Mortality and causes of death in persons with Down syndrome in California

Steven M Day* PhD;
David J Strauss PhD FASA;
Robert M Shavelle PhD MBA;
Robert J Reynolds MPH, Life Expectancy Project, San Francisco, CA, USA.

**Correspondence to first author at* Life Expectancy Project, 1439 17th Avenue, San Francisco, CA 94122-3402, USA.
E-mail: Day@LifeExpectancy.com

This study investigated mortality and causes of death between 1988 and 1999 in 14 781 persons (6702 female) with Down syndrome in California, comparing age, sex, ethnicity, and other factors. Mean age at the start of follow-up was 14 years 8 months (SD 14y 10mo). During the study period 600 persons died. The standardized mortality ratio (SMR) for the population was 5.5. Blacks were at greater risk than whites, Hispanics, or Asians (relative risk=1.5). Mortality declined during the period, especially for children with congenital heart defects. Leukemia (SMR=17), respiratory illnesses (SMR=27), congenital anomalies (SMR=72), and circulatory diseases (SMR=5.3) accounted for most of the excess mortality. With the exception of leukemia, cancer mortality was not different from that of the general population.

See end of paper for list of abbreviations.

It is well documented that persons with Down syndrome (DS) have higher mortality rates than the general population (Dupont et al. 1986, Baird and Sadovnick 1987, Eyman et al. 1991, Strauss and Eyman 1996, Strauss and Zigman 1996, Hayes et al. 1997, Hijii et al. 1997, Singer and Strauss 1997, Strauss and Shavelle 1998, Frid et al. 1999, Hermon et al. 2001, Yang et al. 2002). Death rates in DS have been shown to increase sharply after age 40 years (Dupont et al. 1986, Eyman et al. 1991, Strauss and Eyman 1996, Strauss and Shavelle 1998), while motor and cognitive skills decline (Strauss and Zigman 1996, Day 2001).

Survival in DS has improved over the past few decades (Dupont et al. 1986, Baird and Sadovnick 1987, Hayes et al. 1997, Eyman et al. 1991, Hermon et al. 2001, Glasson et al. 2002, Yang et al. 2002); one study has reported a life expectancy nearing 60 years (Glasson et al. 2002).

The most common causes of death in DS include leukemia, respiratory illnesses, congenital circulatory defects, diseases of the digestive system, Alzheimer's disease, and epilepsy (Hermon et al. 2001, Hill et al. 2003). Some have suggested that persons with DS might be at lower risk of some cancer morbidity or mortality (Hasle et al. 2000, Yang et al. 2002) than the general population, but other recent studies have found no significant difference for solid tumors (Hermon et al. 2001) or even a significant excess (Hill et al. 2003).

Racial or ethnic differences in mortality in DS were studied by Yang et al. (2002), who used death certificates to demonstrate that median age at death among blacks with DS was significantly lower than that of whites. In a population with DS in Western Australia, Leonard et al. (2000) found significantly poorer survival among Aboriginal children than among non-Aboriginal children, mirroring the pattern in the general population in Australia. Bishop et al. (1997) reported significant differences in rates of DS births among different racial groups (i.e. a higher rates in Hispanics compared with whites at maternal ages under 40 years), even after controlling for prenatal diagnosis and elective abortion.

Congenital heart defects (CHD) are common in DS, with incidence estimates ranging from 25 to 48%, perhaps depending in part on the method of diagnosis (Frid et al. 1999). Surgical repair of heart defects in children with DS has become more common over the past 20 years, resulting in improved survival in children with DS and CHD during this period (Reller and Morris 1998, Malec et al. 1999, Leonard et al. 2000).

The present study focused on the following questions: (1) do mortality rates and life expectancy in DS differ by ethnic group, (2) are mortality rates for DS continuing to fall, and (3) which causes of death are elevated in DS?

Method

PARTICIPANTS

Participants were drawn from persons receiving services from the Department of Developmental Services (DDS) in California between 1 January 1988 and 31 December 1999. Persons were identified as having DS based on an ICD-9 code (World Health Organization 1977) of 758, 758.0, or 758.00 on the Client Development Evaluation Report (CDER; DDS 1986). The CDER contains psychological, medical, functional, behavioral, and cognitive items. Reliability of the functional items and some medical items has been assessed and judged satisfactory (Citygate Associates 1998). According to Eyman et al.

(1991, p 605): 'Down syndrome is usually diagnosed at birth, and chromosomal studies are usually performed shortly thereafter. Regional Center physicians are responsible for confirming, or making, the diagnosis of Down syndrome and if karyotyping has not been carried out the physicians arrange for it to be performed'.

MORTALITY INFORMATION

Mortality information was obtained from the State of California annual electronic death records (State of California 1988–1999). For each age group the number of observed deaths divided by the number of person-years of exposure gave the mortality rate. Person-years were stratified to make univariate comparisons of mortality rates. Logistic regression on person-years was used to make controlled comparisons. In this method, each person-year is associated with an outcome variable, such as death, and explanatory variables such as sex, age, ethnicity, or calendar year. This person-year approach has been used frequently in the Framingham heart study (Cupples et al. 1998) and elsewhere (Strauss et al. 1999, 2000).

EXPOSURE

Exposure was calculated as the time from first CDER indicating DS until the earliest of the following: (1) date of death, (2) end of the study period (31 December 1999), or (3) 3 years after the last CDER. The third criterion was included to reduce potential bias owing to the migration of persons from California. Deaths of such people would not appear in our records, but because of the third condition the exposure time during which they might have died would be brief.

STATISTICS

Comparisons of mortality rates across different ethnic or racial groups were made in pairwise fashion, controlling for age with Cochran–Mantel–Haenszel statistics. Observed deaths and exposure were sufficient to obtain reliable estimates of mortality rates for the study group up to ages 65 to 69 years. Beyond age 69 years the relative risk from the age group 65 to 69 years was used to adjust mortality rates in the US general population (mixed 60% male to 40% female to match the study population). Life tables based on resulting mortality rates at all ages were constructed by standard methods (Anderson 1999).

Table I: First evaluation at age 2 years or older of persons with Down syndrome

Parameter	*Number*	*%*
All persons (*n*=14 781)		
Condition		
Congenital heart defect	1709	11.6
Epilepsy	249	1.7
Tube fed	121	0.8
Leukemia	28	0.2
Ethnicity		
White	6412	43.4
Hispanic	5231	35.4
Asian	675	4.6
African American	771	5.2
Other/missing	1692	11.4
Sex		
Male	8079	54.7
Female	6702	45.3
Ages 10 and older only (*n*=9890)		
Walking		
Does not walk	166	1.7
Walks only with support	164	1.7
Walks unsteadily alone at least 10 feet	341	3.4
Walks well alone at least 20 feet, balances well	9219	93.2
Level of mental retardation[a]		
None	88	0.9
Mild	2438	25.1
Moderate	4245	43.7
Severe	1638	16.9
Profound	773	8.0
Suspected/undetermined	524	5.4
Word usage		
No use of words	1198	12.1
Uses simple (one-syllable) words and associates words with appropriate objects	4476	45.3
Uses complex words and associates words with appropriate objects, but has a limited vocabulary	3320	33.6
Has a broad vocabulary, understands meaning of words and uses them in appropriate contexts	896	9.1

[a]UK usage: learning disability.

Table II: Mortality rates for 14 781 persons with Down syndrome

Age (y)	*Exposure (person–years)*	*Observed deaths*	*Mortality rate*[a]
2–4	14 888	54	0.0036
5–9	20 233	39	0.0019
10–14	11 992	25	0.0021
15–19	8342	16	0.0019
20–24	8684	27	0.0031
25–29	8066	32	0.0040
30–34	6623	39	0.0059
35–39	5680	36	0.0063
40–44	4408	47	0.0107
45–49	2941	77	0.0262
50–54	1758	66	0.0375
55–59	976	55	0.0564
60–64	480	54	0.1124
65–69	156	25	0.1602
70–74	70	6	0.0861
75–79	4	2	0.4807
All	95 301	600	0.0063

[a]Observed deaths divided by exposure.

Table III: Abbreviated life table for whites, Hispanics, and Asians with Down syndrome, including those with chronic heart defects, leukemia, and those requiring tube feeding

Age (y)	*L (n)*	*MR*	*LE (y)*
2	100 000	0.0036	53.5
5	99 084	0.0015	51.0
10	98 136	0.0021	46.4
20	96 070	0.0024	37.3
30	92 984	0.0054	28.4
40	87 414	0.0099	19.9
50	73 900	0.0375	12.4
60	46 566	0.1121	6.7
70	11 789	0.2159	3.7
80	458	0.5163	1.8

L, number living at beginning of age interval; MR, mortality rate during age interval (deaths per person-year); LE, life expectancy at beginning of age interval.

We tested for a decline in age-specific mortality rates during the study period by stratifying the occurrence and exposure data by age and by two time periods, 1988 to 1993 and 1994 to 1999. This was performed separately for persons with and without CHD.

Cause-specific death rates in DS were compared with those in the Californian general population by the following method. (1) For each cause of death considered, age-specific mortality rates (deaths per 100 000 person-years of exposure) in the Californian general population were computed from state mortality data (State of California 1988–1999) and population data (State of California, Department of Finance 1988) over the period 1988 to 1999. (2) For the persons with DS the total number of person-years at risk of death, or exposure time,

Table IV: Comparison of mortality rates for persons with Down syndrome with and without congenital heart defects (CHD)

Age (y)	*No CHD*			*CHD*			*CHD vs No CHD*		*p*
	Exposure[a]	*Deaths*[b]	*Mortality rate*[c]	*Exposure*[a]	*Deaths*[b]	*Mortality rate*[c]	*RR*	*EDR*[e]	
2–4	11728	36	0.0031	3160	18	0.0057	1.9	0.0026	<0.05
5–9	16621	27	0.0016	3612	12	0.0033	2.0	0.0017	<0.05
10–19	18553	31	0.0017	1781	10	0.0056	3.4	0.0039	<0.001
20–29	15842	47	0.0030	909	12	0.0132	4.5	0.0102	<0.001
30–39	11673	57	0.0049	630	18	0.0286	5.8	0.0237	<0.001
40–49	7069	112	0.0158	280	12	0.0429	2.7	0.0270	<0.001
50+	3336	198	0.0593	108	10	0.0930	1.6	0.0336	*ns*
All	84822	508	0.0060	10479	92	0.0088	1.5	0.0028	<0.001

p values are based on a χ^2 variable with 1 degree of freedom and a null hypothesis that a CHD has no effect on mortality. RR, relative risk, equal to ratio of mortality rates for CHD and no CHD. EDR, excess death rate; *ns*, not significant. [a]Number of person-years, rounded to nearest year. [b]Observed number of deaths. [c]Mortality rate, equal to observed deaths divided by exposure. [e]Excess death rate, equal to difference between mortality rates for CHD and no CHD.

Table V: Cause-specific mortality in persons with Down syndrome compared with general population of California

Cause of death (ICD-9 codes)	*Observed deaths*	*Expected deaths*[a]	*SMR*[b]	*95% CI*[c]
All malignant neoplasms (140–208)	44	19.9	2.2	(1.6–3.0)
Leukemia (204–208)	26	1.5	17.0	(11–25)
Lung, bronchus (162)	0	4.0	0.0	(0.0–0.8)
Other	18	14.4	1.3	(0.7–2.0)
All congenital anomalies (740–759)	194	2.7	71.7	(62–82)
Of circulatory system (745–748)	75	0.8	93.6	(74–117)
Down syndrome (758)	115	0.1	1605.9	(1312–1899)
Other	4	1.8	2.2	(0.6–5.6)
All circulatory diseases (390–459)	92	17.3	5.3	(4.3–6.5)
Ischemic heart disease (410–414)	31	7.3	4.3	(2.9–6.1)
Pulmonary circulatory disease (415–417)	5	0.4	12.0	(3.9–28)
Cerebrovascular disease (430–438)	20	2.7	7.5	(4.6–12)
Arteries, arterioles, capillaries (440–448)	6	0.6	9.4	(3.4–20)
Other	30	6.3	4.8	(3.2–6.8)
All respiratory diseases (460–519)	111	4.2	26.6	(22–32)
Pneumonia, not aspiration (480–487)	77	1.4	53.8	(42–63)
Aspiration pneumonia (507)	12	0.1	140.4	(73–245)
Other	22	2.6	8.3	(5.2–13)
All nervous system, sense organs (320–389)	24	3.3	7.3	(4.7–11)
Alzheimer's disease (331)	8	0.1	154.6	(67–305)
Epilepsy, convulsions (345)	5	0.3	14.3	(4.6–33)
Other	11	2.9	3.8	(1.9–6.8)
All digestive system (520–579)	24	4.9	4.9	(3.1–7.2)
Cirrhosis and other liver diseases (571)	5	3.1	1.6	(0.5–3.7)
Other	19	1.8	10.4	(6.3–16)
All endocrine, nutritional, metabolic (240–279)	10	2.5	4.0	(1.9–7.3)
Diabetes mellitus (250)	6	1.5	4.1	(1.5–8.9)
Other	4	1.0	3.8	(1.0–9.8)
All accidents (800–949)	30	21.8	1.4	(0.9–2.0)
Inhalation of foreign body (911–912)	8	0.2	52.7	(23–104)
Other	22	21.7	1.0	(0.6–1.5)
All other causes	71	32.8	2.2	(1.7–2.7)

[a]Age-adjusted expected number of deaths in general California population for same age and sex distribution. [b]Ratio of observed number of deaths to expected number. [c]Confidence interval based on assumption that observed deaths follow a Poisson distribution. ICD-9 codes, International Statistical Classification of Diseases, Injuries and Causes of Death, 9th revision (World Health Organization 1977); SMR, standardized mortality ratios.

was determined. (3) Mortality rates from step 1 were applied to the exposure times in step 2 to determine expected numbers of deaths due to each cause for each age group. (4) The observed number of deaths due to each cause in the DS population at each age group was noted. (5) Standardized mortality ratios (SMRs) were computed for each age group as the ratio of the observed number of deaths to the expected number (Kahn and Sempos 1989). By summing observed and expected numbers over age groups, overall SMRs for each cause were computed. (6) Confidence intervals (CIs) for the SMRs, based on the assumption that the observed number of deaths follows a Poisson distribution, were derived by using the tables given in Brackenridge and Elder (1998).

By determining causes of death in the DS group using the same source of mortality information as in the general California population, the effect on resulting SMRs of various sources of potential reporting bias was minimized.

ETHICAL APPROVAL

This study received ethical approval from the Institutional Review Board of the Office of Research Affairs, University of California, Riverside.

Results

Table I describes the 1988 to 1999 study population of 14 781 persons with DS. There were 600 deaths among persons with DS during the study period. Table II provides the person-years of exposure, observed numbers of deaths, and mortality rates by age group for the entire study population. Mortality rates did not differ significantly by sex, and deaths and exposure were combined across sexes for subsequent analyses. No significant difference in mortality rates among whites, Hispanics, and Asians with DS was found, and these three groups were combined for further comparisons. Although mortality rates for blacks did not differ significantly from other ethnic groups within any age stratum, overall mortality rates for blacks were higher than for the white/Hispanic/Asian group: Cochran–Mantel–Haenszel common odds ratio 1.53 (95% CI 1.04 to 2.27). For these comparative analyses, person-years were excluded for those with CHDs, leukemia, or those who had ever been tube fed.

Table III is the life table for the white/Hispanic/Asian group with DS, giving a life expectancy of 53.5 additional years for 2-year-olds with DS. Exposure and numbers of observed deaths for blacks were insufficient to give reliable estimates of mortality rates in some age strata, but adjusting mortality rates for the white/Hispanic/Asian group according to the common odds ratio of 1.53 resulted in a life table for blacks (not shown) with a life expectancy of 48.7 additional years for 2-year-olds. This is 9% less than for the white/Hispanic/Asian group. By comparison, 2-year-old blacks in the US general population have a life expectancy 8% less than that of whites.

Persons with DS and CHD had significantly higher mortality rates than those without CHD. Table IV shows the rates for each group, relative risks, and excess death rates.

Mortality rates were lower in the later half of the study period (1994 to 1999) than in the earlier part (1988 to 1993). Differences were generally not significant within an age stratum, although children aged 2 to 4 years with CHD presented a notable exception (earlier to later relative risk=6.1, $p<0.001$). Cochran–Mantel–Haenszel statistics showed a significant secular trend overall, with common odds ratios comparing mortality rates in the later period with those in the earlier of 0.54 (95% CI 0.35 to 0.81) for persons with CHD and 0.75 (95% CI 0.63 to 0.90) for those without.

Table V gives observed and age-adjusted expected numbers of deaths due to specific causes, with expected numbers based on Californian general population mortality rates for 1988 to 1999. In all, there were 600 deaths observed and 109.5 expected, giving an overall SMR of 5.5 and a total of 491 more deaths than expected. Excluding 115 deaths in which the underlying cause was 'Down syndrome', there remained 376 excess deaths. Causes of death accounting for 78% of these 376 excess deaths were leukemia ($n=17$, SMR=17, 95% CI 11 to 25), congenital anomalies of the circulatory system ($n=75$, SMR=94, 95% CI 74 to 117), respiratory diseases ($n=111$, SMR=27, 95% CI 22 to 32), and diseases of the circulatory system, other than congenital ($n=92$, SMR=5.3, 95% CI 4.3 to 6.5).

Cancers other than leukemia accounted for 18 deaths, with 18.4 deaths expected (SMR=1, not significant). No one in the study died of lung cancer, although four deaths were expected.

Discussion

Our study finding that mortality rates did not differ by sex is consistent with previous work (Thase 1982, Strauss and Eymann 1996), although a recent Australian study found lower rates for males (Glasson et al. 2002).

Consistent with Yang et al. (2002), we found higher mortality in blacks than in whites, a pattern consistent with that of the US general population. The reason for this difference in DS, as

Table VI: Comparison of standardized mortality ratios between studies

Cause of death	*Standardized mortality ratio*		
	Present study (n=600)	*Hermon et al. (2001; n=622)*	*Hill et al. (2003; n=742)*
Leukemia	17	13	33
Other malignant neoplasms	1.0 (18)	1.8 (6)	4.6 (16)
Diabetes	4.1	11.4	9.8
Alzheimer's disease	155	220	54[a]
Pneumonia	54	30	83
Ischemic heart disease	4.3	1.1	3.9
All causes, including Down syndrome	5.5	6.22	11.1
All causes, excluding Down syndrome	4.4	–	7.8

Results in parentheses are numbers of deaths. [a]Includes dementia. –, information on Down syndrome as cause of death not provided.

in the general population (Guralnik et al. 1993, Wong et al. 2002) remains unclear and warrants further investigation.

Our results on causes of death largely agree with two other recent studies (Hermon et al. 2001, Hill et al. 2003). Table VI compares the three studies. Differences may be attributable to different age distributions, sampling variation, different methods of coding causes of death, or possible biases in identifying causes of death.

The significantly small number of observed deaths due to lung cancer (observed=0, expected=4) might be explained by the low incidence of tobacco use in the DS population, as suggested by Hasle et al. (2000). The number of cancer deaths other than leukemia was similar to that expected in the general population, contrary to Yang et al. (2002) but consistent with others (Hermon et al. 2001, Hill et al. 2003).

In our population of persons with DS, the proportion with CHD was about 12%. This is lower than other studies have suggested (Frid et al. 1999). The difference might be partly due to the fact that the CDER does not identify mild cases of CHD. According to the CDER manual (California Department of Developmental Services 1986, chapter VII, section 12, p 1) a medical condition included in a client's annual report 'indicates the presence of major, chronic medical problems that limit or impede the client or significantly impact the provision of services'. Mild CHD or a successfully repaired CHD might have little impact on a patient's well-being (Hijii et al. 1997) and thus might not be noted on the CDER.

It was not surprising to find that persons with CHD had higher mortality rates than those without. This difference was substantially *larger* in adults than in children: adults with CHD were subject to an extra mortality rate of about 10 deaths per 1000 person-years at ages 20 to 29 years, rising to more than 34 deaths per 1000 person-years at age 50 years and above. A trend over time toward more frequent repair of CHD in DS children, or recent improvements in surgical techniques, might explain this pattern. Another possible explanation is that the adverse effect of CHD might become worse with increasing age. In either case, this finding could have implications for possible surgical treatment of adults with CHD.

The decline in mortality over time has been reported by others (Dupont et al. 1986, Baird and Sadovnick 1987, Eyman et al. 1991, Hayes et al. 1997, Hermon et al. 2001, Yang et al. 2001). In the present study, death rates declined markedly among children 2 to 4 years of age with CHD, from 10.6 deaths per 1000 person-years in the earlier period (1988 to 1993) to 1.7 per 1000 in the later period (1994 to 1999). A smaller, but still statistically significant, decline was observed for older children. However, no significant trend was observed for adult mortality. As noted above and elsewhere, this finding might be explained in part by increasing surgical repair of CHD in children with DS, and by improvements in surgical procedures (Reller and Morris 1998, Malec et al. 1999, Leonard et al. 2000). Because we do not currently have information in our database indicating whether a person's heart defect was surgically repaired, we were unable to explore this conjecture.

Mortality rates of persons with DS remain higher overall than those of the general population with many, though not all, major causes of death contributing to the difference. The findings reported here suggest many further questions and research opportunities, especially regarding the causal mechanisms of the mortality differences, including possible genetic links to aging or cancer. The findings here and in the future may have important implications for persons with and without DS.

DOI: 10.1017/S0012162205000319

Accepted for publication 19th May 2004.

Acknowledgement
We thank Dr Quanhe Yang, Dr Sonja Rasmussen, and Dr JM Friedman for their valuable comments and suggestions during the early stages of this research.

References

Anderson RN. (1999) United States Life Tables, 1997. *National Vital Statistics Reports Vol. 47 No. 28.* Hyattsville, MD: National Center For Health Statistics.

Baird PA, Sadovnick AD. (1987) Life expectancy in Down syndrome. *J Pediatr* **110:** 849–854.

Bishop J, Huether CA, Torfs C, Lorey F, Deddens J. (1997) Epidemiologic study of Down syndrome in a racially diverse California population, 1989–1991. *Am J Epidemiol* **145:** 134–147.

Brackenridge RDC, Elder JW, editors. (1998) *Medical Selection of Life Risks.* 4th edn. New York: Stockton Press.

California Department of Developmental Services. (1986) *Client Development Evaluation Report (CDER).* Sacramento, CA: California Department of Developmental Services.

Citygate Associates. (1998) *Independent Evaluation of the Department of Developmental Services' Community Placement Practices: Final Technical Report.* Sacramento, CA: Citygate Associates.

Cupples LA, D'Agostino RB, Anderson K, Kannel WB. (1998) Comparison of baseline and repeated measure covariate techniques in the Framingham Heart Study. *Stat Med* **7:** 205–222.

Day SM. (2001) Estimators of long-term transition probabilities in multistate stochastic processes. (PhD dissertation.) University of California at Riverside.

Dupont A, Vaeth M, Videbech P. (1986) Mortality and life expectancy of Down's syndrome in Denmark. *J Ment Defic Res* **30:** 111–120.

Eyman RK, Call TL, White JF. (1991) Life expectancy of persons with Down syndrome. *Am J Ment Retard* **95:** 603–612.

Frid C, Drott P, Lundell B, Rasmussen F, Anneren G. (1999) Mortality in Down's syndrome in relation to congenital malformations. *J Intellect Disabil Res* **43:** 234–241.

Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, Bittles AH. (2002) The changing survival profile of people with Down's syndrome: implications for genetic counselling. *Clin Genet* **62:** 390–393.

Guralnik JM, Land KC, Blazer D, Fillenbaum GG, Branch LG. (1993) Educational status and active life expectancy among older blacks and whites. *N Engl J Med* **329:** 110–116.

Hasle H, Clemmensen IH, Mikkelsen M. (2000) Risks of leukaemia and solid tumours in individuals with Down's syndrome. *Lancet* **355:** 165–169.

Hayes C, Johnson Z, Thornton L, Fogarty J, Lyons R, O'Connor M, Delany V, Buckley K. (1997) Ten-year survival of Down syndrome births. *Int J Epidemiol* **26:** 822–829.

Hermon C, Alberman E, Beral V, Swerdlow AJ, for The Collaborative Study Group of Genetic Disorders. (2001) Mortality and cancer incidence in persons with Down's syndrome, their parents and siblings. *Ann Hum Genet* **65:** 167–176.

Hijii T, Fukushige J, Igarashi H, Takahashi N, Ueda K. (1997) Life expectancy and social adaptation in individuals with Down syndrome with and without surgery for congenital heart disease. *Clin Pediatr (Phila)* **36:** 327–332.

Hill DA, Gridley G, Cnattingius S, Mellemkjaer L, Linet M, Adami H, Olsen JH, Nyren O, Fraumeni JF. (2003) Mortality and cancer incidence among individuals with Down syndrome. *Arch Intern Med* **163:** 705–711.

Kahn HA, Sempos CT. (1989) *Statistical Methods in Epidemiology.* Oxford: Oxford University Press.

Leonard S, Bower C, Petterson B, Leonard H. (2000) Survival of infants born with Down's syndrome: 1980–1996. *Paediatr Perinat Epidemiol* **14:** 163–171.

Malec E, Mroczek T, Pajak J, Januszewska K, Zdebska E. (1999) *Pediatr Cardiol* **20:** 351–354.

Reller MD, Morris CD. (1998) Is Down syndrome a risk factor for poor outcome after repair of congenital heart defects? *J Pediatr* **132:** 738–741.
Singer RB, Strauss D. (1997) Comparative mortality in mentally retarded patients in California with and without Down's syndrome, 1986–1991. *J Insur Med* **29:** 172–184.
State of California, Department of Finance. (1988) *Race/ethnic Population with Age and Sex Detail, 1970–2040.* Sacramento, CA: State of California, Department of Finance.
State of California. (1988–1999) *Department of Health Services, Center for Health Statistics, Office of Health Information and Research Annual Electronic Death Records.* Sacramento, CA: State of California, Department of Health Services.
Strauss D, Eyman RK. (1996) Mortality of people with mental retardation in California with and without Down syndrome, 1986–1991. *Am J Ment Retard* **100:** 643–653.
Strauss D, Shavelle R. (1998) Life expectancy of persons with chronic disabilities. *J Insur Med* **30:** 96–108.
Strauss DJ, Shavelle RM, Ashwal S. (1999) Life expectancy and median survival time in the permanent vegetative state. *Pediatr Neurol* **21:** 626–631.
Strauss D, Shavelle R, DeVivo MJ, Day S. (2000) An analytic method for longitudinal mortality studies. *J Insur Med* **32:** 217–225.
Strauss D, Zigman WB. (1996) Behavioral capabilities and mortality risk in adults with and without Down syndrome. *Am J Ment Retard* **101:** 269–281.
Thase ME. (1982) Longevity and mortality in Down's syndrome. *J Ment Defic Res* **26:** 177–192.
Wong MD, Shapiro MF, Boscardin WJ, Ettner SL. (2002) Contribution of major diseases to disparities in mortality. *N Engl J Med* **347:** 1585–1592.
World Health Organization. (1977) *International Statistical Classification of Diseases, Injuries, and Causes of Death.* 9th Revision. Geneva:World Health Organization.
Yang Q, Rasmussen SA, Friedman JM. (2002) Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. *Lancet* **359:** 1019–1025.

List of abbreviations

CDER	Client Development Evaluation Report
CHD	Congenital heart defects
DDS	Department of Developmental Studies
DS	Down syndrome
SMR	Standardized mortality ratio