Life-Long Morbidity Among Danes With Poliomyelitis

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ABSTRACT. Nielsen NM, Rostgaard K, Askgaard D, Skinhøj P, Aaby P. Life-long morbidity among Danes with poliomyelitis. Arch Phys Med Rehabil 2004;85:385-91.

Objective: To estimate long-term morbidity in a cohort of Danish poliomyelitis patients.

Design: A historical prospective cohort study of 27,047 persons.

Setting: Denmark.

Participants: A total of 5421 persons hospitalized for poliomyelitis between 1919 to 1954 in Copenhagen, Denmark, and 21,626 age- and gender-matched Danes. Participants were followed up on average for 20.6 years, yielding a total of 555,884 person-years of follow-up.

Interventions: Not applicable

Main Outcome Measures: The exposed (poliomyelitis) cohort and the unexposed (control) cohort were followed up for somatic hospitalization from 1977 to 1999 in the Danish Hospital Discharge Register. The incidence rate ratio (IRR) was calculated as the ratio between the incidence rate of disease in the exposed and unexposed cohorts.

Results: Overall, polio patients had a 1.2- to 1.3-fold increased risk of being hospitalized with pulmonary diseases, heart diseases, gastrointestinal disorders, or diseases of the locomotive apparatus. Among paralytic polio patients, long-term morbidity seems to be associated with the acute severity of poliomyelitis, as well as young age at infection. Paralytic patients, who contracted respiratory polio under the age of 5, had the highest risk of being hospitalized with lung diseases (IRR=7.26; 95% confidence interval [CI], 3.06–18.33), diseases of the locomotive apparatus (IRR=4.05; 95% CI, 1.66–9.86), heart diseases (IRR=1.70; 95% CI, 0.65–3.98), and diseases of the digestive system (IRR= 2.23; 95% CI, 1.03–4.62). Surprisingly, patients without paralyses, especially women, also had an increased morbidity.

Conclusions: Overall, a history of poliomyelitis was associated with a slightly increased morbidity measured by hospitalizations. Long-term morbidity was highest among respiratory polio patients; however, patients presumably left without any residual symptoms also had an increased morbidity.

Key Words: Denmark; Morbidity; Poliomyelitis; Rehabilitation.

POLIOMYELITIS IS A SEVERE viral infection of the central nervous system. According to symptoms, clinical polio is divided into either nonparalytic polio, resembling a viral meningitis, or paralytic polio, characterized by the development of more or less severe flaccid paralysis. Fortunately, acute poliomyelitis is nowadays an uncommon disease, but "old" poliomyelitis is still a major cause of long-term disabilities.[1]

Apart from a few cohort studies, which have suggested an increased risk of Parkinson's disease, multiple sclerosis (MS), and female breast cancer,[2-4] most of the research concerning comorbidity among previous polio patients have been focused on the development of the so-called postpolio syndrome (PPS), defined by development of new muscular weakness and fatigue decades after paralytic polio.[5-9]

Based on results from studies of patients disabled by spinal cord injury or cerebral palsy, we would expect that paralytic polio patients, because of their impaired mobility, would be more prone to develop cardiovascular diseases (CVDs), hypertension, lung diseases, diabetes, and orthopedic problems such as osteoporosis, fractures, and scoliosis.[10-14] A few case studies[14-16] have reported episodes of heart disease, hypertension, diabetes, bowel dysfunction, asthma, emphysema, and arthritis among paralytic polio patients. However, none of these case studies[14-16] has assessed the morbidity among less severely paralyzed polio patients and certainly not among nonparalytic polio patients.

To estimate nonparalytic and paralytic polio patients' long-term morbidity caused by CVDs, lung diseases, gastrointestinal diseases, and locomotor disorders, we took advantage of historical medical archives on patients hospitalized with poliomyelitis in Copenhagen, Denmark, between 1919 and 1954 and a nationwide hospital discharge register.

METHODS

The Polio Cohort (Exposed Cohort)

Throughout the first half of the 20th century, 1 hospital, the Blegdamshospital, served as the primary center for patients suspected of or diagnosed with acute poliomyelitis in the area of greater Copenhagen. All medical records on patients admitted to the hospital have been stored at the Copenhagen City Archives. To identify patients diagnosed with poliomyelitis between 1919 and 1954, more than 80,000 consecutive hospital records were reviewed. Information extracted from the records included name, sex, date and place of birth, date of admission and discharge, and details concerning the acute severity of the disease.

Only cases with a discharge diagnosis of paralytic polio, nonparalytic polio, suspected polio, or primary lymphocytic meningitis were included in the analysis. Occurring during the same season as polio, primary lymphocytic meningitis was generally considered to be nonparalytic polio, after other pos-

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sible viral infections such as mumps had been excluded based on the clinical symptoms.[17]

The distinction among paralytic, nonparalytic, and suspected polio is not clear. According to the literature, cases resembling poliomyelitis with symptoms such as fever, headache, vomiting, pain, rigidity of back and neck, and more than 3 cells/mm^3 in the spinal fluid were considered as cases of poliomyelitis, whereas cases with fever and meningeal symptoms but no pleocytosis were classified as suspected polio.[18] The diagnosis of paralytic polio was verified by the existence of the characteristic asymmetrical flaccid paralysis. We further divided paralytic polio patients into 3 groups, according to severity: (1) patients who had no or only mild paralysis of the extremities and no respiratory difficulties, (2) patients with severe paralysis of at least 1 extremity but no respiratory difficulties, and (3) patients who received artificial ventilation because of respiratory failure during the acute phase of the disease. (Many patients treated for respiratory failure did eventually start breathing spontaneously.[15]) Groups 1 and 2 together are referred to as nonrespiratory paralytic polio.

Since April 1, 1968, all Danish citizens have been assigned a unique identification number (CRS number), which is recorded in the Danish Civil Registration System along with information on, for example, place of birth and place of residence. Using name, sex, and date of birth as keys, the polio cohort was linked to the Civil Registration System to identify individual CRS numbers.[19] Overall, 5421 polio patients were alive on January 1, 1977, the date that the Danish Hospital Discharge Register (NHDR) was established.

The Cohort of Nonpolio Patients (Unexposed Cohort)

For each polio patient, 4 persons were identified in the Danish Civil Registration System and matched by sex, age, and geographical residence as of January 1, 1977.

Morbidity Data

By means of the CRS number, the poliomyelitis and the control cohorts were linked to the NHDR, a population-based registration of all somatic hospitalizations since January 1, 1977.[20] From 1977 to 1993, the diseases were coded according to the *International Classification of Diseases, 8th Revision* (ICD-8); from 1994 to 1999, they were coded according to ICD-10 codes.[21,22] Because the underlying causes of morbidity were distributed over several hundred different diagnoses, it was necessary to aggregate the diagnoses into explicit groups. Having looked into cancer and some of the neurologic diseases,[2-4] we decided to focus on CVDs, lung diseases, digestive disorders, and orthopedic disorders. Subgroup analysis within each main disease category was chosen according to previous comorbidity studies among disabled persons.[23]

Data Analysis

The polio and nonpolio cohorts were followed from January 1, 1977, until the date of first hospitalization with the respective disease, disappearance, emigration, death, or December 31, 1999, whichever came first. Only the patient's first hospitalization with the respective disease was included in the analysis; subsequent hospitalizations for the same disorder were ignored. The disease incidence rate for the respective disease in the polio cohort was calculated as the number of polio patients who were registered as being hospitalized with the disease divided by the total follow-up time in person-years among the polio patients. Similarly, the incidence rate of the same disease was calculated among the persons in the unexposed cohort. The ratio between disease incidence rates in the exposed and unexposed cohorts, respectively, was the measure of the incidence rate ratio (IRR), which approaches the relative risk when the event studied is rare. The 95% confidence intervals (CIs) for the IRR were estimated from the Wald test assuming a Poisson distribution of the observed cases.

RESULTS

Overall, 6551 persons were hospitalized with poliomyelitis at the Blegdamshospital from 1919 to 1954. Of the 6207 patients surviving hospitalization, CRS numbers were identified for 5759 (93%); 228 (4%) patients had died or moved before the CRS numbers were introduced in 1968. Among the 5759 identified patients, 5421 (87%) were alive and residents of Denmark on January 1, 1977, and 90% of this group had contracted poliomyelitis between 1942 and 1954. A cohort of 21,626 nonexposed age- and gender-matched persons were chosen from the Danish population (for a very few cases, it was impossible to find 4 matched, nonexposed controls). The age of the persons included in the study was on average 39.1 years (range, 22.7–90.4y) on January 1, 1977; they were followed up for 20.6 years (range, 0–23.0y), yielding a total of 555,884 person-years of follow-up (table 1). Overall, 78% of the polio patients had been hospitalized at least once from January 1, 1997, and December 31, 1999, versus 71% in the nonexposed cohort. The risk of hospitalization was especially high among respiratory polio patients, because 86% had been admitted to a hospital at least once (data not shown).

Cardiovascular Diseases

Overall, 26% of the polio patients had been hospitalized due to CVDs. Thus, compared with the nonexposed cohort, polio patients had a 17% (IRR=1.17; 95% CI, 1.10–1.24) higher risk of heart disease. Differentiating the CVDs (table 2) showed a modestly increased risk of coronary heart diseases and hypertension. Furthermore, analyzing the data according to severity of poliomyelitis, it was shown that patients who had suffered from respiratory failure during the epidemics had a high risk of valvular heart diseases (IRR=6.62; 95% CI, 1.89–25.89) and cor pulmonale (IRR=3.85; 95% CI, 1.35–10.73) (see table 2).

Lung Diseases

More than 15% of the polio patients had a lung disease diagnosed at a hospital, corresponding to a 34% increased risk of being hospitalized with a respiratory disease. Dividing the lung diseases into more specific categories, we found that the risk of pneumonia was increased by 41% (IRR=1.41; 95% CI, 1.25–1.59), the risk of asthma and bronchitis by 38% (IRR=1.38; 95% CI, 1.18–1.62), and the risk of emphysema and chronic lung diseases by 54% (IRR=1.54; 95% CI, 1.31–1.82).

Patients who had suffered from breathing difficulties during the acute phase of poliomyelitis had the highest risk of developing lung diseases (IRR=3.51; 95% CI, 2.47–4.94) (see table 2). Examining age at first hospitalization, we found that the respiratory patients had an extraordinarily high risk of being hospitalized with a lung disease before the age of 45 years (IRR=8.70; 95% CI, 4.17–19.37), whereas their excess risk of debuting with a respiratory disease after 45 years of age (IRR=2.78; 95% CI, 1.83–4.15) was significantly lower (data not shown). Likewise, respiratory polio patients had 3- to 7-fold increased risks of being hospitalized with pneumonia, asthma, bronchitis, emphysema, and atelectasis (see table 2).

Patients with nonparalytic polio and nonrespiratory paralytic polio had only a modest increase in their risk of being hospitalized with a lung disease; however, women with suspected

Table 1: Demographic Characteristics of the Cohorts

Patient Group	Polio Cohort		Age- and Gender-Matched Cohort	
	Persons at Risk	Person-Years at Risk	Persons at Risk	Person-Years at Risk
All polio cases				
Men	3025	62,433	12,045	243,194
Women	2396	50,527	9581	199,730
Total	5421	112,960	21,626	442,924
Nonrespiratory paralytic polio				
Men	960	19,582	3810	75,379
Women	887	18,836	3545	73,733
Total	1847	38,418	7355	149,111
Respiratory polio				
Men	78	1456	312	6196
Women	78	1495	312	6577
Total	156	2951	624	12,773
Nonparalytic polio				
Men	1737	36,298	6924	141,724
Women	1190	25,208	4760	99,642
Total	2927	61,506	11,684	24,365
Suspected polio				
Men	250	5096	999	19,896
Women	241	4988	964	19,779
Total	491	10,085	1963	39,674

polio had a 3-fold increase in their risk of asthma, bronchitis, and emphysema.

Diseases of the Locomotive Apparatus

Because the incidence of diseases associated with the locomotive apparatus and the gastrointestinal system did not differ between paralytic polio patients with and without respiratory failure, we analyzed paralytic polio patients as a single group.

The risk of being hospitalized with a disease affecting muscles, bones, or connective tissue was only slightly increased (IRR=1.30; 95% CI, 1.21–1.40). Only 17% of the polio patients had been admitted to the hospital for a disease of the locomotive apparatus. The risk of arthrosis was increased by 16% (IRR=1.16; 95% CI, 1.00–1.34), the risk of osteoporosis by 100% (IRR=2.10; 95% CI, 1.54–2.83), and the risk of developing spinal deformities by more than 140% (IRR=2.41; 95% CI, 1.47–3.86). The risk of rheumatoid arthritis was not increased, nor was the risk of diseases of the connective tissue. Patients treated for nonparalytic polio and suspected polio seemed to have a higher risk of being diagnosed with a locomotor disease than did paralytic polio patients. However, paralytic polio patients did have a 4-fold higher risk of being hospitalized because of spinal deformities (IRR=4.39; 95% CI, 2.28–8.52) (table 3).

Diseases of the Digestive System

Overall, 23% of the polio patients had been hospitalized because of a digestive system disorder, leading to 1.3-fold (IRR=1.27; 95% CI, 1.19–1.36) increased risk of gastrointestinal diseases. The incidence of hospitalization due to paralytic ileus, bowel dysfunctions, liver and pancreas diseases, inflammatory bowel diseases, and ulcers was increased by 30% to 40%. Except for a 2-fold increased risk of paralytic ileus among men with paralytic polio, the higher incidence of diseases associated with the stomach and intestine was restricted to patients without paralysis (see table 3).

Other Diseases

Overall, an increased risk of kidney and urinary tract disorders was only observed in women with suspected polio (IRR=2.99; 95% CI, 1.60–5.49). However, differentiating the diseases showed that paralytic polio patients had a 39% higher risk of renal and urinary tract stones (IRR=1.39; 95% CI, 1.01–1.90) (data not shown). Women with suspected polio had a 2-fold (IRR=2.51; 95% CI, 1.18–5.10) increased risk of diabetes. Otherwise, the incidence of diabetes and thyroid diseases was not increased among polio patients (data not shown).

Morbidity, by Poliomyelitis Severity and Age at Onset

To simplify the analysis, we did not differentiate gender in this analysis; however, as shown in previous tables, women with suspected polio tended to have a higher morbidity than men with suspected polio.

Overall, no difference in morbidity according to age of contracting poliomyelitis was observed. However, paralytic patients who contracted polio before the age of 5 years had a higher long-term morbidity of lung diseases, heart disorders, gastrointestinal disorders, and locomotor diseases. This age effect was, however, only significant for respiratory polio patients and long-term morbidity due to gastrointestinal diseases and diseases of the locomotive apparatus. No age effect was observed among polio patients with nonparalytic polio or suspected polio. Patients who had suspected polio before the age of 5 years did, however, tend to have a higher risk of lung diseases, compared with those contracting suspected polio after the age of 5 years (table 4).

Among the paralytic polio patients who were infected with polio before the age of 5 years, long-term morbidity from lung diseases was associated with the acute severity of poliomyelitis. Respiratory polio patients had the highest risk of hospitalization (IRR=7.26; 95% CI, 3.06–18.33), followed by patients who developed severe paralysis of at least 1 extremity (IRR=1.47; 95% CI, 0.98–2.16) and finally by patients who developed no or only mild paralysis (test for trend, $P<.01$). The same trend was seen for disorders of the locomotive apparatus ($P=.02$) (see table 4).

Table 2: Incidence of Heart and Lung Diseases in the Cohort of 5421 Polio Patients in 1977–1999

	All Polio Patients			Nonrespiratory Paralytic Polio			Respiratory Polio			Nonparalytic Polio			Suspected Polio		
	No.	IRR	95% CI	No.	IRR	95% CI	No.	IRR	95% CI	No.	IRR	95% CI	No.	IRR	95% CI
CVDs															
Men	803	1.14	1.05–1.23	258	1.11	0.97–1.27	24	1.26	0.78–1.94	451	1.14	1.02–1.26	70	1.22	0.93–1.59
Women	587	1.21	1.11–1.33	209	1.12	0.96–1.30	19	1.31	0.77–2.13	271	1.16	1.01–1.33	88	1.79	1.39–2.29
Total	1390	1.17	1.10–1.24	467	1.12	1.01–1.24	43	1.28	0.90–1.78	722	1.15	1.06–1.25	158	1.49	1.24–1.78*
Coronary heart disease															
Men	318	1.17	1.03–1.32	89	0.97	0.77–1.22	11	1.41	0.68–2.69	188	1.26	1.07–1.48	30	1.31	0.85–1.95
Women	174	1.25	1.05–1.48	60	1.11	0.83–1.47	1	0.25	0.01–1.24	81	1.23	0.95–1.57	32	2.12	1.37–3.23
Total	492	1.20	1.08–1.33	149	1.02	0.85–1.22	12	1.02	0.52–1.85	269	1.25	1.09–1.43	62	1.64	1.21–2.19
Valvular heart diseases															
Men	28	0.93	0.61–1.39	8	0.79	0.34–1.60	2	4.30	0.52–35.82	14	0.81	0.44–1.40	4	1.96	0.52–6.23
Women	34	1.37	0.92–2.01	7	0.81	0.33–1.71	4	9.05	1.77–65.27	14	1.26	0.66–2.23	9	1.99	0.85–4.31
Total	62	1.13	0.85–1.50	15	0.80	0.44–1.35	6	6.62	1.89–25.89	28	0.99	0.64–1.47	13	1.97	0.98–3.77
Arrhythmia															
Men	159	1.11	0.93–1.32	62	1.29	0.96–1.70	3	0.85	0.20–2.59	78	0.96	0.74–1.22	16	1.57	0.85–2.75
Women	111	1.34	1.08–1.66	41	1.33	0.93–1.88	4	3.64	0.90–13.75	53	1.37	1.00–1.87	13	1.03	0.54–1.84
Total	270	1.20	1.04–1.37	103	1.31	1.04–1.63	7	1.54	0.61–3.48	131	1.10	0.90–1.33	29	1.27	0.82–1.91
Hypertension															
Men	196	1.57	1.32–1.84	68	1.53	1.15–2.02	8	3.51	1.34–8.89	103	1.54	1.22–1.92	17	1.46	0.82–2.50
Women	137	1.44	1.18–1.74	44	1.23	0.87–1.71	2	0.63	0.10–2.24	68	1.41	1.06–1.85	23	2.84	1.65–4.81
Total	333	1.51	1.33–1.71	112	1.40	1.12–1.73	10	1.83	0.83–3.71	171	1.48	1.24–1.77	40	2.03	1.38–2.95
Cor pulmonale															
Men	31	0.90	0.60–1.31	11	0.96	0.47–1.80	2	1.43	0.21–6.19	14	0.73	0.39–1.25	4	1.74	0.47–5.35
Women	36	1.29	0.88–1.87	11	0.94	0.46–1.74	5	11.3	2.44–78.98	18	1.32	0.75–2.20	2	0.99	0.15–3.96
Total	67	1.08	0.82–1.40	22	0.95	0.58–1.48	7	3.85	1.35–10.73	32	0.97	0.65–1.41	6	1.39	0.50–3.35
Lung diseases															
Men	420	1.20	1.08–1.34	133	1.11	0.91–1.34	25	2.55	1.55–4.12	226	1.16	1.00–1.34	36	1.46	0.98–2.12
Women	406	1.51	1.34–1.69	142	1.36	1.12–1.64	30	4.95	2.99–8.19	185	1.41	1.19–1.66	49	1.77	1.26–2.46
Total	826	1.34	1.23–1.44	275	1.23	1.07–1.40	55	3.51	2.47–4.94	411	1.26	1.13–1.40	85	1.62	1.26–2.08
Pneumonia															
Men	175	1.25	1.05–1.47	59	1.23	0.91–1.64	12	2.54	1.21–5.09	94	1.21	0.95–1.52	10	1.05	0.48–1.98
Women	180	1.61	1.35–1.91	66	1.41	1.06–1.86	17	5.15	2.59–10.28	80	1.62	1.24–2.09	17	1.39	0.78–2.37
Total	355	1.41	1.25–1.59	125	1.32	1.07–1.61	29	3.64	2.22–5.90	174	1.37	1.15–1.62	27	1.23	0.78–1.87
Asthma and bronchitis															
Men	83	1.06	0.82–1.33	23	0.90	0.56–1.40	6	2.87	0.96–7.97	44	0.99	0.70–1.36	10	1.52	0.70–3.05
Women	127	1.74	1.41–2.14	40	1.53	1.05–2.19	5	3.22	0.95–10.08	62	1.61	1.19–2.15	20	2.90	1.61–5.12
Total	210	1.38	1.18–1.62	63	1.22	0.91–1.61	11	3.03	1.37–6.47	106	1.27	1.02–1.58	30	2.22	1.41–3.44
Emphysema etc															
Men	81	1.32	1.02–1.69	35	1.75	1.16–2.59	8	3.22	1.25–7.96	27	0.82	0.53–1.21	11	1.88	0.88–3.77
Women	114	1.76	1.41–2.19	39	1.61	1.10–2.32	17	13.29	5.52–36.83	41	1.21	0.84–1.69	17	3.22	1.68–6.10
Total	195	1.54	1.31–1.82	74	1.67	1.27–2.19	25	6.71	3.65–12.64*	68	1.01	0.77–1.31	28	2.51	1.55–4.02

*Significant difference between women and men ($P<.05$).

DISCUSSION

Overall, we found a modest but significantly increased morbidity among persons previously diagnosed with poliomyelitis. Among the paralytic polio patients, long-term morbidity was associated with acute severity of poliomyelitis and age at the polio infection; patients with onset of respiratory polio before the age of 5 years had the highest incidence of heart, lung, and locomotor diseases. However, contrary to previous expectations, morbidity was also increased among polio patients without paralyses, especially among women diagnosed with suspected polio.

Clinical poliomyelitis occurs in a limited fraction of those exposed to the virus and even less in persons who developed paralytic polio (<1%). This phenomenon could be related to host factors, environment factors, or factors related to the process of transmission of the virus.[24-33] It has been suggested that the severity of poliomyelitis is related to an immunogenetic mechanism associated with the major histocompatibility system in humans.[25,26] However, if genetic susceptibility were a major determinant of the risk of developing paralytic polio, one would expect a higher incidence of immunopathic disorders such as rheumatoid arthritis, diabetes, thyroid diseases, and connective tissue diseases among the paralytic polio patients and not among the nonparalytic polio patients. This was not the case. However, in a previous study[3] based on the linkage between the total polio cohort and a Danish nationwide register of MS, we observed a 1.7-fold increase in the risk of MS among polio patients, irrespective of severity of poliomyelitis.

The present observed association between severe polio and lung diseases is in line with previous studies. However, the incidence of CVDs, hypertension, diabetes, and especially musculoskeletal disorders among paralytic polio patients seems slightly lower than what we would have expected based on the

Table 3: Incidence of Diseases of the Locomotor Apparatus and Digestive System in 5421 Polio Patients, 1977–1999

	All Polio Patients			Paralytic Polio			Nonparalytic Polio			Suspected Polio		
	No.	IRR	95% CI	No.	IRR	95% CI	No.	IRR	95% CI	No.	IRR	95% CI
Locomotive apparatus												
Men	427	1.23	1.10–1.37	123	0.98	0.80–1.20	267	1.39	1.21–1.60	37	1.22	0.83–1.75
Women	471	1.38	1.24–1.53	174	1.27	1.07–1.50	226	1.34	1.15–1.55	71	1.97	1.48–2.59
Total	898	1.30	1.21–1.40	297	1.13	0.99–1.29	493	1.37	1.23–1.51	108	1.61	1.29–2.01*
Arthrosis												
Men	98	1.07	0.86–1.34	23	0.68	0.43–1.04	66	1.32	0.99–1.74	9	1.18	0.53–2.39
Women	139	1.24	1.02–1.49	52	1.16	0.84–1.56	62	1.19	0.89–1.57	25	1.65	1.02–2.59
Total	237	1.16	1.00–1.34	75	0.95	0.73–1.22	128	1.25	1.02–1.52	34	1.48	0.99–2.17
Osteoporosis etc												
Men	13	2.53	1.23–5.04	5	2.15	0.66–6.24	8	4.46	1.60–12.73	0	—	—
Women	50	2.02	1.43–2.82	17	1.72	0.95–3.00	25	1.94	1.18–3.10	8	3.99	1.47–10.83
Total	63	2.10	1.54–2.83	22	1.80	1.06–2.94	33	2.23	1.44–3.40	8	2.62	1.03–6.35
RA and connective tissue												
Men	21	1.22	0.73–1.95	11	1.78	0.84–3.55	9	0.98	0.44–1.94	1	0.56	0.03–3.13
Women	31	0.72	0.48–1.04	8	0.43	0.19–0.84	19	0.97	0.57–1.57	4	0.79	0.23–2.10
Total	52	0.86	0.63–1.15	19	0.77	0.45–1.22*	28	0.97	0.63–1.45	5	0.73	0.25–1.74
Deformities of the back												
Men	7	1.60	0.62–3.71	6	4.66	1.40–16.16	1	0.35	0.02–1.82	0	—	—
Women	20	2.94	1.63–5.21	13	4.30	1.95–9.56	5	1.52	0.49–4.03	2	3.98	0.48–33.12
Total	27	2.41	1.47–3.86	19	4.39	2.28–8.52	6	0.98	0.36–2.25	2	2.62	0.35–15.84
Digestive system												
Men	676	1.20	1.10–1.30	213	1.04	0.89–1.20	404	1.29	1.15–1.44	59	1.33	0.98–1.77
Women	557	1.37	1.25–1.51	198	1.09	0.93–1.27	275	1.48	1.29–1.70	84	2.18	1.67–2.83
Total	1233	1.27	1.19–1.36	411	1.06	0.95–1.18	679	1.36	1.25–1.48	143	1.72	1.41–2.09*
Paralytic ileus etc												
Men	42	1.45	1.01–2.05	21	2.04	1.18–3.42	18	1.07	0.61–1.75	3	1.67	0.36–6.03
Women	73	1.41	1.07–1.84	25	1.06	0.67–1.63	37	1.67	1.13–2.43	11	1.82	0.86–3.63
Total	115	1.42	1.14–1.75	46	1.36	0.96–1.88	55	1.40	1.02–1.90	14	1.78	0.92–3.28
IBD												
Men	36	0.97	0.66–1.37	13	0.92	0.48–1.62	20	1.01	0.60–1.62	3	0.90	0.21–2.78
Women	71	1.75	1.32–2.31	24	1.48	0.91–2.34	34	1.78	1.17–2.64	13	2.49	1.21–4.91
Total	107	1.37	1.10–1.71	37	1.22	0.83–1.74	54	1.39	1.01–1.88	16	1.86	1.00–3.31
Liver and pancreas												
Men	173	1.30	1.09–1.54	46	1.00	0.71–1.36	114	1.49	1.20–1.85	13	1.22	0.63–2.21
Women	186	1.34	1.13–1.58	62	0.92	0.69–1.20	89	1.55	1.20–1.97	35	2.49	1.62–3.77
Total	359	1.32	1.17–1.48	108	0.95	0.77–1.17	203	1.52	1.29–1.78	48	1.93	1.36–2.71
Ulcers												
Men	202	1.39	1.18–1.63	64	1.20	0.90–1.58	122	1.51	1.22–1.85	16	1.44	0.79–2.50
Women	156	1.34	1.12–1.61	55	1.08	0.79–1.44	76	1.42	1.08–1.83	25	2.23	1.35–3.60
Total	358	1.37	1.21–1.55	119	1.14	0.93–1.39	198	1.47	1.25–1.73	41	1.84	1.26–2.64

Abbreviations: IBD, inflammatory bowel disease; RA, rheumatoid arthritis.
*Significant difference between women and men ($P<.05$).

results of similar studies.[14,16,34-37] However, most previous follow-up studies were restricted to a selected group of paralytic polio patients, such as patients at postpolio clinics or members of polio societies. Such patient groups are undoubtedly dominated by the most severely handicapped polio survivors. Furthermore, those analyses used self-reported diseases in contrast to our study, which is based on severe diseases that demand hospitalization.

According to Danish National Board of Health statistics, more than 84% of the patients with paralytic polio and more than 89% of patients with nonparalytic polio in the County of Copenhagen were hospitalized at the Blegdamshospital during the 20th century[4,38] and more than 87% of this group of polio patients were included in the follow-up cohort. It is possible that the relatively low morbidity among the paralytic polio patients may be explained partly because only the most healthy polio patients survived to the beginning of the study (January 1977). Nevertheless, we believe that the present study provides a more detailed description of the comorbidity among a broader group of polio patients, ranging from very severely paralyzed to nonparalytic polio patients.

By restricting the outcome to diseases registered in the NHDR, we examined only the incidence of severe and life-threatening disorders. However, almost all somatic hospitalizations since 1977 are registered in the NHDR, which may be considered close to 100% complete. Validations studies have indicated 75% to 90% agreement between the register and secondary recoding of hospital files performed by specialized physicians. Overall, 97% of cases with Crohn's disease are recorded as such in the NHDR, whereas diagnoses such as hypertension and acute myocardial infarction have a lower validity (40%–66%). Many cases are coded in related categories. Grouping the diseases into broader categories, as done in the present study, is therefore supposed to increase validity.[39-41]

Table 4: Incidence of Diseases by Age at Hospitalization for Poliomyelitis and Degree of Disability Among Polio Patients

	0–4y			≥5y		
	No.	IRR	95% CI	No.	IRR	95% CI
Heart diseases						
Paralytic polio	125	1.23	1.00–1.50	385	1.11	0.99–1.25
None or mild paralysis of the extremities	79	1.19	0.92–1.53	249	1.19	1.03–1.37
Severe paralysis of at least 1 extremity	39	1.25	0.86–1.77	100	0.93	0.74–1.15
Respiratory polio	7	1.70	0.65–3.98	36	1.28	0.87–1.82
Nonparalytic polio	113	1.20	0.97–1.48	609	1.15	1.05–1.26
Suspected polio	14	1.08	0.57–1.90	144	1.57	1.30–1.90
Total	252	1.20	1.05–1.39	1138	1.18	1.10–1.26
Lung diseases						
Paralytic polio	100	1.44	1.14–1.80	230	1.37	1.17–1.58
None or mild paralysis of the extremities	53	1.18	0.86–1.60	122	1.23	1.00–1.50
Severe paralysis of at least 1 extremity	34	1.47	0.98–2.16	66	1.20	0.90–1.57
Respiratory polio	13	7.26	3.06–18.33	42	3.09	2.09–4.52
Nonparalytic polio	71	1.07	0.82–1.38	340	1.32	1.16–1.49
Suspected polio	13	2.37	1.16–4.67	72	1.54	1.17–2.01
Total	184	1.30	1.10–1.53	642	1.36	1.24–1.48
Locomotor apparatus						
Paralytic polio	108	1.24	0.99–1.53	189	1.08	0.92–1.27
None or mild paralysis of the extremities	64	1.08	0.81–1.42	126	1.09	0.89–1.32
Severe paralysis of at least 1 extremity	34	1.34	0.89–1.95	46	1.02	0.73–1.40
Respiratory polio	10	4.05	1.66–9.86	17	1.21	0.69–2.02
Nonparalytic polio	115	1.45	1.17–1.79	378	1.35	1.20–1.51
Suspected polio	16	1.69	0.92–3.00	92	1.62	1.27–2.05
Total	239	1.36	1.17–1.57	659	1.29	1.18–1.41
Diseases of the digestive system						
Paralytic polio	132	1.15	0.94–1.39	279	1.03	0.90–1.17
None or mild paralysis of the extremities	89	1.17	0.92–1.47	170	0.99	0.84–1.17
Severe paralysis of at least 1 extremity	32	0.94	0.62–1.36	89	1.16	0.91–1.47
Respiratory polio	11	2.23	1.03–4.62	20	0.85	0.51–1.34
Nonparalytic polio	157	1.46	1.22–1.75	522	1.34	1.21–1.48
Suspected polio	17	1.55	0.86–2.68	126	1.78	1.44–2.18
Total	306	1.31	1.15–1.49	927	1.27	1.18–1.37

Despite the fact that validity varies between diagnoses, diagnoses reported by a physician are likely to be more reliable than self-reported disorders.

PPS is not coded in the ICD; however, "polio sequelae" (paralysis or any conditions specified as late effect after polio) is listed as a specific disease with a code in ICD-8 (code 44.99) and ICD-10 (code B91.1). More than 50% of the respiratory polio patients and 15% of the nonrespiratory polio patients were hospitalized because of polio sequelae. Because of the surprisingly low incidence of locomotor disorders, many muscle and bone disorders were probably hidden in the diagnosis of polio sequelae.

We observed an increased morbidity among patients with nonparalytic polio and patients diagnosed with suspected polio. To date, late effects of polio have only been associated with paralytic polio. However, recent studies[42-44] have suggested that nonparalytic polio patients and even patients without weakness or nuchal spinal rigidity might have lost several neurons because of the poliovirus infection and, like the paralytic polio patient, those people might develop late-onset muscle weakness and fatigue.

There are a number of potential sources of bias that need to be considered. Polio patients might seek medical attention more often than other persons. If so, one would expect a much higher morbidity among the polio patients with paralyses and no increased morbidity among patients who had nonparalytic polio or suspected polio. However, this was not the case. Polio patients, irrespective of degree of paralysis, are characterized by doing well in society, are well educated, hard working, and generally self-supported,[45,46] all factors indicative of high socioeconomic status. If socioeconomic status were linked to hospitalizations, our results would have been biased by polio patients having easier access to the hospitals. However, in Denmark, health care, including hospitalization, is free and easily accessible to all citizens. Confounding from socioeconomic factors is therefore an unlikely explanation of the observed increased hospitalization rate.

Within the cohort of polio patients, a misclassification between the different types of poliomyelitis might have occurred. Many cases of paralytic polio might have been misclassified as suspected polio or nonparalytic polio as a result of failure to detect minimal degrees of muscle weakness. Accordingly, these patients might not have received the correct treatment and attention during the acute phase of poliomyelitis and, furthermore, later symptoms might have been ignored or considered without relation to their previous polio disease.

To estimate whether polio patients had a higher morbidity than expected, we compared polio patients with an age- and gender-matched group of Danes who lived in the same period. Among this group of people considered as not having had polio, some might have had nonparalytic or undiagnosed polio infection not requiring hospitalization. Had we been able to avoid this kind of misclassification, our results on differential morbidity would presumably have been stronger.

CONCLUSIONS

The present investigation suggests that persons with a history of poliomyelitis have a slightly increased morbidity compared with an age- and gender-matched cohort. As expected, persons who suffered from respiratory failure during the epidemics had the highest morbidity. Surprisingly, individuals presumably left without residual symptoms after the acute phase of poliomyelitis, especially women, also had an increased morbidity compared with control subjects from the Danish population. The mechanism underlying this association is unknown and further studies are needed.

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References

1. United Nations Children's Fund. Countdown to polio eradication. A world free of polio: with commitment from every nation, this will be our priceless gift to the 21st century. New York: UNICEF; 1999. Available at: http://www.unicef.org/polio/poliobook.htm. Accessed May 20, 2003.
2. Nielsen NM, Rostgaard K, Hjalgrim H, Askgaard DS, Aaby P. Parkinson's disease and poliomyelitis. JAMA 2002;287:1650-1.
3. Nielsen NM, Wohlfahrt J, Melbye M, et al. Multiple sclerosis and poliomyelitis. A Danish historical cohort study. Acta Neurol Scand 2000;101:384-7.
4. Nielsen NM, Wohlfahrt J, Aaby P, et al. Cancer risk in a cohort of polio patients. Int J Cancer 2001;92:605-8.
5. Owen RR. Postpolio syndrome and cardiopulmonary conditioning. West J Med 1991;154:5:557-8.
6. Jublet B, Drucker J. Post-polio syndrome: an update. Semin Neurol 1993;13:283-9.
7. Jubelt B, Cashman NR. Neurological manifestations of post-polio syndrome. Crit Rev Neurobiol 1987;3:199-200.
8. Ramlow J, Alexander M, LaPorte R, Kaufmann C, Kuller L. Epidemiology of the post-polio Syndrome. Am J Epidemiol 1992; 136:7:769-86.
9. Klingman J, Chui H, Corgiat M, Perry J. Functional recovery. A major risk factor for the development of post poliomyelitis muscular atrophy. Arch Neurol 1988;45:645-7.
10. Kemp BJ, McNeal DR. The importance of aging with a disability to assistive technology. Assist Technol 1999;11:81-3.
11. Garland DE, Stewart CA, Adkins RH, et al. Osteoporosis after spinal cord injury. J Orthop Res 1992;10:371-8.
12. Murphy KP, Molnar GE, Lankasky K. Medical and functional status of adults with cerebral palsy. Dev Med Child Neurol 1995; 37:1075-84.
13. Bauman WA, Spungen AM, Adkins RH, Kemp BJ. Metabolic and endocrine changes in persons ageing with spinal cord injury. Assist Technol 1999;11:88-96.
14. Campbell ML, Sheets B, Strong PS. Secondary health condition among middle-aged individuals with chronic physical disabilities: implication for unmet needs for services. Assist Technol 1999;11: 105-22.
15. Astrup P, Bjørneboe M, Neukirch F. Polioepidemien i København 1952. Bibliotek Laeger/Medicinsk Forum 1989;7:9-111.
16. Schanke AK, Stanghelle JK, Fatigue in polio survivors. Spinal Cord 2001;39:243-51.
17. Lassen HC. [Comparative studies of primary lymphocytic meningitis and paralytic polio] [Danish]. Ugeskr Laeger 1939;3:73-80.
18. Bjerglund R, Bang HO. Poliomyelitisepidemien i København 1950. Ugeskr Laeger 1953;4:879-84.
19. Malig C. CRS. The Civil Registration System in Denmark. Copenhagen: CRS Office, Ministry of the Interior; 1995.
20. Rasmussen S, Madsen M. Registre inden for sundhedsområdet. Copenhagen: National Institute of Public Health; 1997.
21. Danish National Board of Health. International statistical classification of diseases and health related problems. 8th revision. Copenhagen: Danish National Board of Health; 1965.
22. Danish National Board of Health. International statistical classification of diseases and health related problems. 10th revision. Copenhagen: Danish National Board of Health; 1993.
23. Gabriel SE, Crowson CS, O'Fallon WM. Comorbidity in arthritis. J Rheumatol 1999;26:2475-9.
24. Weinstein L. Influence of age and sex on susceptibility and clinical manifestation in poliomyelitis. N Engl J Med 1957;257: 2:47-52.
25. Reedy JJ. Recessive inheritance of susceptibility to poliomyelitis. J Hered 1957;48:37-44.
26. Pietch MC, Morris PJ. An association of HL-A3 and HL-A7 with paralytic poliomyelitis. Tissue Antigen 1974;4:50-5.
27. van Eden W, Persijn G, Bijkerk H, de Vries RR, Schuurman RK, van Rood JJ. Differential resistance to paralytic poliomyelitis controlled by histocompatibility leukocyte antigens. J Infect Dis 1983;147:422-6.
28. Von Magnus H. Poliomyelitis. Faktorer af betydning for udvikling af lammelser. Ugeskr Laeger 1952;31:1032-4.
29. Wyatt HV. Provocation of poliomyelitis by multiple injections. Trans R Soc Trop Med Hyg 1985;79:355-8.
30. Aaby P, Bukh J, Hoff G, et al. High measles mortality in infancy related to intensity of exposure. J Pediatr 1986;109:40-4.
31. Aaby P. Malnourished or overinfected. An analysis of the determinants of acute measles mortality [thesis]. Copenhagen: Copenhagen Univ; 1988.
32. Aaby P, Coovadia H, Bukh J, et al. Severe measles: a reappraisal of the role of nutrition, overcrowding and virus dose. Med Hypotheses 1985;18:93-112.
33. Wyatt HV. Is poliomyelitis a genetically-determined disease: I: a genetic model. Med Hypotheses 1975;1:35-42.
34. Wekre LL, Stanghelle JK, Lobben B, Øyhaugen S. The Norwegian Polio Study 1994: a nation-wide survey of problems in long-standing poliomyelitis. Spinal Cord 1998;36:280-4.
35. Halstead LS, Rossi CD. Postpolio syndrome: clinical experience with 132 consecutive outpatients. Birth Defects Orig Artic Ser 1987;23:13-26.
36. Farbu E, Gilhus NE. Poliomyelitis: long-time consequences for social life. Acta Neurol Scand 1997;96:353-8.
37. Frustace SJ. Poliomyelitis: late and unusual sequelae. Am J Phys Med 1988;66:328-36.
38. Nielsen NM. Poliomyelitis; acute severity and long-term consequences [thesis]. Copenhagen: Univ Copenhagen; 1999.
39. Jürgensen HJ, Frølund C, Gustafsen J, Mosbech H, Guldhammer B. [Registration of diagnoses in a national patient register. Preliminary assessment of the validity of the register] [Danish]. Ugeskr Laeger 1984;146:3303-8.
40. Madsen M, Balling H, Eriksen LS. [The validity of the diagnosis of acute myocardial infarction in 2 registries: the Heart Registry compared to the National Patient Registry] [Danish]. Ugeskr Laeger 1990;152:308-14.
41. Fonager K, Sørensen HT, Rasmussen SN, Møller-Petersen J, Vyberg M. Assessment of the diagnoses of Crohn's disease and ulcerative colitis in a Danish Hospital Information System. Scand J Gastroenterol 1996;31:154-9.
42. Sabin AB, Steigman AJ. Poliomyelitis virus of low virulence in patients with epidemic "summer grippe or sore throat." Am J Hyg 1949;49:176-93.
43. Bodian D. Histopathological basis of clinical findings in poliomyelitis. Am J Med 1949;6:63-78.
44. Bruno RL. Paralytic vs. "nonparalytic" polio: distinction without a difference? Am J Phys Med Rehabil 2000;79:4-12.
45. Farbu E, Rekand T, Aarli JA, Gilhus NE. Polio survivors—well educated and hard working. J Neurol 2001;248:500-5.
46. Lønnberg F. Late onset polio sequelae in Denmark. Results of a nation-wide survey of 3607 polio survivors. Scand J Rehabil Med Suppl 1993;28:1-32.