were discounted in favor of privacy. This judgment seemed to be founded on the premise that no one ordinarily needs to see a medical record except the patient’s personal physician. This, of course, is neither true nor desirable if we are to deliver effective and efficient integrated medical care.”

L. Joseph Melton MD
Mayo Clinic

Source: NEJM Vol 337 1997
Proportion of Ethics Approved Research Projects using Name Identified & Data Linked Administrative Health Information WA 1990-2003

**Figure** Proportions of ethics-approved research projects (N=408) using name-identified and data-linked administrative health information in Western Australia 1990-2003

Our Health System Needs Effective Evaluation

- Spiraling costs of care
- Increase complex diseases
- New technologies, drugs - harmful side effects
- Patient expectations
- Concerns over safety
- Poor data for service planning
4. Modernity’s paradox and the imperative for good data
Modernity’s Paradox

• Increasing prosperity
• Increasing problems for children and youth
• Increasing inequalities in outcomes and opportunities

Source: Keating & Hertzman 1999
Indicators of Poor Developmental Health which are Increasing in Australian Children and Youth

Health Outcomes
- Low birth weight
- Complex diseases (asthma, diabetes, obesity)
- Mental Health problems, suicide

Lifestyle risk factors
- Child abuse/neglect/domestic violence
- Behavioural problems, substance abuse

Others
- Juvenile crime
- Learning disorders
- Disabilities (intellectual, physical)

Source: Stanley, 2000 Millennium Year Book
Trends in Problems Affecting Children & Youth in Today’s World

• Many are increasing in incidence
• Complex problems (eg mental health, obesity)
• Demand complex information to monitor, study & prevent them
• Costly to treat & manage
• Crisis in child & youth services (health, mental health, education & crime)
• Research in silos
• Services in silos
Bad Parenting....

1. Mother duck leads her ducklings.
2. Mother duck notices something.
3. Mother duck tries to save her ducklings from the drain.
Overview of databases and trajectories

Cross Sectional & Cohort Data

- RASCAL
- WACHS WAACHS
- WACHS WAACHS
- WACHS WAACHS
- WACHS WAACHS

Population Level Data

- MCHRDB
- HMDS
- HMDS DCD
- HMDS DCD
- HMDS DCD
- HMDS DCD
- HMDS DCD
- HMDS DCD
- HMDS DCD

Developmental Trajectories

- Pregnancy
  - Maternal health, SES
  - Parenting, SES, SEIFA

- Infancy
  - Parenting, SES, SEIFA
  - Parental wellbeing
  - Family environment

- Early childhood
  - Parenting, SES, SEIFA
  - Parental wellbeing
  - Family environment

- Late childhood
  - Parenting, SES, SEIFA
  - Parental wellbeing

- Adolescence
  - Parenting, SES, SEIFA
  - Parental wellbeing

- Education, delinquency

- Health, disability, child protection

- Health, disability, child protection

- Health, disability, child protection education

- Health, disability, child protection education

- Health, disability, child protection education
“In the late 20th century, scholars and politicians posed a key question ‘What desires and needs do you have as an autonomous rights bearing person to privacy, liberty and free enterprise?’ Now it is important to ask another kind of question ‘What kind of community do you want and deserve to live in, and what personal interests are you willing to forgo to achieve a good and healthy society?’”

Prof Lawrence O Gostin 2004
University of Georgetown
Rationale for ARACY

• Rise in complex problems (e.g., mental health, obesity)
• Demand complex information to monitor, study & prevent them
• Research is fragmented, done in separate silos and does not inform solutions
• Policy in silos, not using research
• Most research and policy ignore major socioeconomic drivers of poor outcomes
WA Data Linkage Unit
MCHRDB 2004 Onwards

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* geocoded
Cerebral Palsy by Gestational age in Western Australia, 1980-1999

SIDS by Aboriginal status and Birth Year Groups, WA births 1980-2001

Source: J Freemantle 2004
Privacy Concerns

- Abuse, particularly genetic risk data, by insurers or employers
- Sensitive information on individuals given out without their knowledge
- Government control of personal data
- Prefer consent for record linkage
- However, in focus groups: (McCallum et al 1993, Kelman 2005)
  - Strong support for public good research
  - Trusted research in universities
  - Acknowledged low risk
UK Privacy & Medical Research

Personal data for public good: using health information in medical research

- Increased complex laws/regulations
- Variable interpretation
- Many projects blocked/delayed
- Increase in costs
- Poor public awareness of value and methods of research

Commentary Lancet, 2006

Source: Academy of Medical Sciences, 2006