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Hospitalizations among persons with Down syndrome: a national cohort study in Denmark

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Summary

Background—Most persons with Down syndrome (DS) now survive to adulthood, but their health care needs beyond childhood are not well described. We examined hospitalizations among persons with DS in Denmark.

Methods—We followed 3,212 persons with DS (1910-2007), identified from the Danish Cytogenetic Register, and a random sample of persons without DS from the general population (as comparison group), through the National Hospital Register from January 1, 1977, to May 31, 2008. Poisson regression was used to calculate rate ratios for numbers of overnight hospital admissions and hospital days.

Findings—During this time period, persons with DS had more than twice the rate of hospital admissions and nearly three times as many bed-days as the population as whole. Malformations, diseases of the respiratory system, and diseases of the nervous system or sensory organs were the principal indications for hospital admissions. The higher rate ratios for hospital admissions were mainly seen among persons less than 20 years of age, and hospitalization for neoplasms or for diseases of the musculoskeletal system or connective tissue was much less frequent than expected among adults with DS. Persons with DS who had congenital heart defects were far more likely to be hospitalized than those without.

Interpretation—Persons with DS in Denmark are hospitalized more frequently and for more days than persons without DS; however, hospitalization usage differs by age (with a higher burden at younger ages) and by presence of a congenital heart defect. As survival among persons with DS

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continues to improve, these data are helpful for health care planning, although results may be different within other health care systems.

Keywords

Down syndrome; hospitalization; comorbidity; congenital heart defects

Introduction

Down syndrome (DS), caused by an extra copy of the genetic material on chromosome 21, is the most common identifiable genetic cause of cognitive impairment, occurring in approximately one in 700 births.[1] People with DS have congenital heart defects,[2] and gastrointestinal tract defects more often than the general population.[3,4] In addition, some studies show that persons with DS are at increased risk for other health problems,[5] including childhood leukemia,[6] hypothyroidism,[7] infectious diseases,[8,9] certain autoimmune disorders like celiac disease and diabetes,[7,10] and Alzheimer's disease.[11]

Most people with DS in countries with good health care now survive to adulthood,[12,13] and planning for their health care requires information on the health problems they experience as they age.[14-16] Most information about health conditions and health care utilization for persons with DS is still limited to childhood,[17-19] and most studies are based on small sample sizes. In addition, studies on DS co-morbidities are often done using selected clinical samples,[20] that may not be representative of all people with DS.

We conducted a population-based follow-up study using nationwide Danish health registry data collected prospectively as part of routine health care to examine patterns of hospitalizations among children and adults with DS in comparison to the general population.

Methods

Study design

This is a national register-based follow-up study of people with DS in Denmark. First, a cohort of all persons with DS was identified using the Danish Cytogenetic Register. Then a reference cohort was randomly selected from the general population in the Civil Registration System, matching on birth year. The DS and reference cohorts were linked to a number of national registers, including the Civil Registration System and the National Patient Register. All data linkages were based upon the unique personal identification number assigned to each Danish resident since 1968. The personal identification number includes information on birth date and sex and allows complete follow-up for death, emigration, and hospitalizations.

Identification of persons with DS

The Danish Cytogenetic Register was founded in 1968 to collect information on constitutional chromosomal abnormalities in Denmark. The register is based on reports from cytogenetic laboratories throughout the country and provides virtually complete coverage of constitutional chromosomal abnormalities diagnosed in Denmark since 1961. The

Cytogenetic Register contained information on 3551 individuals with a postnatal cytogenetic diagnosis of DS by 2007 (i.e. including those who were born before April 1968 and alive on April 1, 1968 and those who were born between April 1968 and December 2007). A karyotype based on a peripheral blood sample was available from all patients. All reported karyotypes were reviewed (by SAR, JMF and HH), with five patients reclassified as not having trisomy 21 and 16 individuals excluded because they had another cytogenetic aberration (such as XYY, XXY, XXX, translocations, inversions, or deletion). We also excluded 114 patients with mosaic trisomy 21, 198 patients who died or emigrated before January 1, 1977, and six patients who died on the date of birth. A total of 3212 patients with non-mosaic DS (born between 1910 and 2007), including 3075 with standard trisomy 21 and 137 with Robertsonian translocations, remained for analysis (Table 1).

Selection of reference cohort

Based on the initial cohort of persons with DS (n=3551), 71020 persons without DS were randomly selected from the Civil Registration System, with a sampling frame of 20:1 and matching on birth year. With the subsequent exclusion of 135 cases with DS from the initial cohort (see above), 2700 matched persons in the reference cohort were dropped. We also excluded from the reference cohort 1074 persons who died or emigrated before January 1, 1977, and 42 persons who died on the date of birth, resulting in 67,204 individuals available for comparison in the final reference cohort (Table 1).

Data on hospitalizations

Data on hospitalizations were obtained by data linkage to the National Patient Register using the unique personal identification numbers. The National Hospital Register has collected nationwide data on all hospital admissions since 1977. Up to 20 diagnoses for each admission were recorded in the register, using the 8th Revision of International Classification of Diseases (ICD8) before 1994 and the 10th Revision of International Classification of Diseases (ICD10) since 1994. Diseases were categorized on organ systems (Table 2).

We included all data on inpatient hospitalizations lasting more than one day (i.e., the discharge date was different from the admission date) between January 1, 1977, and May 31, 2008. We used all available information on diagnoses related to each hospitalization; one hospitalization counted once for “any” hospitalization and also counted in all relevant disease categories. Outpatient use is not included in this analysis.

Information on covariates and civil status

Information on sex (female, male) and date of birth (before April 1968, 1968-1979, 1980-1989, 1990-1999, 2000-2007) was extracted from the personal identification number. Information on congenital heart defect (ICD8: 746-747·4; ICD10: Q20-Q26) was obtained from the National Hospital Register, and information on vital status and emigration was obtained from the Civil Registration System.

Data analysis

We used Poisson regression to calculate rate ratios for the frequency of hospital admissions and number of hospital days among persons with DS compared with the reference cohort. Follow-up started at the date of birth for those born after January 1, 1977, or was left-truncated at January 1, 1977, for those born before that date, and ended at date of death, date of emigration, or end of follow-up (May 31, 2008), whichever came first. DS is present at birth and, although not always diagnosed immediately, we started our observation at birth, assuming that all children with DS who died would be diagnosed prior to death. We used a robust method to calculate 95% confidence intervals, accounting for the dependence between hospitalizations within each person. We included sex and birth cohort as covariates in the Poisson regression models, and we also included age group as a covariate for analyses among all persons.

First, we performed Poisson regression analyses for hospital admission for any reason, comparing individuals with DS to the reference cohort at any age and within each age group (<1, 1-4, 5-19, 20-49, and 50+ years). Then we conducted Poisson regression analyses for hospital admission for each disease category, comparing individuals with DS to the reference cohort at any age and within each age group. Next, we performed similar analyses on hospital days. Finally, we estimated associations of sex, age group, birth cohort, and congenital heart defects with the overall frequency of hospital admission and number of hospital days among persons with DS. All analyses were performed with STATA software (version SE 9·2).

Role of the funding source

The US federal government, the funding source for this study, employs some of the study authors (AC, DS, and SAR). The report received approval for publication from other employees of the US government. The first author had full access to all data in the study and he and the other authors had final responsibility for the decision to submit for publication.

Results

We followed 3,212 persons with DS for more than 30 years (from January 1, 1977 to May 31, 2008), and recorded a total of 16,815 hospital admissions and 108,042 hospital days over 63,489 person-years at risk. Among 67,204 individuals in the population-based reference cohort matched for birth year and followed over the same time period, there were 186,416 hospital admissions and 980,246 hospital days over 1,520,470 person-years at risk.

Overall, persons with DS were admitted to hospital more than twice as often as the reference population (Table 3). The most common reasons for hospitalization among people with DS were malformations, diseases of the respiratory system, and diseases of the nervous system or sensory organs. Hospitalization for most causes was more frequent than expected among people with DS, compared to the reference cohort. For example, the rate ratio for hospitalization due to malformations (excluding chromosomal abnormalities) among people with DS was 22·7 (95% CI 21·7-23·7). The rate ratios of hospital admissions for diseases of the respiratory system and for diseases of the nervous system or sensory organs were five

times higher among persons with DS than those seen in the reference cohort. The highest rate ratios of hospital admission for persons with DS were seen before 20 years of age for almost all disease categories (Table 3). The rate ratios of hospitalization for neoplasms or diseases of the musculoskeletal system or connective tissue were lower than expected among adults with DS.

The pattern seen with days of hospitalization was similar, but the overall rate ratio for people with DS was even higher (2·7, 95% CI 2·6-2·8) (Table 4). Many diseases contributed to this high use, but malformations play an especially important role, and diseases of the respiratory system and diseases of the nervous system or sensory organs are very frequently responsible. The higher than expected use of hospital days in people with DS was mainly in the first five years of life. Strikingly low rate ratios for days of hospitalization were seen for neoplasms (0·1, 95% CI 0·1-0·2) or for diseases of the musculoskeletal system or connective tissue (0·2, 95% CI 0·1-0·3) among persons with DS over 50 years of age.

Analyses among DS persons showed that males had slightly more hospital admissions and used more bed-days than females. Children with DS under five years of age had the highest rate ratios for hospital admissions and for bed-days, whereas adults with DS aged 20-49 years had the lowest rate ratios for admissions and for bed-days. The age-adjusted rate of hospital admission remained constant for those born in 1970s and later, but use of bed-days decreased with time. Persons with DS who had congenital heart defects had more hospital admissions and used more bed-days than persons with DS but no cardiac malformations (Table 5).

Discussion

In this historical population-based study that covers over 30 years of observation in Denmark, we found that people with DS had more overnight hospital admissions and spent more days in hospital than the general population, especially before the age of 20. Malformations, diseases of the respiratory system, and diseases of the nervous system or sensory organs were the main reasons for hospitalization, and persons with DS who also had congenital heart defects were often hospitalized than persons with DS but no cardiac malformations. The rate ratios of hospitalization for neoplasms or for diseases of the musculoskeletal system or connective tissue were much lower than expected among adults with DS. Use of hospital bed-days decreased over time among people with DS, following a general population trend.[21]

Our results were obtained in the Danish health care system with tax-paid hospital care to all residents free of charge, but our findings are generally consistent with reports from other countries or regions. A study of 117 children with DS aged 6-14 years in the United Kingdom reported that 88% of the children had been hospitalized at some time in their life, compared with 45% of children aged 11 years in the general population.[22] Among 196 neonates with DS who participated in a two-year randomized clinical trial in Holland, the hospital admission rate was about 2·8 times higher than expected in the neonatal period and about 2·2 times higher than expected thereafter.[19] A study in the United States that used Tennessee Hospital Discharge Data System records from 1997 through 2002 showed that

children with DS had been hospitalized in the first year of life at a rate 4·1 times that expected nationally.[18] A recent study examining health insurance hospital discharge claims in Taiwan in 2005 reported that the annual length of stay in hospital was twice as great for persons with DS as for the general population.[23] Date from 120 Israeli adults with DS who were hospitalized at Hadassah Medical Centers during the years 1988-2007 revealed a similar trend.[24]

Our findings differ, however, from two previous studies from Denmark,[25,26] which suggested that the number of hospital admissions was higher for 41-50-year-old adults with DS,[25] but not for adolescents with DS,[26] in comparison to the general population. However, both of these earlier studies included very small numbers of persons with DS identified in a Danish county (38 adults and 43 adolescents with DS).

Our findings indicating lower rates of hospitalization in recent years are consistent with recent studies from Sweden and Australia. The Swedish study identified 211 children with DS from registers and followed them up to 24 years of age. The authors found that the children with DS born between 1995 and 1998 had a shorter mean duration of neonatal and postneonatal care in hospital than those born between 1973 and 1980.[17] The Australian study used data from two cross-sectional surveys in school-aged children with DS (5-17 years old) and found fewer bed-days per hospital admission in 2004 than in 1997.[27]

We found that malformations, diseases of the respiratory system, and diseases of the nervous system or sensory organs were the main reasons for hospitalization among people with DS. This is in accordance with most studies.[17-20,22,27-29] Our finding that persons with DS who have congenital heart defects were more likely to be hospitalized and to stay longer in the hospital than persons with DS but no cardiac malformations is also in agreement with previous reports.[17,18,20]

We found lower than expected rates of hospital admission and of days of hospitalization for neoplasms and diseases of the musculoskeletal system or connective tissue among adults with DS, especially those over 50 years of age. Common musculoskeletal diseases of later life such as osteoarthritis and osteoporosis are frequent among older adults with Down syndrome,[30-32] so the low rate ratio for hospitalization related to musculoskeletal conditions in this age group is surprising. On the other hand, we were not surprised to find that hospitalization for neoplasia was infrequent among older adults with Down syndrome. The incidence of solid tumours[33,34] and deaths from malignant neoplasms other than leukemia[13] have been reported to be much less frequent than expected among older adults with DS, and a recent health survey of older persons with DS also noted a low rate of cancer.[31]

Our study had a number of strengths. We identified an unselected national cohort of persons with DS and followed them over an extended period. The Danish Cytogenetic Register includes all persons diagnosed with DS during the study period in Denmark, and all patients had cytogenetic confirmation. We excluded persons with mosaic DS, because they had better survival compared to persons with non-mosaic DS[35] and the number of persons with mosaic DS was too small for separate analysis. Our study included a random sample from the general population as a reference group. Information on hospitalizations for persons with

DS and the comparison population was obtained from the Danish National Hospital Register by using unique personal identification numbers.

Our study also has some limitations. Some errors in coding are likely to occur in the Danish National Hospital Register; however, we expect that the rate of errors would be similar among persons with and without DS. If hospitalization leads to a cytogenetic diagnosis of DS for persons born before 1968, some overestimation of health problems among these older persons with DS may have occurred. However, in more recent decades, most persons with DS in our cohort were diagnosed within the first year of life.

Our data show that persons with DS had more hospital admissions and more days hospitalized than the general population in Denmark, and that this was most pronounced during their childhood and adolescence. These population-based findings have important implications for planning health care as survival among persons with DS improves.

Panel: Research in Context

Systematic review

We searched PubMed in January 2012 for reports that contained the terms “Down syndrome” and “hospitalization” as well as relevant articles cited by these reports. Almost all previous studies on hospitalization are limited to children with DS, and most are based on small sample sizes.

Interpretation

In this national cohort study that followed 3,212 Danish persons with DS for more than 30 years, we found that people with DS had more overnight hospital admissions and spent more days in hospital than the general population, in particular before the age of 20 years. Hospitalizations for most causes were more frequent among persons with DS than among persons without DS, while hospitalizations for neoplasms and for diseases of the musculoskeletal system or connective tissue occurred less commonly among adults with DS than among the general Danish population.

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Table 1

Distribution of persons with Down syndrome and reference population by sex and birth year, Denmark, 1977-2008

	Persons with Down syndrome		Reference population	
	n	%	n	%
Total	3212	100·0	67204	100·0
Sex				
Female	1450	45·1	32865	48·9
Male	1762	54·9	34339	51·1
Birth cohort				
Before April 1968	1158	36·1	23672	35·2
1968-1979	621	19·3	14810	22·0
1980-1989	475	14·8	9525	14·2
1990-1999	614	19·1	12306	18·3
2000-2007	344	10·7	6891	10·3

Table 2

Disease categorization according to the International Classification of Diseases, the 8th and 10th revisions (ICD8 and ICD10 codes)

Disease categories	ICD 10 codes	ICD 8 codes
Any	A00-Z99	000-796, E800-E999, N800-N999, Y00-Y95
Infectious and parasitic diseases	A00-B99	000-136
Neoplasms	C00-D48	140-239
Diseases of the blood (-forming) organs, immunological disorders	D50-D89	280-289
Endocrine, nutritional and metabolic diseases	E00-E90	240-279
Mental and behavioral disorders	F00-F99	290-315
Diseases of the nervous system and the sensory organs	G00-H95	320-389
Diseases of the circulatory system	I00-I99	390-444·1, 444·3-458, 782·4
Diseases of the respiratory system	J00-J99	460-519
Diseases of the digestive system	K00-K93	520-577, 444·2
Diseases of the skin and subcutaneous tissue	L00-L99	680-709
Diseases of the musculoskeletal system/connective tissue	M00-M99	710-738
Diseases of the genitourinary system	N00-N99	580-629, 792
Complications of pregnancy, childbirth and puerperium	O00-O99	630-678
Certain conditions originating in the perinatal period	P00-P96	760-779
Congenital malformations*	Q00-Q89	740-759·2, 759·6-759
Congenital heart defects	Q20-D26	746-747·4
Gastrointestinal tract defects	Q38-Q45	750-751
Other*	Q00-Q18, Q27-Q37, Q50-Q89	740-745, 747·5-749, 752-759·2, 759·6-759
Symptoms, signs, abnormal findings, ill-defined causes	R00-R99	780-782·3, 782·5-791, 793-796
External causes of injury and poisoning	V01-Y89, S00-T98	E800-E999, N800-N999
Factors influencing health status and contact with health services	Z00-Z99, U00-U89	Y00-Y95

* Chromosomal abnormalities (ICD10: Q90-Q99; ICD8: 759·3-759·5) were excluded in these categories.

Table 3

Rate ratios for hospital admissions in persons with Down syndrome, compared with the reference population, by age group and disease category, Denmark, 1977-2008

	<1 year		1-4 year		5-19 year		20-49 year		50+ year		All ages	
	N	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)
Any	4814	3·0 (2·8-3·1)	3511	6·8 (6·4-7·1)	3668	3·4 (3·3-3·6)	3570	1·0 (1·0-1·1)	1252	1·2 (1·1-1·3)	16815	2·2 (2·1-2·2)
Infectious and parasitic diseases	154	3·6 (3·0-4·2)	252	4·4 (3·8-5·0)	182	3·3 (2·8-3·9)	165	1·9 (1·6-2·2)	57	2·2 (1·7-2·9)	810	3·0 (2·8-3·2)
Neoplasms	23	4·8 (3·0-7·5)	324	17·5 (15·0-20·5)	182	4·1 (3·5-4·9)	146	0·6 (0·5-0·8)	41	0·2 (0·2-0·3)	716	1·5 (1·3-1·6)
Diseases of the blood (-forming) organs, immuno-logical disorders	50	13·3 (9·3-19·1)	51	5·3 (3·9-7·2)	39	2·5 (1·8-3·5)	76	3·4 (2·7-4·3)	9	0·4 (0·2-0·8)	225	3·0 (2·6-3·5)
Endocrine, nutritional and metabolic diseases	59	3·5 (2·6-4·6)	85	5·4 (4·2-6·8)	178	4·0 (3·4-4·7)	350	2·6 (2·3-3·0)	97	1·0 (0·8-1·2)	769	2·4 (2·3-2·7)
Mental and behavioral disorders	14	4·0 (2·2-7·0)	19	3·8 (2·4-6·2)	51	2·2 (1·6-2·9)	108	1·2 (1·0-1·5)	64	1·6 (1·3-2·1)	256	1·6 (1·4-1·8)
Diseases of the nervous system and the sensory organs	158	4·0 (3·4-4·8)	454	6·1 (5·5-6·8)	769	8·6 (7·9-9·4)	636	4·9 (4·5-5·4)	288	4·7 (4·2-5·4)	2305	5·9 (5·6-6·2)
Diseases of the circulatory system	134	39·6 (29·7-52·8)	115	56·3 (39·8-79·6)	136	10·7 (8·7-13·2)	313	1·7 (1·5-1·9)	133	0·4 (0·4-0·5)	831	1·6 (1·5-1·8)
Diseases of the respiratory system	859	8·6 (7·9-9·4)	1612	8·2 (7·7-8·8)	930	6·0 (5·6-6·5)	403	2·6 (2·4-2·9)	279	2·2 (1·9-2·4)	4083	5·5 (5·3-5·7)
Diseases of the digestive system	93	3·2 (2·6-4·0)	193	5·0 (4·3-5·9)	441	4·2 (3·8-4·7)	440	1·5 (1·4-1·7)	153	1·2 (1·0-1·5)	1320	2·3 (2·1-2·4)
Diseases of the skin and subcutaneous tissue	27	3·0 (2·0-4·6)	32	2·1 (1·4-3·0)	91	3·1 (2·5-3·8)	136	1·7 (1·4-2·1)	34	2·1 (1·5-3·0)	320	2·1 (1·9-2·4)
Diseases of the musculoskeletal system/ connective tissue	9	3·4 (1·7-6·8)	19	2·3 (1·4-3·7)	131	3·1 (2·6-3·7)	137	0·7 (0·6-0·8)	23	0·2 (0·2-0·4)	319	0·9 (0·8-1·0)
Diseases of the genitourinary system	37	4·1 (2·9-5·9)	42	2·6 (1·9-3·6)	113	1·8 (1·5-2·2)	300	1·0 (0·9-1·2)	89	1·0 (0·8-1·2)	581	1·2 (1·1-1·4)
Complications of pregnancy, childbirth and puerperium	0		0		0		23	0·0 (0·0-0·0)	0		23	0·0 (0·0-0·0)
Certain conditions originating in the perinatal period	951	3·4 (3·1-3·7)	18	12·1 (6·9-21·4)	2	3·3 (0·7-14·7)	1	0·4 (0·1-3·2)	0		972	3·4 (3·1-3·7)
Congenital malformations	2320	33·1 (30·7-35·8)	1193	34·5 (31·2-38·1)	885	13·9 (12·7-15·3)	434	11·4 (10·1-13·0)	26	4·9 (3·2-7·4)	4858	22·7 (21·7-23·7)

	<1 year		1-4 year		5-19 year		20-49 year		50+ year		All ages	
	N	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)	n	Rate ratio (95% CI)
Congenital heart defects	1913	110·4 (98·1-124·3)	960	121·6 (103·2-143·2)	583	89·5 (74·7-107·2)	330	68·3 (54·6-85·6)	5	7·1 (2·7-18·7)	3791	100·4 (92·9-108·6)
Gastrointestinal tract defects	367	28·1 (23·8-33·1)	159	33·1 (25·7-42·5)	135	40·1 (30·4-53·0)	8	7·1 (3·2-15·8)	0		669	29·4 (26·0-33·1)
Other	290	6·6 (5·7-7·5)	152	6·2 (5·2-7·5)	234	4·2 (3·6-4·9)	104	3·2 (2·6-4·0)	21	4·9 (3·1-7·7)	801	5·0 (4·6-5·4)
Symptoms, signs, abnormal findings, ill-defined causes	141	2·6 (2·2-3·2)	148	2·0 (1·7-2·3)	206	1·9 (1·6-2·1)	339	1·6 (1·4-1·8)	165	2·0 (1·7-2·3)	999	1·9 (1·8-2·0)
External causes of injury and poisoning	331	0·8 (0·7-0·9)	93	1·6 (1·3-2·0)	247	0·9 (0·8-1·1)	316	0·7 (0·7-0·8)	154	1·5 (1·3-1·8)	1141	0·9 (0·8-1·0)
Factors influencing health status and contact with health services	1425	1·2 (1·1-1·2)	106	4·2 (3·4-5·2)	228	3·8 (3·3-4·4)	349	0·4 (0·3-0·4)	60	0·7 (0·5-0·9)	2168	0·9 (0·9-1·0)

Poisson regression; Adjusted for sex and birth cohort (for all ages, additionally adjusted for age group); CI: confidence interval.

Time (person-years) at risk for persons with DS: 1535 for <1 years, 5938 for 1-4 years, 21089 for 5-19 years, 30160 for 20-49 years, 4767 for 50+ years, and 63489 for all age groups.

Table 4

Rate ratios for hospital days in persons with Down syndrome, compared with the reference population, by age group and disease category, Denmark, 1977-2008

	<1 year		1-4 year		5-19 year		20-49 year		50+ year		All ages	
	days	Rate ratio (95% CI)	days	Rate ratio (95% CI)	days	Rate ratio (95% CI)	days	Rate ratio (95% CI)	days	Rate ratio (95% CI)	days	Rate ratio (95% CI)
Any	45552	5·7 (5·4-6·1)	19774	10·5 (9·6-11·5)	17797	3·8 (3·5-4·2)	18252	1·1 (1·0-1·2)	6667	0·8 (0·8-0·9)	108042	2·7 (2·6-2·8)
Infectious and parasitic diseases	1272	4·6 (3·5-6·1)	1363	6·7 (5·3-8·6)	1218	4·6 (3·6-6·1)	1089	1·8 (1·4-2·4)	282	1·1 (0·8-1·5)	5224	3·3 (2·9-3·7)
Neoplasms	194	6·0 (2·4-14·9)	2504	29·1 (21·7-39·2)	1084	4·7 (3·5-6·3)	1069	0·8 (0·5-1·0)	192	0·1 (0·1-0·2)	5042	1·5 (1·3-1·7)
Diseases of the blood (-forming) organs, immunological disorders	820	24·0 (14·0-41·1)	412	5·6 (3·1-10·1)	234	2·8 (1·6-4·8)	362	2·4 (1·6-3·5)	53	0·3 (0·1-0·8)	1881	3·5 (2·8-4·4)
Endocrine, nutritional and metabolic diseases	1014	5·1 (3·2-8·0)	435	4·3 (3·0-6·1)	1104	3·2 (2·5-4·2)	2251	2·8 (2·3-3·3)	747	0·8 (0·5-1·2)	5550	2·3 (2·0-2·6)
Mental and behavioral disorders	233	7·3 (3·1-17·1)	181	4·4 (2·1-9·2)	317	1·6 (1·0-2·6)	498	1·1 (0·8-1·5)	605	1·6 (0·9-2·7)	1834	1·7 (1·3-2·1)
Diseases of the nervous system and the sensory organs	2197	6·9 (5·0-9·6)	2382	7·8 (6·2-9·8)	3200	7·4 (6·2-8·8)	3252	3·6 (2·9-4·4)	1668	2·8 (2·1-3·8)	12699	5·0 (4·5-5·5)
Diseases of the circulatory system	1902	51·5 (31·2-85·0)	1165	133·7 (76·5-233·9)	918	11·0 (7·6-15·8)	2013	1·6 (1·3-2·1)	727	0·3 (0·2-0·4)	6725	1·7 (1·5-2·0)
Diseases of the respiratory system	8092	15·3 (13·1-18·0)	8404	12·9 (11·3-14·8)	4211	7·1 (6·2-8·2)	3343	4·5 (3·8-5·5)	2381	2·2 (1·8-2·8)	26431	7·3 (6·8-7·8)
Diseases of the digestive system	727	4·5 (3·0-6·9)	955	7·3 (5·2-10·2)	1842	4·1 (3·2-5·2)	1864	1·1 (1·0-1·3)	556	0·6 (0·5-0·8)	5944	1·8 (1·6-2·0)
Diseases of the skin and subcutaneous tissue	365	5·7 (3·3-10·0)	151	1·8 (1·0-3·3)	412	2·3 (1·6-3·2)	587	1·1 (0·8-1·5)	399	1·8 (1·0-3·3)	1914	1·8 (1·5-2·2)
Diseases of the musculoskeletal system/connective tissue	32	1·5 (0·6-4·0)	57	1·5 (0·8-2·8)	697	2·6 (2·0-3·4)	1029	0·7 (0·5-0·9)	163	0·2 (0·1-0·3)	1978	0·7 (0·6-0·9)
Diseases of the genitourinary system	478	7·3 (3·9-13·5)	230	3·2 (2·0-5·3)	634	2·3 (1·5-3·3)	1382	1·0 (0·8-1·2)	401	0·7 (0·5-0·9)	3125	1·3 (1·1-1·5)
Complications of pregnancy, childbirth and puerperium	0		0		0		104	0·0 (0·0-0·0)	0		104	0·0 (0·0-0·0)
Certain conditions originating in the perinatal period	12607	5·0 (4·5-5·7)	103	13·2 (5·9-29·5)	9	6·8 (1·0-47·1)	19	1·4 (0·2-10·6)	0		12738	5·0 (4·5-5·7)
Congenital malformations	27112	46·0 (40·5-52·2)	8607	53·4 (45·6-62·5)	5593	18·7 (15·9-21·9)	2348	9·2 (7·4-11·4)	109	2·6 (1·5-4·6)	43768	31·9 (29·5-34·5)
Congenital heart defects	22926	98·7 (80·0-121·8)	7343	184·6 (141·6-240·7)	4074	112·8 (84·3-150·9)	1794	53·4 (36·7-77·6)	24	3·5 (0·8-15·9)	36160	103·2 (89·0-119·6)
Gastrointestinal tract defects	4802	43·1 (32·6-57·1)	1249	55·8 (35·5-87·8)	746	47·1 (31·0-71·6)	109	9·1 (2·3-35·6)	0		6906	41·8 (33·7-51·8)
Other	2834	8·9 (7·0-11·3)	850	7·7 (5·1-11·6)	1243	4·7 (3·7-6·0)	489	2·3 (1·7-3·2)	85	2·6 (1·4-4·8)	5500	5·9 (5·1-6·8)
Symptoms, signs, abnormal findings, ill-defined causes	1191	3·7 (2·7-5·1)	863	3·5 (2·6-4·8)	1214	3·3 (1·8-6·2)	1144	1·5 (1·2-1·7)	697	1·2 (0·9-1·5)	5109	2·2 (1·8-2·6)
External causes of injury and poisoning	1625	1·2 (1·0-1·4)	525	2·9 (1·9-4·3)	1475	1·3 (1·0-1·8)	2598	1·2 (0·9-1·6)	1081	1·2 (0·8-1·6)	7304	1·3 (1·1-1·5)
Factors influencing health status and contact with health services	9315	1·8 (1·6-2·0)	501	5·4 (3·5-8·2)	758	3·2 (2·4-4·2)	1257	0·3 (0·2-0·4)	221	0·3 (0·2-0·6)	12051	1·2 (1·1-1·3)

Poisson regression; Adjusted for sex and birth cohort (for all ages, additionally adjusted for age group); CI: confidence interval·

Time (person-years) at risk for persons with DS: 1535 for <1 years, 5938 for 1-4 years, 21089 for 5-19 years, 30160 for 20-49 years, 4767 for 50+ years, and 63489 for all age groups.

Table 5

Associations of covariates with overall hospital admissions and hospital days in people with Down syndrome, Denmark, 1977-2008

	Hospital admissions			Hospital days		
	RR	95% CI		RR	95% CI	
Sex						
Female	1·0			1·0		
Male	1·1	1·1	1·1	1·1	1·0	1·2
Age group, years						
<1	15·5	14·5	16·6	36·8	32·7	41·4
1-4	3·0	2·9	3·3	4·2	3·7	4·8
5-19	1·0			1·0		
20-49	0·7	0·7	0·8	0·6	0·5	0·7
50+	1·7	1·5	1·9	1·4	1·2	1·7
Birth cohort						
Before April 1968	1·2	1·1	1·3	1·5	1·3	1·7
1968-1979	1·0			1·0		
1980-1989	1·0	1·0	1·1	0·8	0·7	0·9
1990-1999	1·0	1·0	1·1	0·6	0·5	0·7
2000-2007	1·0	0·9	1·1	0·6	0·5	0·7
Congenital heart defects						
No	1·0			1·0		
Yes	2·1	2·0	2·2	2·5	2·3	2·8

Poisson regression; Adjusted for covariates in the table; RR: rate ratio; CI: confidence interval.