GENETIC COUNSELLING

About two thirds of cases are new mutations. Genetic counselling to affected parents is straightforward as non-penetrance is a rare event[35] so their offspring have a 50:50 risk of being affected and affected individuals have a 60–70% risk of seizures and a 50% risk of learning difficulty. Counselling apparently normal parents about the risk of a second affected child is more difficult. Accurate counselling can only be given after full clinical examination of both parents, including ultraviolet light examination of the skin in a darkened room and direct fundoscopy through dilated pupils. Although rarely helpful, cranial computed tomography and renal ultrasound should also be offered as a positive finding significantly alters the risk assessment. Single renal cysts are ignored but polycystic disease or angiomyolipoma are significant. Echocardiography for genetic counselling is unreliable[36] and skeletal survey is unhelpful,[37] but echocardiography is helpful in screening the at risk newborn. Siblings of an affected isolated case should be offered the same screening as their parents because it is known that parents have a 2% recurrence risk even if they have been previously screened. Antenatal diagnosis is now possible for very large affected kindreds who show clear linkage to chromosome 16 but not for other families. Gene deletions are difficult to detect but where detected offer more reliable diagnosis than linkage: at present this remains a research technique. With the exception of very large families, those families who link to the TSC1 gene on chromosome 9 or who are too small for linkage analysis will have to wait for further progress in the isolation of the gene before DNA techniques will help them.

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1 Sampson JR, Stephenson JBF, Mann L, Connor JM. Genetic aspects of tuberous sclerosis in the west of Scotland. *J Med Genet* 1989; **26:** 28–31.
2 Osborne JP, Fryer AE, Webb DW. Epidemiology of tuberous sclerosis. *Ann NY Acad Sci* 1991; **615:** 125–7.
3 Webb DW, Osborne JP, Fryer AE. On the incidence of fits and mental retardation in tuberous sclerosis. *J Med Genet* 1991; **28:** 385–8.
4 Wiederholt WC, Gomez MR, Kurland LT. Incidence and prevalence of tuberous sclerosis in Rochester, Minnesota, 1950–1982. *Neurology* 1985; **35:** 600–3.
5 Ahlsen G, Gillberg IC, Lindblom R, Gillberg C. Tuberous sclerosis in western Sweden. A population study of cases with early childhood onset. *Arch Neurol* 1994; **51:** 76–81.
6 Pampiglione P, Pugh F. Infantile spasms and subsequent development of tuberous sclerosis syndrome. *Lancet* 1975; ii: 1046.
7 Gomez MR. *Tuberous sclerosis.* 2nd Ed. New York: Raven Press, 1988.
8 Webb DW, Thomas RD, Osborne JP. Cardiac rhabdomyomas and their association with tuberous sclerosis. *Arch Dis Child* 1993; **68:** 367–70.
9 Webb DW, Super M, Normand ICS, Osborne JP. Tuberous sclerosis and polycystic kidney disease. *BMJ* 1993;**306:** 1258–9.
10 Margo CE, Barletta JP, Staman JA. Giant cell astrocytoma of the retina in tuberous sclerosis. *Retina* 1993; **13:** 155–9.
11 Webb DW, Kabala J, Osborne JP. A population study of renal disease in tuberous sclerosis. *Br J Urol* 1994; **74:** 151–4.
12 Menor F, Marti-Bonmati L, Mulas F, Poyatos C, Cortina H. Neuroimaging in tuberous sclerosis: a clinicoradiological evaluation in pediatric patients. *Pediatr Radiol* 1992; **22:** 485–9.
13 Altman NR, Purser RK, Donovan Post MJ. Tuberous sclerosis: characteristics at CT and MRI imaging. *Radiology* 1988; **167:** 527–32.
14 Smith H, Watson GH, Patel RG, Super M. Cardiac rhabdomyomas in tuberous sclerosis: their course and diagnostic value. *Arch Dis Child* 1989; **64:** 106–200.
15 Jozwiak S, Pedich M, Rajszys P, Michalowicz R. Incidence of hepatic hamartomas in tuberous sclerosis. *Arch Dis Child* 1992; **67:** 1363–5.
16 Chiron C, Dulac O, Luna D, *et al.* Vigabatrin in infantile spasms. *Lancet* 1990; **335:** 363–4.
17 Appleton RE, Montiel-Viesca F. Vigabatrin in infantile spasms, why add on? *Lancet* 1993; **341:** 962.
18 Bebin EM, Kelly PJ, Gomez MR. Surgical treatment for epilepsy in cerebral tuberous sclerosis. *Epilepsia* 1993; **34:** 651–7.
19 Hunt A, Stores G. Sleep disorder and epilepsy in children with tuberous sclerosis: a questionnaire based study. *Dev Med Child Neurol* 1994; **36:** 108–15.
20 Deonna T, Ziegler AL, Moura-Serra J, Innocenti G. Autistic regression in relation to limbic pathology and epilepsy: report of two cases. *Dev Med Child Neurol* 1993; **35:** 166–76.
21 Smalley SL, Tanguay PE, Smith M, Gutierrez G. Autism and tuberous sclerosis. *J Autism Dev Disord* 1992; **22:** 339–55.
22 Pasyk KA, Argenta LC. Argon laser surgery of skin lesions in tuberous sclerosis. *Ann Plast Surg* 1988; **20:** 426–33.
23 Drake DB, Morgan RF, Cooper PH. Shave excision and dermabrasion for facial angiofibroma in tuberous sclerosis. *Ann Plast Surg* 1992; **28:** 377–8.
24 Smythe JF, Dyck JD, Smallhorn JF, Freedom R. Natural history of cardiac rhabdomyomas in infancy and childhood. *Am J Cardiol* 1990; **66:** 1247–9.
25 Van Baal JG, Smits NJ, Keeman JN, Verhoef S. The evolution of renal angiomyolipomas in patients with tuberous sclerosis. *J Urol* 1994; **152:** 35–8.
26 Pirson Y. Renal transplantation in tuberous sclerosis. *BMJ* 1992; **305:** 313.
27 Shepherd CW, Scheithaur B, Gomez MR, *et al.* Brain tumours in tuberous sclerosis. A clinicopathological study of the Mayo Clinic experience. *Ann NY Acad Sci* 1991; **615:** 378–9.
28 Webb DW, Fryer AE, Osborne JP. On the morbidity associated with tuberous sclerosis. *Dev Med Child Neurol* (in press).
29 Webb DW, Thomson JLG, Osborne JP. Cranial magnetic resonance imaging in patients with tuberous sclerosis and normal intellect. *Arch Dis Child* 1991; **66:** 1375–7.
30 Shepherd CW, Gomez MR, Crowson CS. Causes of death in patients with tuberous sclerosis. *Mayo Clin Proc* 1991; **66:** 792–6.
31 Fryer AE, Chalmers A, Connor JM, *et al.* Evidence that the gene for tuberous sclerosis is on chromosome 9. *Lancet* 1987; i: 659–61.
32 Kandt RS, Haines JL, Smith M, *et al.* Linkage of an important gene locus for tuberous sclerosis to a chromosome 16 marker for polycystic kidney disease. *Nature Genetics* 1992; **2:** 37–41.
33 The European chromosome 16 tuberous sclerosis consortium. Identification and characterization of the tuberous sclerosis gene on chromosome 16. *Cell* 1993; **75:** 1305–15.
34 Green AJ, Yates JRW. Loss of heterozygosity on chromosome 16p in hamartomata from patients with tuberous sclerosis. *Am J Hum Genet* 1993; **53** (suppl): 244.
35 Webb DW, Osborne JP. Non-penetrance in tuberous sclerosis. *J Med Genet* 1991; **28:** 417–9.
36 Webb DW, Thomas RG, Osborne JP. Echocardiography for genetic counselling in tuberous sclerosis. *J Med Genet* 1992; **29:** 487–9.
37 Fryer AE, Chalmers AH, Osborne JP. The value of investigation for genetic counselling in tuberous sclerosis. *J Med Genet* 1990; **27:** 217–23.

Use of registers in child health

The role of registers in the planning and provision of health care for children and in health services research has been much debated over the last 20 years. Recently, in the UK, the debate has focused on the resource implications of maintaining registers,[1] on concerns about confidentiality,[2] and on organisational changes in the NHS which appear to threaten the infrastructure of many regionally based information systems, including registers.[3]

It is timely, therefore, to consider the aims and objectives of registers, the extent to which these are fulfilled, and to respond to the challenge that some of these objectives could be met in other ways. From these considerations, I hope the essential and unique characteristics of registers will emerge together with some of the problems of setting them up and maintaining them.

Definition of a register

A register is a list of children with a particular predefined attribute. This attribute is usually a disease or condition

but registers can also contain children with a particular impairment or disability, children who are thought to be 'at risk', for example of physical or sexual abuse, or those who have had a particular treatment. Indeed, the term 'register' may be used to describe everyone within a particular age group living in a given area, for example the basic module or 'child register' of many district based child health information systems.

Aims and objectives of registers

These can be considered under three headings:

(1) TO ASSESS THE HEALTH NEEDS OF A POPULATION

In order to measure health care needs, the prevalence of health 'problems' in the population need to be known. Routinely collected data on morbidity are limited. Some are available from the hospital inpatient data, from contacts with general practitioners and from notification of some communicable diseases, but these are restricted to children who have sought and received care. This does not necessarily reflect the numbers of children with the condition in the population nor are the characteristics of those who are seen for treatment likely to be the same as those who are not seen.

On the other hand, a diagnostic register that is based on a population who are currently resident in a geographically defined area and which is compiled from multiple sources, maintained and updated, can provide a more precise estimate of the numbers and characteristics of children with a particular condition. Further information may be needed, however, to assess the health, educational, and other needs of such children. In these cases information on how the condition affects the child's ability to function in every day life, the level of severity of the condition, and details of associated impairments and disabilities also need to be recorded.

The focus on 'function' has led to the development of 'special needs registers' in which the attribute which determines the inclusion of the child is not a diagnosis, but a disability for which the child needs special help. Special needs registers are now held by many district health authorities. Some are 'free standing'[4] but many are integrated with a computerised child health system.[5] This allows information from the special needs register to be linked with the child register and enhances the information available on each child.

The quality of the information on health, educational, and social needs of children that is held at a local level varies considerably, however. Although the basic module or child register of the district based child health information system together with information on immunisation is remarkably complete, the information on impairment and disability is often of poor quality. If the aims of the local disability registers were clarified, if agreement could be reached on a standard description of impairment and disability, and if information could be linked to maternity and neonatal datasets, data quality might improve and the information become more relevant and useful.

(2) TO EVALUATE CARE PROVIDED BY THE HEALTH SERVICE

The use of registers to provide information for health professionals who are considering whether or not the health care they are providing is beneficial and cost effective can be considered under four headings:

(A) Evaluation of preventive measures

Diagnostic registers at both local and national level can provide a way of evaluating primary preventive measures for example, the rubella immunisation programme can be monitored using data about the numbers of children with congenital rubella embryopathy. The impact of prenatal folic acid administration can be assessed by examining the numbers of conceptions with a neural tube defect. The Office of Population Censuses and Surveys notification scheme for congenital malformations has been used to monitor these effects at national level and there are a number of locally based congenital anomaly registers. The latter, such as a neural tube register in the Oxford area,[6] and the regional fetal abnormality survey in the former Northern region[7] tend to much more complete and reliable than the national system. A further problem with the national system at present is that it does not include malformations in fetal deaths and stillbirths. A working party has recently recommended a number of changes that if implemented would address some of these shortcomings.[8] Even if data are more complete there will still be problems in interpreting trends, of course. Although changes in the rates of conditions may reflect effective preventive measures, other factors may also be exerting their effect at the same time.

(B) Evaluation of screening programmes

Fetuses, babies, and children are subjected to various types of screening in order to detect conditions, on the assumption that early detection and intervention will be beneficial and cost effective. For example, screening programmes for the prenatal diagnosis of Down's syndrome are widely used, and in the neonatal period babies are screened for congenital dislocation of the hip, phenylketonuria, congenital hypothyroidism, and other metabolic disorders. Preterm babies are screened for retinopathy of prematurity and during the first year most babies are screened for sensorineural deafness. In order to evaluate these programmes the number of children later diagnosed as having a particular condition needs to be known, and the extent to which the screening test correctly identifies them. Without a population register of the children with the condition (which should include fetuses with the condition where appropriate), such as the national Down's syndrome cytogenetic register,[9] the register of children with congenital hypothyroidism,[10] the national register of children with phenylketonuria,[11] and a local register of children with sensorineural deafness,[12] it is impossible to determine accurately the sensitivity and specificity of the screening test and the false positive and false negative detection rates. Where such registers do not exist, as for example for congenital dislocation of the hip, the effectiveness of the widespread neonatal screening which is currently done is not known and indeed has been challenged.[13]

It is arguable that before screening programmes are established, registers of the condition being sought need to be set up and funded. It is not clear whether the responsibility for this funding lies centrally or locally. In view of the change in function of NHS regions, this area needs further clarification. Many of the existing registers which are linked to national screening programmes are well designed and maintained. This is particularly important as the conditions are rare and the registers need to be complete and accurate in order to avoid misleading conclusions.

(C) Evaluation of perinatal care

For many years, it has been assumed that there is a link between care for mothers and babies around the time of birth and some disabling disorders of children. For example, the birthweight specific rate of cerebral palsy was

thought to reflect the quality of perinatal care. It is now clear, however, that cerebral palsy may originate at any time during the development of the brain and trends observed on cerebral palsy registers need to be interpreted with care.[14] The value of a cerebral palsy register in the evaluation of perinatal care lies more in its ability to provide information on the outcome of babies who are enrolled in randomised controlled trials of obstetric and neonatal interventions and as a framework for case-control studies.

(D) Evaluation of services for children with chronic disorders and disability

Population registers of children with disabilities can provide a good framework for evaluative studies and audit. For example, an evaluation of a change in management policy for young diabetics was based on a local register of juvenile diabetics.[15] Similarly, interventions such as physiotherapy and conductive education for children with cerebral palsy have rarely been systematically or fully evaluated and can be studied using a register as a sampling frame. This can allow a population of children free from selection bias and subgroups of children with similar levels of disability to be identified. Registers have rarely been used in this way and we need to explore their potential further in service evaluation and in audit.

(3) TO IMPROVE UNDERSTANDING OF AETIOLOGY

Over the years, disease registers have played a useful part in both understanding the natural history of diseases and conditions, and in the generation and testing of aetiological hypotheses. Observations of geographic clustering of cases and trends over time in the prevalence of conditions have raised important questions, particularly when using the very successful child cancer registers. Registers of genetically determined conditions provide a basis not only for compiling information on the rapidly increasing number of such conditions but can also be used to identify carriers and those at risk of having affected children. This, of course, raises a number of the ethical issues surrounding registers, in particular that of confidentiality.

Ethical issues and confidentiality

A potential conflict can arise between the need to ensure that personal health information is confidential to that person and the caregiver, and the benefit of disclosure of information in order to provide and plan care and services, and to conduct research. As names and other identifiers are often included on registers (to enable linkage and to identify duplicate entries), clear guidelines are needed. Recently a working group of the Royal College of Physicians has recommended that the use of data from registers for public health practice (such as audit, monitoring morbidity indices, needs assessment) and research that does not involve direct contact with the patient, does not require independent ethical review.[16] Despite this reassurance, consideration still needs to be given to issues such as patients' and parents' dislike of 'labelling', and the need for careful control and supervision of access to register data.

To what extent can a particular register fulfil more than one role?

It has been stated that the aims and objectives of any one register should be predefined at the outset. There needs to be a clear distinction between registers which are primarily a managerial tool, such as the child protection register, those whose aim is to ensure that the service needs of individual children are met, such as the registers of disabled children held by social services and those whose aim is to provide data about a geographically defined population. Registers are rated as 'successful' if they meet their prestated objectives. Attempts to use them for other purposes are usually not successful. There may be ways, however, of meeting several different objectives with one register. For example, in the new BD8 form which is used for registering people with blindness or partial sight, parts 1–4 of the form provide the information needed to plan appropriate services, and part 5 is an epidemiological return which is anonymised and sent directly to the Office of Population Censuses and Surveys.[17] This model could perhaps be used in other diagnostic registers, for example the special needs registers which form part of the child health information systems.

Issues of data quality

Ways of validating the quality of data need to be considered when establishing a register. Using clear case definitions, with exclusions clearly stated, and an agreed standard simple description of clinical characteristics and levels of disability will mean that a register is more likely to be reliable and complete. It is generally agreed that using multiple sources of ascertainment and cross checking between sources helps to ensure as complete a register as possible. Although reporting to registers is usually voluntary in the UK, this is not so in all countries. In Nordic countries, it is mandatory to register children with visual impairment using a standard system of description. Registers that are linked to disability benefits, as with the BD8 registration system in the UK, can also potentially enhance completeness of data, although there is under reporting of children with blindness and partial sight as the benefits do not apply until later on in life. In general, however, the most successful registers are those which provide information which is useful for and used by those who in turn contribute reliable and accurate data to them.

Conclusion

It is clear that registers can potentially answer questions about the health and educational needs of children in the population, and the effectiveness of preventive measures and screening programmes. They can contribute to the evaluation of treatment and services, and provide a framework for aetiological research. Indeed they form a vital part of the information infrastructure of the health service and should not be considered in isolation but recognised as complementary to other sources of information. It is time to consider whose responsibility it is to fund, maintain, and utilise these invaluable sources of information about the health of children.

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1 Donaldson L. Registering a need. *BMJ* 1992; **305:** 597–8.
2 Knox EG. Confidential medical records and epidemiological research. *BMJ* 1992; **304:** 727–8.
3 Information Management Group, NHS Management Executive. *An information management and technology strategy for the NHS in England.* London: Department of Health, 1992.
4 Colver AF, Robinson A. Establishing a register of children with special needs. *Arch Dis Child* 1989; **64:** 1200–3.
5 Woodruffe C, Abra A. A special conditions register. *Arch Dis Child* 1991; **66:** 927–30.
6 Hey K, O'Donnell M, Murphy M, Jones N, Botting B. Use of local neural tube defect registers to interpret national trends. *Arch Dis Child* 1994; **71:** 198–202.

7 Northern Regional Survey Steering Group. Fetal abnormality: an audit of its recognition and management. *Arch Dis Child* 1992; **67:** 770–4.
8 Office of Population Censuses and Surveys. *The OPCS monitoring scheme for congenital malformations: a review by a working group of the Registrar General's Medical Advisory Committee.* Occasional paper No 43. London: OPCS, 1995.
9 Mutton DE, Ide R, Alberman E, Bobrow M. Analysis of national register of Down's syndrome in England and Wales: trends in prenatal diagnosis. *BMJ* 1993; **306:** 431–2.
10 Grant DB, Smith I. Survey of neonatal screening for primary hypothyroidism in England, Wales and Northern Ireland 1982–84. *BMJ* 1988; **296:** 1355–8.
11 Beasley HG, Costello PM, Smith I. Outcome of treatment in young adults with phenylketonuria detected by routine neonatal screening between 1964 and 1971. *Q J Med* 1994; **87:** 155–60.
12 Johnson A, King R. A regional register of early childhood impairments: a discussion paper. *Community Medicine* 1989; **11:** 352–63.
13 Clark NMP. Diagnosing congenital dislocation of the hip [Editorial]. *BMJ* 1992; **305:** 435–6.
14 Pharaoh P, Cooke T, Cooke RW, Rosenbloom L. Birthweight specific trends in cerebral palsy. *Arch Dis Child* 1990; **65:** 602–6.
15 Swift PGF, Hearnshaw JR, Botha JL, Wright G, Raymond NT, Jamieson KF. A decade of diabetes; keeping children out of hospital. *BMJ* 1993; **307:** 96–8.
16 Report of a working group to the Royal College of Physicians Committee in ethical issues in medicine: independent ethical review of studies involving personal medical records. *J R Coll Physicians Lond* 1994; **28:** 439–43.
17 Evans JR, Wormald RPL. Epidemiological functions of BD8 certification. *Eye* 1993; **7:** 172–9.