

Supplementary Appendix:

MORTALITY AFTER CHILDHOOD GROWTH HORMONE TREATMENT – THE SAGHE STUDY

Table S1: Mortality by diagnosis for risk group 2 and 3

Diagnosis	Risk group 2					Risk group 3				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Central nervous system tumour						272	11.5	25,032.0	23.6 (21.0, 26.6)	104.1 (91.5, 117.8)
Central nervous system tumour craniopharyngioma						65	5.1	10,567.1	12.8 (10.0, 16.3)	56.7 (42.7, 73.6)
Non central nervous system tumour						20	1.1	2,435.9	18.5 (11.9, 28.6)	77.7 (45.7, 122.4)
Hematologic malignancy						65	6.0	11,828.7	10.9 (8.5, 13.8)	49.9 (37.4, 65.0)
Chronic renal failure and renal diseases						31	2.5	4,666.4	12.3 (8.6, 17.5)	61.0 (39.7, 88.9)
Turner syndrome	52	16.7	60,068.9	3.1 (2.4, 4.1)	5.9 (3.7, 8.6)					
Syndromes and chronic diseases	77	11.2	23,866.9	6.9 (5.5, 8.6)	27.6 (20.8, 35.6)	3	0.4	666.9	7.1 (2.3, 22.0)	38.7 (2.9, 125.1)
Multiple pituitary hormone deficiency - organic GHD	53	20.3	34,401.2	2.6 (2.0, 3.4)	9.5 (5.6, 14.3)					
Skeletal dysplasias	10	1.8	3,928.1	5.7 (3.0, 10.5)	21.0 (7.7, 42.3)					

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

Table S2a: Comprehensive mortality data for all countries (risk group 1a and 1b)

	Risk group 1a					Risk group 1b				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	90	84.2	151004	1.1 (0.9, 1.3)	0.4 (-0.8, 1.8)	49	33.5	66229	1.5 (1.1, 1.9)	2.3 (0.4, 4.7)
Country										
Belgium	3	3.5	5784	0.8 (0.3, 2.6)	-0.9 (-5.0, 9.0)	1	1.6	2702	0.6 (0.1, 4.4)	-2.3 (-5.9, 14.7)
Switzerland	0	1.4	3590	0.0 (., .)	-3.9 (., 6.4)	0	0.3	897	0.0 (., .)	-3.6 (., 37.5)
France	63	56.8	88786	1.1 (0.9, 1.4)	0.7 (-0.9, 2.7)	30	17.7	31398	1.7 (1.2, 2.4)	3.9 (0.8, 8.0)
Germany	5	4.2	10264	1.2 (0.5, 2.9)	0.8 (-2.5, 7.3)	1	0.9	2318	1.1 (0.2, 7.8)	0.4 (-3.8, 20.1)
Italy	2	3.4	9409	0.6 (0.1, 2.4)	-1.5 (-3.3, 4.1)	2	0.5	1444	3.7 (0.9, 14.7)	10.1 (-2.1, 46.3)
The Netherlands	3	2.1	6512	1.5 (0.5, 4.5)	1.4 (-2.2, 10.3)	1	1.1	3838	0.9 (0.1, 6.4)	-0.3 (-2.8, 11.6)
Sweden	9	7.8	17793	1.2 (0.6, 2.2)	0.7 (-2.1, 5.2)	7	4.8	10766	1.5 (0.7, 3.1)	2.1 (-1.8, 8.9)
UK	5	5.1	8867	1.0 (0.4, 2.4)	-0.1 (-3.9, 7.4)	7	6.5	12867	1.1 (0.5, 2.3)	0.4 (-2.9, 6.1)
Sex										
Male	76	70.8	102986	1.1 (0.9, 1.3)	0.5 (-1.1, 2.4)	40	26.6	41421	1.5 (1.1, 2.0)	3.2 (0.5, 6.7)
Female	14	13.4	48018	1.0 (0.6, 1.8)	0.1 (-1.2, 2.1)	9	6.9	24808	1.3 (0.7, 2.5)	0.9 (-1.1, 4.1)
Age started treatment (years)										
0-4	4	7.4	10421	0.5 (0.2, 1.4)	-3.2 (-6.0, 2.8)	5	5.1	7455	1.0 (0.4, 2.4)	-0.1 (-4.6, 8.8)
5-9	19	17.3	44145	1.1 (0.7, 1.7)	0.4 (-1.3, 2.8)	11	8.6	23975	1.3 (0.7, 2.3)	1.0 (-1.3, 4.6)
10-14	56	46.8	82684	1.2 (0.9, 1.6)	1.1 (-0.5, 3.1)	24	16.1	30644	1.5 (1.0, 2.2)	2.6 (-0.2, 6.4)
15-19	11	12.7	13754	0.9 (0.5, 1.6)	-1.2 (-5.2, 5.1)	9	3.7	4155	2.4 (1.3, 4.6)	12.7 (1.0, 32.2)
Time since start of treatment (years)										
0-4	15	19.3	45018	0.8 (0.5, 1.3)	-1.0 (-2.4, 1.2)	10	8.3	18997	1.2 (0.6, 2.2)	0.9 (-1.9, 5.3)
5-9	21	23.2	43607	0.9 (0.6, 1.4)	-0.5 (-2.3, 2.0)	14	8.3	18549	1.7 (1.0, 2.9)	3.1 (-0.3, 8.2)
10-14	30	23.3	36765	1.3 (0.9, 1.8)	1.8 (-0.8, 5.3)	9	9.2	16606	1.0 (0.5, 1.9)	-0.1 (-3.0, 4.8)
15-19	19	15.2	21827	1.3 (0.8, 2.0)	1.7 (-1.7, 6.6)	13	6.1	9760	2.1 (1.2, 3.7)	7.1 (0.9, 16.6)
20-24	5	3.0	3701	1.7 (0.7, 4.0)	5.3 (-3.8, 23.4)	3	1.6	2172	1.9 (0.6, 5.8)	6.4 (-4.6, 32.9)
25-29	0	0.1	87	0.0 (., .)	-10.7 (., 416.0)	0	0.1	144	0.0 (., .)	-8.0 (., 248.5)
Attained age (years)										
0-4	0	4.4	714	0.0 (., .)	-61.3 (., -9.6)	0	3.1	489	0.0 (., .)	-64.2 (., 11.3)
5-9	0	1.3	7872	0.0 (., .)	-1.7 (., 3.0)	1	0.8	4957	1.3 (0.2, 9.2)	0.5 (-1.5, 9.7)
10-14	11	5.0	28739	2.2 (1.2, 4.0)	2.1 (0.2, 5.1)	6	2.3	13724	2.7 (1.2, 5.9)	2.7 (0.0, 7.9)
15-19	27	22.3	44144	1.2 (0.8, 1.8)	1.1 (-1.0, 3.8)	11	8.5	18653	1.3 (0.7, 2.3)	1.4 (-1.6, 6.0)
20-24	22	26.0	36795	0.8 (0.6, 1.3)	-1.1 (-3.3, 2.0)	14	9.7	15424	1.4 (0.9, 2.4)	2.8 (-1.3, 8.9)
25-29	15	16.2	22979	0.9 (0.6, 1.5)	-0.5 (-3.4, 3.7)	11	5.8	9025	1.9 (1.1, 3.4)	5.8 (-0.3, 15.4)
30-34	14	7.7	8803	1.8 (1.1, 3.1)	7.1 (-0.1, 17.9)	6	2.7	3388	2.2 (1.0, 4.9)	9.6 (-1.6, 30.5)
35-39	1	1.2	943	0.8 (0.1, 5.8)	-2.4 (-12.8, 46.0)	0	0.6	552	0.0 (., .)	-11.5 (., 55.4)
40-44	0	0.0	16	0.0 (., .)	-21.1 (., 2341.1)	0	0.0	16	0.0 (., .)	-16.5 (., 2234.0)
Duration of treatment (years)										
<2	26	16.3	25771	1.6 (1.1, 2.3)	3.8 (0.3, 8.5)	14	5.6	10159	2.5 (1.5, 4.2)	8.3 (2.0, 17.6)
2	12	15.0	23716	0.8 (0.5, 1.4)	-1.3 (-3.7, 2.5)	9	5.6	10440	1.6 (0.8, 3.1)	3.2 (-1.4, 11.0)
3	15	13.9	23443	1.1 (0.7, 1.8)	0.5 (-2.3, 4.6)	8	5.0	9454	1.6 (0.8, 3.2)	3.1 (-1.7, 11.3)
4-5	14	15.4	28813	0.9 (0.5, 1.5)	-0.5 (-2.7, 2.8)	8	6.4	13058	1.3 (0.6, 2.5)	1.3 (-2.2, 7.2)
6-9	12	11.0	24190	1.1 (0.6, 1.9)	0.4 (-2.0, 4.1)	5	5.8	13513	0.9 (0.4, 2.1)	-0.6 (-3.1, 4.4)
≥10	4	5.7	9986	0.7 (0.3, 1.9)	-1.7 (-4.6, 4.5)	3	3.4	5861	0.9 (0.3, 2.8)	-0.6 (-4.7, 9.2)
Unknown	7	6.8	15084	1.0 (0.5, 2.1)	0.1 (-2.7, 5.0)	2	1.8	3745	1.1 (0.3, 4.5)	0.6 (-4.1, 14.6)

Mean r-hGH dose (µg/kg/d)										
<15	3	4.3	5571	0.7 (0.2, 2.1)	-2.4 (-6.7, 8.0)	3	1.8	2316	1.7 (0.5, 5.2)	5.2 (-5.1, 30.1)
15-19	20	19.7	29074	1.0 (0.7, 1.6)	0.1 (-2.6, 3.9)	7	5.8	9342	1.2 (0.6, 2.5)	1.3 (-3.2, 9.2)
20-24	11	14.4	25222	0.8 (0.4, 1.4)	-1.4 (-3.5, 2.1)	9	5.1	9442	1.8 (0.9, 3.4)	4.2 (-1.0, 12.7)
25-29	10	10.0	18339	1.0 (0.5, 1.9)	0.0 (-2.8, 4.6)	5	4.3	8903	1.2 (0.5, 2.8)	0.8 (-3.0, 8.3)
30-34	7	7.1	15255	1.0 (0.5, 2.1)	-0.1 (-2.8, 4.8)	8	4.8	10576	1.7 (0.8, 3.3)	3.0 (-1.3, 10.3)
35-39	2	2.3	5012	0.9 (0.2, 3.5)	-0.5 (-4.0, 9.9)	0	1.3	3060	0.0 (., .)	-4.2 (., 7.9)
40-49	3	1.8	4160	1.7 (0.5, 5.2)	2.9 (-2.8, 16.7)	0	1.2	2783	0.0 (., .)	-4.3 (., 9.0)
≥50	0	1.0	2454	0.0 (., .)	-4.2 (., 10.9)	8	3.0	7088	2.7 (1.4, 5.4)	7.1 (0.7, 18.1)
Unknown	34	23.6	45917	1.4 (1.0, 2.0)	2.3 (0.0, 5.2)	9	6.3	12720	1.4 (0.7, 2.8)	2.2 (-1.7, 8.5)

Birth weight SDS										
<-4	0	0.0	97	0.0 (., .)	-3.4 (., 375.3)	2	1.1	2357	1.9 (0.5, 7.4)	3.9 (-3.6, 26.1)
-3 to -4	0	0.2	345	0.0 (., .)	-7.0 (., 100.1)	4	2.3	4662	1.7 (0.6, 4.6)	3.6 (-2.7, 17.0)
-2 to -3	0	0.7	1396	0.0 (., .)	-5.3 (., 21.1)	6	7.4	14999	0.8 (0.4, 1.8)	-1.0 (-3.5, 3.8)
-1 to -2	14	13.2	24967	1.1 (0.6, 1.8)	0.3 (-2.2, 4.1)	18	9.9	19480	1.8 (1.2, 2.9)	4.2 (0.4, 9.5)
0 to -1	21	24.9	44744	0.8 (0.5, 1.3)	-0.9 (-2.7, 1.6)	8	6.7	11969	1.2 (0.6, 2.4)	1.1 (-2.7, 7.6)
0 to 1	14	14.8	24845	0.9 (0.6, 1.6)	-0.3 (-2.9, 3.5)	1	2.4	4259	0.4 (0.1, 3.0)	-3.2 (-5.5, 7.5)
1 to 2	5	3.7	6092	1.3 (0.6, 3.2)	2.1 (-3.4, 13.1)	0	0.6	955	0.0 (., .)	-5.9 (., 32.7)
2 to 3	1	1.2	1791	0.9 (0.1, 6.1)	-0.9 (-6.3, 24.6)	1	0.2	356	4.6 (0.6, 32.4)	21.9 (-5.4, 150.3)
Unknown	35	25.4	46727	1.4 (1.0, 1.9)	2.0 (-0.2, 5.0)	9	3.0	7191	3.0 (1.6, 5.9)	8.4 (1.6, 19.7)

Cumulative r-hGH dose (mg/kg)										
<25	31	35.2	55891	0.9 (0.6, 1.3)	-0.8 (-2.5, 1.6)	20	13.7	23172	1.5 (0.9, 2.3)	2.7 (-0.6, 7.4)
25-49	17	18.5	34609	0.9 (0.6, 1.5)	-0.4 (-2.5, 2.5)	15	7.7	16449	1.9 (1.2, 3.2)	4.4 (0.4, 10.3)
50-99	10	9.6	19751	1.0 (0.6, 1.9)	0.2 (-2.4, 4.4)	4	6.0	13488	0.7 (0.2, 1.8)	-1.5 (-3.7, 3.1)
≥100	2	2.4	5160	0.8 (0.2, 3.3)	-0.9 (-4.3, 9.3)	3	2.2	5296	1.4 (0.4, 4.3)	1.5 (-3.0, 12.4)
Unknown	30	18.4	35593	1.6 (1.1, 2.3)	3.3 (0.5, 6.9)	7	3.9	7825	1.8 (0.9, 3.8)	3.9 (-1.4, 13.4)

By cause										
Infectious and parasitic disease (A00-B99)	3	1.1	140740	2.7 (0.9, 8.2)	0.1 (0.0, 0.5)	0	0.5	63911	0.0 (., .)	-0.1 (., 0.5)
Neoplasms (C00-D48)	7	8.1	151004	0.9 (0.4, 1.8)	-0.1 (-0.3, 0.4)	2	3.4	66229	0.6 (0.1, 2.4)	-0.2 (-0.5, 0.6)
Diseases of blood and blood-forming organs (D50-D89)	3	0.4	151004	8.2 (2.6, 25.4)	0.2 (0.0, 0.6)	1	0.2	66229	6.4 (0.9, 45.2)	0.1 (0.0, 0.8)
Endocrine, nutritional & metabolic disease (E00-E90)	1	1.2	151004	0.8 (0.1, 5.9)	0.0 (-0.1, 0.3)	1	0.6	66229	1.8 (0.2, 12.5)	0.1 (-0.1, 0.8)
Mental & behavioural disorders (F00-F99)	1	1.8	151004	0.6 (0.1, 3.9)	-0.1 (-0.1, 0.2)	0	0.7	66229	0.0 (., .)	-0.1 (., 0.4)
Diseases of nervous system, eye & ear (G00-H95)	2	3.2	140740	0.6 (0.2, 2.5)	-0.1 (-0.2, 0.3)	2	1.5	63911	1.4 (0.3, 5.5)	0.1 (-0.2, 0.9)
Diseases of circulatory system (I00-I99)	9	3.8	151004	2.4 (1.2, 4.6)	0.3 (0.0, 0.9)	6	1.6	66229	3.7 (1.7, 8.3)	0.7 (0.1, 1.7)
Diseases of respiratory system (J00-J99)	2	1.4	151004	1.4 (0.4, 5.7)	0.0 (-0.1, 0.4)	1	0.7	66229	1.5 (0.2, 10.7)	0.1 (-0.1, 0.7)
Diseases of digestive system (K00-K93)	1	0.9	151004	1.1 (0.2, 8.0)	0.0 (-0.1, 0.3)	0	0.4	66229	0.0 (., .)	-0.1 (., 0.5)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	151004	0.0 (., .)	0.0 (., 0.2)	0	0.0	66229	0.0 (., .)	0.0 (., 0.6)
Diseases of musculoskeletal system & connective tissue (M00-M99)	0	0.2	151004	0.0 (., .)	0.0 (., 0.2)	0	0.1	66229	0.0 (., .)	0.0 (., 0.5)
Diseases of genitourinary system (N00-N99)	0	0.2	151004	0.0 (., .)	0.0 (., 0.2)	0	0.1	66229	0.0 (., .)	0.0 (., 0.5)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	151004	0.0 (., .)	0.0 (., 0.2)	0	0.0	66229	0.0 (., .)	0.0 (., 0.6)
Conditions originating in perinatal period (P00-P96)	0	1.2	151004	0.0 (., .)	-0.1 (., 0.2)	0	0.8	66229	0.0 (., .)	-0.1 (., 0.4)
Congenital anomalies (Q00-Q99)	2	2.4	151004	0.8 (0.2, 3.3)	0.0 (-0.1, 0.3)	2	1.3	66229	1.5 (0.4, 6.1)	0.1 (-0.2, 0.9)
Symptoms, signs & ill-defined conditions (R00-R99)	13	7.1	151004	1.8 (1.1, 3.1)	0.4 (0.0, 1.0)	10	2.7	66229	3.7 (2.0, 6.9)	1.1 (0.3, 2.4)
Accidents and violence (V00-Y98)	45	50.0	151004	0.9 (0.7, 1.2)	-0.3 (-1.1, 0.7)	24	18.3	66229	1.3 (0.9, 2.0)	0.9 (-0.4, 2.6)

By circulatory cause										
Ischemic heart disease	1	0.5	151004	2.2 (0.3, 15.7)	0.0 (0.0, 0.3)	0	0.2	66229	0.0 (., .)	0.0 (., 0.5)
Cerebrovascular disease	4	0.9	151004	4.7 (1.8, 12.5)	0.2 (0.0, 0.6)	1	0.4	66229	2.8 (0.4, 20.2)	0.1 (0.0, 0.8)
Other circulatory disease	3	2.3	140740	1.3 (0.4, 4.1)	0.1 (-0.1, 0.5)	5	1.0	63911	5.0 (2.1, 11.9)	0.6 (0.1, 1.7)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S2b: Comprehensive mortality data for all countries (risk group 2 and 3)

	Risk group 2					Risk group 3				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	192	50.0	122319	3.8 (3.3, 4.4)	11.6 (9.5, 14.0)	456	26.7	55392	17.1 (15.6, 18.7)	77.5 (70.1, 85.4)
Country										
Belgium	14	4.5	9876	3.1 (1.9, 5.3)	9.7 (3.2, 19.3)	33	2.1	3862	15.4 (10.9, 21.7)	79.9 (53.3, 114.5)
Switzerland	3	1.1	3369	2.8 (0.9, 8.6)	5.7 (-1.4, 22.8)	10	0.7	1493	14.7 (7.9, 27.3)	62.4 (27.6, 118.6)
France	64	16.7	38104	3.8 (3.0, 4.9)	12.4 (8.6, 17.1)	184	10.8	19693	17.0 (14.7, 19.6)	87.9 (74.9, 102.4)
Germany	7	3.1	9219	2.3 (1.1, 4.8)	4.2 (-0.3, 12.3)	12	1.0	2181	12.3 (7.0, 21.7)	50.5 (24.0, 91.6)
Italy	2	0.4	1609	5.0 (1.2, 19.9)	9.9 (-1.0, 42.4)	0	0.2	475	0.0 (., .)	-3.2 (., 74.4)
The Netherlands	19	3.5	12197	5.4 (3.4, 8.4)	12.7 (6.5, 21.4)	34	1.5	4470	23.1 (16.5, 32.3)	72.8 (49.4, 103.0)
Sweden	28	5.6	15619	5.0 (3.5, 7.3)	14.4 (8.3, 22.3)	49	2.4	5795	20.4 (15.4, 27.0)	80.4 (58.4, 107.7)
UK	55	15.2	32325	3.6 (2.8, 4.7)	12.3 (8.1, 17.5)	134	8.1	17424	16.6 (14.0, 19.7)	72.3 (59.8, 86.5)
Sex										
Male	88	26.0	39508	3.4 (2.7, 4.2)	15.7 (11.3, 20.9)	266	21.0	33379	12.7 (11.2, 14.3)	73.4 (64.1, 83.6)
Female	104	24.0	82811	4.3 (3.6, 5.3)	9.7 (7.4, 12.3)	190	5.7	22013	33.2 (28.8, 38.3)	83.7 (71.9, 96.9)
Age started treatment (years)										
0-4	25	12.4	17593	2.0 (1.4, 3.0)	7.1 (2.1, 13.9)	26	2.1	2705	12.5 (8.5, 18.4)	88.5 (55.1, 133.2)
5-9	59	13.1	45090	4.5 (3.5, 5.8)	10.2 (7.1, 14.0)	145	7.0	19067	20.8 (17.7, 24.5)	72.4 (60.5, 85.8)
10-14	78	19.0	50074	4.1 (3.3, 5.1)	11.8 (8.5, 15.7)	244	14.0	28388	17.5 (15.4, 19.8)	81.0 (70.6, 92.5)
15-19	30	5.5	9561	5.5 (3.8, 7.8)	25.6 (15.4, 39.1)	41	3.8	5232	10.9 (8.0, 14.8)	71.2 (49.1, 99.1)
Time since start of treatment (years)										
0-4	47	16.3	35392	2.9 (2.2, 3.8)	8.7 (5.2, 13.1)	149	6.4	17460	23.2 (19.8, 27.2)	81.7 (68.5, 96.5)
5-9	45	10.9	34132	4.1 (3.1, 5.5)	10.0 (6.4, 14.4)	137	7.4	16040	18.4 (15.6, 21.8)	80.8 (67.1, 96.3)
10-14	51	11.6	29572	4.4 (3.4, 5.8)	13.3 (8.9, 18.8)	91	7.2	13010	12.6 (10.3, 15.5)	64.4 (50.8, 80.3)
15-19	36	8.2	18115	4.4 (3.2, 6.1)	15.4 (9.4, 23.0)	60	4.3	6972	14.1 (11.0, 18.2)	80.0 (59.6, 104.7)
20-24	12	2.8	4824	4.3 (2.4, 7.5)	19.0 (7.0, 37.6)	19	1.3	1775	14.7 (9.4, 23.1)	99.7 (57.2, 159.9)
25-29	1	0.2	285	4.6 (0.6, 32.7)	27.5 (-6.7, 188.0)	0	0.1	135	0.0 (., .)	-9.3 (., 264.4)
Attained age (years)										
0-4	4	8.5	1490	0.5 (0.2, 1.2)	-30.4 (-49.9, 11.5)	0	1.3	204	0.0 (., .)	-65.5 (., 115.3)
5-9	12	1.5	10353	7.9 (4.5, 14.0)	10.1 (4.5, 18.8)	14	0.5	2813	31.0 (18.4, 52.4)	48.2 (25.6, 81.9)
10-14	23	3.8	25161	6.1 (4.1, 9.2)	7.6 (4.3, 12.2)	92	1.9	11150	49.4 (40.3, 60.6)	80.8 (64.8, 99.5)
15-19	49	12.0	34207	4.1 (3.1, 5.4)	10.8 (7.1, 15.4)	145	7.4	16334	19.6 (16.7, 23.1)	84.3 (70.4, 99.9)
20-24	40	12.3	27989	3.3 (2.4, 4.4)	9.9 (5.8, 15.1)	118	8.3	13771	14.3 (11.9, 17.1)	79.7 (64.9, 96.6)
25-29	43	7.4	16034	5.8 (4.3, 7.9)	22.2 (14.8, 31.5)	56	4.8	7871	11.7 (9.0, 15.2)	65.1 (47.7, 86.3)
30-34	17	3.6	6030	4.7 (2.9, 7.6)	22.2 (10.4, 39.1)	24	2.1	2739	11.6 (7.7, 17.2)	80.1 (48.6, 122.8)
35-39	4	0.9	1018	4.4 (1.7, 11.8)	30.5 (1.9, 91.8)	6	0.5	485	11.3 (5.1, 25.1)	112.7 (34.4, 258.2)
40-44	0	0.1	37	0.0 (., .)	-14.2 (., 986.8)	1	0.0	24	27.2 (3.8, 193.2)	399.5 (-4.7, 2295.7)
Duration of treatment (years)										
<2	48	5.1	10822	9.5 (7.2, 12.6)	39.7 (28.0, 54.1)	126	3.9	7405	32.6 (27.4, 38.8)	164.9 (136.5, 197.4)
2	21	4.2	10089	4.9 (3.2, 7.6)	16.6 (8.7, 27.6)	71	3.6	6629	19.9 (15.7, 25.0)	101.7 (78.3, 129.7)
3	24	5.1	12601	4.7 (3.2, 7.0)	15.0 (8.2, 24.3)	56	3.9	7278	14.4 (11.1, 18.7)	71.6 (52.8, 94.6)
4-5	31	8.8	24410	3.5 (2.5, 5.0)	9.1 (5.0, 14.4)	81	5.7	11911	14.2 (11.4, 17.7)	63.2 (49.2, 79.7)
6-9	40	10.6	31853	3.8 (2.8, 5.1)	9.2 (5.6, 13.8)	71	5.4	12683	13.3 (10.5, 16.7)	51.8 (39.5, 66.4)
≥10	9	10.8	19350	0.8 (0.4, 1.6)	-0.9 (-3.5, 3.2)	12	2.0	4159	5.9 (3.4, 10.5)	24.0 (10.1, 45.5)
Unknown	19	5.3	13194	3.6 (2.3, 5.6)	10.4 (4.6, 18.5)	39	2.3	5327	16.8 (12.3, 23.0)	68.9 (47.7, 95.7)

Mean r-hGH dose (µg/kg/d)										
<15	4	1.2	1814	3.5 (1.3, 9.2)	15.7 (-0.3, 50.1)	39	1.9	3246	20.5 (15.0, 28.0)	114.3 (79.6, 158.4)
15-19	15	3.3	5734	4.5 (2.7, 7.4)	20.3 (8.8, 37.3)	59	3.7	7424	15.9 (12.3, 20.6)	74.5 (55.5, 97.5)
20-24	24	4.8	9214	5.0 (3.4, 7.5)	20.9 (11.5, 33.6)	76	5.6	11264	13.7 (10.9, 17.1)	62.5 (48.2, 79.5)
25-29	21	5.9	12421	3.6 (2.3, 5.5)	12.2 (5.7, 21.1)	70	4.2	8973	16.8 (13.3, 21.3)	73.4 (56.2, 93.9)
30-34	21	6.2	15590	3.4 (2.2, 5.2)	9.5 (4.4, 16.6)	53	2.4	5449	22.2 (17.0, 29.0)	92.9 (68.5, 122.8)
35-39	16	5.4	16481	3.0 (1.8, 4.8)	6.4 (2.3, 12.5)	19	1.0	2145	20.0 (12.7, 31.3)	84.1 (48.9, 133.9)
40-49	28	6.6	21948	4.2 (2.9, 6.1)	9.8 (5.5, 15.4)	9	0.9	1787	9.9 (5.2, 19.1)	45.3 (18.0, 90.5)
≥50	10	2.0	5327	5.1 (2.7, 9.5)	15.1 (5.3, 30.8)	8	0.3	676	27.2 (13.6, 54.3)	114.0 (46.7, 228.8)
Unknown	53	14.6	33790	3.6 (2.8, 4.7)	11.4 (7.4, 16.2)	123	6.9	14427	17.9 (15.0, 21.4)	80.5 (66.1, 97.0)

Birth weight SDS										
<-4	3	0.9	1654	3.4 (1.1, 10.6)	12.8 (-1.6, 47.7)	2	0.1	166	25.9 (6.5, 103.7)	115.6 (9.9, 429.8)
-3 to -4	9	1.6	3941	5.8 (3.0, 11.2)	18.9 (6.5, 39.4)	2	0.2	341	10.9 (2.7, 43.4)	53.2 (1.7, 206.3)
-2 to -3	25	4.9	13754	5.1 (3.4, 7.5)	14.6 (8.2, 23.3)	14	0.7	1699	19.7 (11.7, 33.2)	78.2 (40.9, 134.0)
-1 to -2	44	11.1	28604	4.0 (2.9, 5.3)	11.5 (7.3, 16.8)	52	3.1	6595	17.1 (13.0, 22.4)	74.2 (54.3, 98.8)
0 to -1	45	12.6	29067	3.6 (2.7, 4.8)	11.2 (7.0, 16.4)	103	6.7	13742	15.5 (12.7, 18.7)	70.1 (56.3, 86.1)
0 to 1	23	6.8	14726	3.4 (2.2, 5.1)	11.0 (5.3, 18.8)	87	5.2	10445	16.7 (13.6, 20.7)	78.3 (61.7, 97.8)
1 to 2	4	1.9	3917	2.1 (0.8, 5.5)	5.2 (-2.2, 21.2)	29	2.2	4373	13.2 (9.2, 19.0)	61.3 (39.4, 90.2)
2 to 3	4	0.6	1324	6.4 (2.4, 17.0)	25.5 (3.5, 72.7)	5	0.5	949	9.3 (3.9, 22.3)	47.0 (11.4, 117.3)
Unknown	35	9.5	25332	3.7 (2.6, 5.1)	10.1 (5.9, 15.5)	162	8.1	17082	20.0 (17.1, 23.3)	90.1 (76.0, 105.9)

Cumulative r-hGH dose (mg/kg)										
<25	50	13.6	24133	3.7 (2.8, 4.9)	15.1 (9.8, 21.7)	171	8.7	18047	19.7 (17.0, 22.9)	90.0 (76.3, 105.3)
25-49	40	11.3	27513	3.6 (2.6, 4.8)	10.4 (6.3, 15.7)	120	7.7	15567	15.7 (13.1, 18.7)	72.2 (59.0, 87.3)
50-99	45	11.5	32863	3.9 (2.9, 5.3)	10.2 (6.5, 14.8)	59	4.5	9521	13.2 (10.3, 17.1)	57.3 (42.5, 75.3)
≥100	24	5.5	17114	4.4 (2.9, 6.5)	10.8 (5.8, 17.7)	11	0.9	1832	12.8 (7.1, 23.1)	55.4 (25.3, 102.8)
Unknown	33	8.2	20695	4.0 (2.9, 5.6)	12.0 (7.0, 18.4)	95	5.1	10426	18.7 (15.3, 22.8)	86.2 (68.8, 106.5)

By cause										
Infectious and parasitic disease (A00-B99)	0	0.9	113100	0.0 (., .)	-0.1 (., 0.2)	5	0.4	53211	11.9 (5.0, 28.7)	0.9 (0.2, 2.1)
Neoplasms (C00-D48)	14	5.8	122319	2.4 (1.4, 4.1)	0.7 (0.2, 1.4)	334	2.9	55392	117.3 (105.4, 130.6)	59.8 (53.5, 66.6)
Diseases of blood and blood-forming organs (D50-D89)	8	0.3	122319	30.9 (15.5, 61.9)	0.6 (0.3, 1.3)	7	0.1	55392	56.8 (27.1, 119.1)	1.2 (0.5, 2.6)
Endocrine, nutritional & metabolic disease (E00-E90)	18	1.1	122319	16.6 (10.5, 26.4)	1.4 (0.8, 2.2)	4	0.5	55392	8.1 (3.0, 21.5)	0.6 (0.1, 1.8)
Mental & behavioural disorders (F00-F99)	3	1.2	122319	2.5 (0.8, 7.9)	0.1 (0.0, 0.6)	1	0.7	55392	1.4 (0.2, 9.7)	0.0 (-0.1, 0.9)
Diseases of nervous system, eye & ear (G00-H95)	9	2.3	113100	3.9 (2.1, 7.6)	0.6 (0.2, 1.3)	12	1.2	53211	9.7 (5.5, 17.2)	2.0 (0.9, 3.7)
Diseases of circulatory system (I00-I99)	33	2.6	122319	12.8 (9.1, 18.0)	2.5 (1.6, 3.6)	19	1.4	55392	13.9 (8.9, 21.8)	3.2 (1.8, 5.1)
Diseases of respiratory system (J00-J99)	11	1.2	122319	8.8 (4.9, 16.0)	0.8 (0.3, 1.5)	13	0.6	55392	23.3 (13.5, 40.2)	2.2 (1.1, 3.9)
Diseases of digestive system (K00-K93)	3	0.8	122319	3.7 (1.2, 11.6)	0.2 (0.0, 0.7)	8	0.4	55392	20.1 (10.1, 40.2)	1.4 (0.6, 2.8)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	122319	0.0 (., .)	0.0 (., 0.3)	0	0.0	55392	0.0 (., .)	0.0 (., 0.7)
Diseases of musculoskeletal system & connective tissue (M00-M99)	5	0.2	122319	26.9 (11.2, 64.7)	0.4 (0.1, 0.9)	4	0.1	55392	49.6 (18.6, 132.2)	0.7 (0.2, 1.8)
Diseases of genitourinary system (N00-N99)	2	0.1	122319	15.2 (3.8, 60.7)	0.2 (0.0, 0.6)	12	0.1	55392	194.1 (110.2, 341.7)	2.2 (1.1, 3.8)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.2	122319	0.0 (., .)	0.0 (., 0.3)	0	0.0	55392	0.0 (., .)	0.0 (., 0.7)
Conditions originating in perinatal period (P00-P96)	0	1.8	122319	0.0 (., .)	-0.1 (., 0.2)	0	0.3	55392	0.0 (., .)	-0.1 (., 0.6)
Congenital anomalies (Q00-Q99)	33	2.8	122319	11.9 (8.5, 16.7)	2.5 (1.6, 3.6)	10	0.9	55392	11.6 (6.3, 21.6)	1.7 (0.7, 3.2)
Symptoms, signs & ill-defined conditions (R00-R99)	25	4.1	122319	6.1 (4.1, 9.0)	1.7 (1.0, 2.7)	13	1.6	55392	7.9 (4.6, 13.7)	2.1 (1.0, 3.7)
Accidents and violence (V00-Y98)	28	22.5	122319	1.2 (0.9, 1.8)	0.5 (-0.3, 1.5)	14	15.1	55392	0.9 (0.5, 1.6)	-0.2 (-1.3, 1.5)

By circulatory cause										
Ischemic heart disease	2	0.3	122319	7.1 (1.8, 28.3)	0.1 (0.0, 0.6)	1	0.3	55392	5.6 (0.8, 39.5)	0.1 (0.0, 1.0)
Cerebrovascular disease	4	0.6	122319	6.7 (2.5, 17.8)	0.3 (0.0, 0.8)	4	0.8	53211	13.3 (5.0, 35.5)	0.7 (0.1, 1.8)
Other circulatory disease	23	1.5	113100	14.9 (9.9, 22.4)	1.9 (1.2, 2.9)	13	26.7	55392	15.4 (8.9, 26.5)	2.3 (1.1, 4.0)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S3a: Comprehensive mortality data for France only (risk group 1a and 1b)

	Risk group 1a					Risk group 1b				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	63	56.8	88786	1.1 (0.9, 1.4)	0.7 (-0.9, 2.7)	30	17.7	31398	1.7 (1.2, 2.4)	3.9 (0.8, 8.0)
Country										
France	63	56.8	88786	1.1 (0.9, 1.4)	0.7 (-0.9, 2.7)	30	17.7	31398	1.7 (1.2, 2.4)	3.9 (0.8, 8.0)
Sex										
Male	53	48.3	60875	1.1 (0.8, 1.4)	0.8 (-1.4, 3.5)	27	13.8	18089	2.0 (1.3, 2.9)	7.3 (2.2, 14.1)
Female	10	8.4	27911	1.2 (0.6, 2.2)	0.6 (-1.3, 3.6)	3	3.9	13308	0.8 (0.2, 2.4)	-0.7 (-2.5, 3.7)
Age started treatment (years)										
0-4	3	4.3	4969	0.7 (0.2, 2.2)	-2.6 (-7.4, 9.0)	1	2.2	2857	0.5 (0.1, 3.2)	-4.3 (-7.7, 11.7)
5-9	11	9.6	22465	1.2 (0.6, 2.1)	0.6 (-1.8, 4.5)	6	3.9	10385	1.5 (0.7, 3.4)	2.0 (-1.7, 8.8)
10-14	41	32.6	51235	1.3 (0.9, 1.7)	1.6 (-0.6, 4.5)	15	8.8	15468	1.7 (1.0, 2.8)	4.0 (-0.3, 10.3)
15-19	8	10.3	10118	0.8 (0.4, 1.6)	-2.3 (-6.8, 5.4)	8	2.7	2688	2.9 (1.5, 5.9)	19.6 (2.7, 48.5)
Time since start of treatment (years)										
0-4	11	12.5	24905	0.9 (0.5, 1.6)	-0.6 (-2.8, 2.9)	4	4.4	9032	0.9 (0.3, 2.4)	-0.4 (-3.6, 6.5)
5-9	16	15.5	24451	1.0 (0.6, 1.7)	0.2 (-2.6, 4.3)	8	4.7	8865	1.7 (0.9, 3.4)	3.8 (-1.4, 12.5)
10-14	18	16.3	23182	1.1 (0.7, 1.8)	0.7 (-2.4, 5.2)	8	5.1	8390	1.6 (0.8, 3.2)	3.5 (-1.9, 12.7)
15-19	15	10.9	14535	1.4 (0.8, 2.3)	2.8 (-1.7, 9.5)	8	3.2	4634	2.5 (1.3, 5.1)	10.5 (0.7, 27.2)
20-24	3	1.6	1714	1.9 (0.6, 6.0)	8.4 (-5.5, 42.1)	2	0.4	477	4.5 (1.1, 18.1)	32.6 (-4.2, 142.2)
25-29										
Attained age (years)										
0-4	0	2.8	374	0.0 (., .)	-74.9 (., 23.8)	0	1.5	206	0.0 (., .)	-71.5 (., 107.2)
5-9	0	0.7	4023	0.0 (., .)	-1.8 (., 7.4)	0	0.4	2105	0.0 (., .)	-1.6 (., 15.9)
10-14	8	2.8	14926	2.8 (1.4, 5.7)	3.5 (0.4, 8.7)	2	1.1	6261	1.8 (0.5, 7.3)	1.4 (-1.4, 9.8)
15-19	16	13.8	24048	1.2 (0.7, 1.9)	0.9 (-1.9, 5.1)	4	4.5	8771	0.9 (0.3, 2.4)	-0.5 (-3.8, 6.6)
20-24	18	17.8	22465	1.0 (0.6, 1.6)	0.1 (-3.2, 4.7)	11	5.3	7626	2.1 (1.1, 3.7)	7.4 (0.2, 18.8)
25-29	11	12.0	15995	0.9 (0.5, 1.7)	-0.6 (-4.0, 4.8)	8	3.2	4641	2.5 (1.2, 5.0)	10.3 (0.5, 27.0)
30-34	9	5.9	6364	1.5 (0.8, 2.9)	4.8 (-2.9, 17.5)	5	1.5	1602	3.4 (1.4, 8.2)	22.0 (0.9, 63.6)
35-39	1	0.9	586	1.2 (0.2, 8.4)	2.6 (-14.1, 80.5)	0	0.3	185	0.0 (., .)	-14.5 (., 185.2)
40-44	0	0.0	5	0.0 (., .)	-23.9 (., 7192.8)	0	0.0	1	0.0 (., .)	-23.9 (., 27871.8)
Duration of treatment (years)										
<2	21	13.0	18757	1.6 (1.1, 2.5)	4.3 (0.0, 10.2)	7	3.4	5507	2.1 (1.0, 4.4)	6.6 (-1.0, 20.1)
2	11	12.2	17650	0.9 (0.5, 1.6)	-0.7 (-3.8, 4.2)	7	4.1	7246	1.7 (0.8, 3.6)	4.0 (-1.8, 14.2)
3	12	10.4	15858	1.1 (0.7, 2.0)	1.0 (-2.7, 6.6)	6	3.5	6030	1.7 (0.8, 3.8)	4.1 (-2.2, 15.8)
4-5	8	10.2	17014	0.8 (0.4, 1.6)	-1.3 (-4.0, 3.3)	7	3.0	5600	2.3 (1.1, 4.9)	7.1 (-0.4, 20.4)
6-9	8	5.4	10277	1.5 (0.7, 3.0)	2.6 (-1.8, 10.1)	2	1.9	3735	1.1 (0.3, 4.3)	0.3 (-4.4, 14.3)
≥10	1	2.6	3822	0.4 (0.1, 2.7)	-4.3 (-6.9, 7.7)	1	0.8	1078	1.3 (0.2, 9.5)	2.4 (-6.7, 44.8)
Unknown	2	2.9	5410	0.7 (0.2, 2.7)	-1.7 (-5.0, 7.9)	0	1.1	2202	0.0 (., .)	-4.8 (., 11.9)
Mean r-hGH dose (µg/kg/d)										
<15	3	4.0	5009	0.7 (0.2, 2.3)	-2.0 (-6.8, 9.5)	2	1.5	1751	1.4 (0.3, 5.4)	3.0 (-7.0, 32.9)
15-19	19	18.5	26823	1.0 (0.7, 1.6)	0.2 (-2.6, 4.2)	6	5.1	8156	1.2 (0.5, 2.6)	1.1 (-3.5, 9.8)
20-24	10	11.8	19660	0.8 (0.5, 1.6)	-0.9 (-3.6, 3.3)	8	3.5	6291	2.3 (1.1, 4.5)	7.1 (-0.1, 19.5)
25-29	4	6.2	10665	0.6 (0.2, 1.7)	-2.1 (-4.8, 3.8)	2	2.0	3814	1.0 (0.3, 4.1)	0.1 (-4.5, 13.8)
30-34	2	1.3	2695	1.5 (0.4, 6.0)	2.5 (-4.0, 21.9)	0	0.5	1009	0.0 (., .)	-5.1 (., 31.4)
35-39	1	0.2	434	4.6 (0.6, 32.7)	18.0 (-4.4, 123.3)	0	0.2	507	0.0 (., .)	-4.6 (., 68.2)
40-49	2	0.2	417	8.5 (2.1, 33.9)	42.3 (0.2, 167.6)	0	0.2	517	0.0 (., .)	-3.5 (., 67.9)
≥50	0	0.2	420	0.0 (., .)	-5.0 (., 82.7)	6	1.5	3337	4.1 (1.9, 9.2)	13.6 (2.3, 34.8)
Unknown	22	14.2	22663	1.5 (1.0, 2.4)	3.4 (-0.2, 8.4)	6	3.3	6018	1.8 (0.8, 4.1)	4.5 (-1.8, 16.2)

Birth weight SDS										
<-4	0	0.0	17	0.0 (., .)	-4.5 (., 2137.2)	0	0.1	180	0.0 (., .)	-7.4 (., 197.1)
-3 to -4	0	0.1	103	0.0 (., .)	-6.7 (., 352.9)	1	0.8	1235	1.3 (0.2, 9.4)	2.0 (-5.9, 39.0)
-2 to -3	0	0.2	429	0.0 (., .)	-5.3 (., 80.6)	2	3.5	6017	0.6 (0.1, 2.3)	-2.5 (-5.4, 6.2)
-1 to -2	9	7.8	13676	1.1 (0.6, 2.2)	0.8 (-2.7, 6.8)	12	5.9	10686	2.0 (1.2, 3.6)	5.7 (0.3, 14.1)
0 to -1	14	18.2	29380	0.8 (0.5, 1.3)	-1.4 (-3.6, 1.8)	5	3.4	5304	1.5 (0.6, 3.5)	3.0 (-3.4, 15.5)
0 to 1	11	10.7	16019	1.0 (0.6, 1.9)	0.2 (-3.3, 5.6)	1	1.2	1592	0.8 (0.1, 6.0)	-1.1 (-7.2, 27.6)
1 to 2	4	2.9	4114	1.4 (0.5, 3.7)	2.8 (-4.3, 17.9)	0	0.2	278	0.0 (., .)	-8.3 (., 124.5)
2 to 3	1	1.0	1478	1.0 (0.1, 6.9)	-0.1 (-6.7, 30.8)	1	0.1	169	7.4 (1.0, 52.3)	51.2 (-6.5, 321.9)
Unknown	24	15.9	23571	1.5 (1.0, 2.3)	3.5 (-0.2, 8.4)	8	2.5	5938	3.2 (1.6, 6.5)	9.3 (1.7, 22.4)

Cumulative r-hGH dose (mg/kg)

<25	25	28.9	42466	0.9 (0.6, 1.3)	-0.9 (-3.0, 1.9)	13	9.3	14761	1.4 (0.8, 2.4)	2.5 (-1.6, 8.7)
25-49	12	12.3	20605	1.0 (0.6, 1.7)	-0.1 (-2.9, 4.2)	9	4.2	8238	2.2 (1.1, 4.1)	5.9 (-0.1, 15.7)
50-99	6	3.8	7047	1.6 (0.7, 3.5)	3.1 (-2.3, 13.1)	3	1.7	3925	1.8 (0.6, 5.5)	3.3 (-2.8, 18.0)
≥100	0	0.6	1070	0.0 (., .)	-5.2 (., 29.3)	0	0.2	449	0.0 (., .)	-5.0 (., 77.2)
Unknown	20	11.2	17599	1.8 (1.2, 2.8)	5.0 (0.6, 11.2)	5	2.3	4025	2.2 (0.9, 5.3)	6.8 (-1.6, 23.4)

By cause

Infectious and parasitic disease (A00-B99)	3	0.8	88786	3.6 (1.2, 11.2)	0.2 (0.0, 0.9)	0	0.3	31398	0.0 (., .)	-0.1 (., 1.1)
Neoplasms (C00-D48)	6	5.2	88786	1.2 (0.5, 2.6)	0.1 (-0.3, 0.9)	1	1.7	31398	0.6 (0.1, 4.3)	-0.2 (-0.5, 1.2)
Diseases of blood and blood-forming organs (D50-D89)	1	0.2	88786	4.1 (0.6, 29.2)	0.1 (0.0, 0.6)	1	0.1	31398	11.8 (1.7, 84.1)	0.3 (0.0, 1.7)
Endocrine, nutritional & metabolic disease (E00-E90)	1	0.7	88786	1.4 (0.2, 10.0)	0.0 (-0.1, 0.5)	0	0.3	31398	0.0 (., .)	-0.1 (., 1.1)
Mental & behavioural disorders (F00-F99)	1	1.0	88786	1.0 (0.1, 7.0)	0.0 (-0.1, 0.5)	0	0.3	31398	0.0 (., .)	-0.1 (., 1.1)
Diseases of nervous system, eye & ear (G00-H95)	2	2.2	88786	0.9 (0.2, 3.7)	0.0 (-0.2, 0.6)	1	0.7	31398	1.4 (0.2, 10.0)	0.1 (-0.2, 1.5)
Diseases of circulatory system (I00-I99)	6	2.3	88786	2.6 (1.2, 5.9)	0.4 (0.0, 1.2)	4	0.7	31398	5.7 (2.1, 15.1)	1.0 (0.1, 3.0)
Diseases of respiratory system (J00-J99)	1	0.9	88786	1.1 (0.2, 8.1)	0.0 (-0.1, 0.5)	0	0.3	31398	0.0 (., .)	-0.1 (., 1.1)
Diseases of digestive system (K00-K93)	0	0.5	88786	0.0 (., .)	-0.1 (., 0.4)	0	0.2	31398	0.0 (., .)	-0.1 (., 1.1)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	88786	0.0 (., .)	0.0 (., 0.4)	0	0.0	31398	0.0 (., .)	0.0 (., 1.2)
Diseases of musculoskeletal system & connective tissue (M00-M99)	0	0.1	88786	0.0 (., .)	0.0 (., 0.4)	0	0.0	31398	0.0 (., .)	0.0 (., 1.2)
Diseases of genitourinary system (N00-N99)	0	0.1	88786	0.0 (., .)	0.0 (., 0.4)	0	0.0	31398	0.0 (., .)	0.0 (., 1.2)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	88786	0.0 (., .)	0.0 (., 0.4)	0	0.0	31398	0.0 (., .)	0.0 (., 1.2)
Conditions originating in perinatal period (P00-P96)	0	0.7	88786	0.0 (., .)	-0.1 (., 0.3)	0	0.4	31398	0.0 (., .)	-0.1 (., 1.1)
Congenital anomalies (Q00-Q99)	1	1.4	88786	0.7 (0.1, 5.1)	0.0 (-0.2, 0.5)	0	0.6	31398	0.0 (., .)	-0.2 (., 1.0)
Symptoms, signs & ill-defined conditions (R00-R99)	12	5.9	88786	2.0 (1.2, 3.6)	0.7 (0.0, 1.7)	9	2.0	31398	4.6 (2.4, 8.8)	2.2 (0.7, 4.8)
Accidents and violence (V00-Y98)	29	34.0	88786	0.9 (0.6, 1.2)	-0.6 (-1.6, 0.9)	14	10.1	31398	1.4 (0.8, 2.4)	1.3 (-0.8, 4.3)

By circulatory cause

Ischemic heart disease	0	0.3	88786	0.0 (., .)	0.0 (., 0.4)	0	0.1	31398	0.0 (., .)	0.0 (., 1.2)
Cerebrovascular disease	3	0.6	88786	5.2 (1.7, 16.1)	0.3 (0.0, 0.9)	1	0.2	31398	5.5 (0.8, 39.3)	0.3 (0.0, 1.7)
Other circulatory disease	3	1.4	88786	2.1 (0.7, 6.5)	0.2 (-0.1, 0.8)	3	0.5	31398	6.6 (2.1, 20.5)	0.8 (0.1, 2.6)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S3b: Comprehensive mortality data for France only (risk group 2 and 3)

	Risk group 2					Risk group 3				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	64	16.7	38104	3.8 (3.0, 4.9)	12.4 (8.6, 17.1)	184	10.8	19693	17.0 (14.7, 19.6)	87.9 (74.9, 102.4)
Country										
France	64	16.7	38104	3.8 (3.0, 4.9)	12.4 (8.6, 17.1)	184	10.8	19693	17.0 (14.7, 19.6)	87.9 (74.9, 102.4)
Sex										
Male	30	7.6	8885	3.9 (2.7, 5.6)	25.2 (14.2, 39.6)	107	8.8	12143	12.2 (10.1, 14.7)	80.9 (65.0, 99.2)
Female	34	9.0	29220	3.8 (2.7, 5.3)	8.5 (5.0, 13.2)	77	2.0	7551	37.8 (30.2, 47.3)	99.3 (77.8, 124.8)
Age started treatment (years)										
0-4	8	3.9	4422	2.1 (1.0, 4.2)	9.4 (-0.9, 26.9)	10	0.6	737	16.7 (9.0, 31.1)	127.6 (57.0, 241.5)
5-9	19	3.7	12983	5.1 (3.3, 8.0)	11.8 (6.0, 20.0)	64	3.0	7544	21.4 (16.8, 27.3)	80.9 (61.4, 104.4)
10-14	23	6.7	17098	3.5 (2.3, 5.2)	9.6 (4.6, 16.3)	96	5.5	9442	17.6 (14.4, 21.5)	95.9 (76.6, 118.4)
15-19	14	2.5	3602	5.7 (3.4, 9.6)	32.0 (14.4, 58.3)	14	1.8	1971	7.8 (4.6, 13.2)	61.9 (29.7, 110.1)
Time since start of treatment (years)										
0-4	15	5.6	10801	2.7 (1.6, 4.5)	8.7 (2.6, 17.8)	58	2.4	6059	24.3 (18.8, 31.5)	91.8 (68.7, 119.8)
5-9	21	3.8	10564	5.5 (3.6, 8.5)	16.3 (8.7, 26.8)	51	3.1	5669	16.3 (12.4, 21.4)	84.4 (61.5, 112.8)
10-14	15	4.1	9992	3.7 (2.2, 6.1)	10.9 (4.3, 20.7)	46	3.2	5033	14.2 (10.7, 19.0)	85.0 (60.5, 115.5)
15-19	13	2.8	6088	4.7 (2.7, 8.0)	16.8 (6.8, 31.9)	25	1.8	2612	13.8 (9.3, 20.4)	88.8 (55.0, 134.4)
20-24	0	0.4	660	0.0 (., .)	-6.1 (., 49.9)	4	0.3	320	14.5 (5.4, 38.6)	116.4 (25.4, 311.5)
25-29										
Attained age (years)										
0-4	1	2.9	414	0.3 (0.0, 2.5)	-45.7 (-69.2, 64.7)	0	0.4	49	0.0 (., .)	-75.8 (., 681.0)
5-9	5	0.5	2896	11.1 (4.6, 26.7)	15.7 (4.1, 38.7)	5	0.2	1096	26.1 (10.9, 62.7)	43.9 (13.1, 104.7)
10-14	10	1.2	7403	8.7 (4.7, 16.1)	12.0 (4.9, 23.3)	39	0.8	4083	52.2 (38.1, 71.4)	93.7 (66.1, 128.7)
15-19	18	3.8	10373	4.7 (3.0, 7.5)	13.7 (6.6, 23.7)	59	3.0	5599	19.9 (15.4, 25.7)	100.1 (74.9, 130.6)
20-24	11	4.3	9073	2.6 (1.4, 4.6)	7.4 (1.3, 17.0)	45	3.6	4943	12.6 (9.4, 16.9)	83.8 (59.2, 114.6)
25-29	11	2.6	5810	4.2 (2.3, 7.5)	14.4 (4.9, 29.3)	26	2.0	2911	12.8 (8.7, 18.8)	82.3 (51.3, 123.9)
30-34	7	1.2	1955	5.7 (2.7, 12.1)	29.6 (8.2, 67.6)	6	0.8	900	7.5 (3.4, 16.7)	57.8 (15.6, 136.3)
35-39	1	0.2	178	4.8 (0.7, 34.3)	44.5 (-10.2, 300.7)	4	0.2	111	25.4 (9.5, 67.7)	345.8 (83.9, 907.5)
40-44	0	0.0	2	0.0 (., .)	-23.9 (., 18257.8)	0	0.0	2	0.0 (., .)	-23.9 (., 19334.8)
Duration of treatment (years)										
<2	19	1.8	3175	10.6 (6.7, 16.6)	54.2 (30.4, 87.8)	52	1.8	3026	29.3 (22.3, 38.4)	166.0 (122.5, 219.5)
2	9	1.7	3505	5.2 (2.7, 9.9)	20.7 (6.8, 43.8)	37	1.6	2515	23.4 (17.0, 32.3)	140.8 (97.3, 196.5)
3	9	2.1	4762	4.3 (2.3, 8.3)	14.5 (4.3, 31.5)	24	1.7	2705	14.5 (9.7, 21.6)	82.6 (50.7, 125.9)
4-5	9	3.4	9059	2.7 (1.4, 5.1)	6.2 (0.8, 15.1)	23	2.4	4433	9.5 (6.3, 14.3)	46.4 (27.4, 72.4)
6-9	11	3.3	10089	3.3 (1.8, 6.0)	7.6 (2.2, 16.2)	22	2.0	4026	11.3 (7.4, 17.1)	49.8 (29.4, 77.9)
≥10	1	2.3	4127	0.4 (0.1, 3.1)	-3.2 (-5.5, 7.9)	4	0.6	1056	6.7 (2.5, 17.8)	32.2 (4.6, 91.3)
Unknown	6	2.1	3388	2.9 (1.3, 6.5)	11.6 (0.4, 32.5)	22	0.9	1932	26.0 (17.1, 39.4)	109.5 (67.0, 168.0)
Mean r-hGH dose (µg/kg/d)										
<15	3	0.5	615	6.6 (2.1, 20.4)	41.4 (2.7, 135.3)	16	0.9	1247	18.7 (11.5, 30.6)	121.4 (66.5, 201.5)
15-19	9	2.1	3287	4.3 (2.2, 8.2)	21.0 (6.1, 45.6)	29	2.0	3607	14.7 (10.2, 21.2)	74.9 (48.4, 110.0)
20-24	11	1.9	3441	5.7 (3.2, 10.3)	26.4 (10.4, 51.6)	38	2.4	4174	15.7 (11.4, 21.6)	85.2 (58.6, 119.2)
25-29	7	1.9	3880	3.8 (1.8, 7.9)	13.3 (2.5, 32.4)	20	1.3	2574	14.9 (9.6, 23.1)	72.5 (42.2, 114.8)
30-34	3	1.3	3944	2.3 (0.7, 7.0)	4.2 (-1.8, 18.9)	3	0.5	1101	6.3 (2.0, 19.5)	22.9 (1.3, 75.3)
35-39	7	2.1	7189	3.4 (1.6, 7.2)	6.9 (1.1, 17.2)	5	0.1	199	58.4 (24.3, 140.2)	246.5 (77.1, 581.0)
40-49	7	1.9	6735	3.7 (1.7, 7.7)	7.5 (1.3, 18.6)	1	0.3	393	3.8 (0.5, 27.0)	18.8 (-6.0, 135.2)
≥50	4	0.3	912	12.0 (4.5, 32.1)	40.2 (8.3, 108.6)	1	0.1	216	8.2 (1.2, 58.1)	40.7 (-4.5, 252.5)
Unknown	13	4.7	8102	2.8 (1.6, 4.8)	10.2 (2.7, 21.6)	71	3.3	6182	21.5 (17.0, 27.1)	109.5 (84.4, 139.5)

Birth weight SDS										
<-4	0	0.1	120	0.0 (., .)	-5.9 (., 302.4)					
-3 to -4	3	0.4	1051	7.8 (2.5, 24.3)	24.9 (2.2, 79.8)	1	0.0	26	45.6 (6.4, 323.4)	374.3 (1.3, 2123.7)
-2 to -3	3	1.6	4685	1.9 (0.6, 6.0)	3.1 (-2.0, 15.4)	6	0.2	376	31.8 (14.3, 70.7)	154.6 (53.6, 342.4)
-1 to -2	13	4.2	11117	3.1 (1.8, 5.4)	8.0 (2.5, 16.3)	14	1.1	2242	13.3 (7.9, 22.4)	57.7 (29.4, 100.1)
0 to -1	22	4.4	9308	5.0 (3.3, 7.7)	19.0 (10.1, 31.1)	44	3.0	5632	14.6 (10.8, 19.6)	72.8 (51.4, 99.5)
0 to 1	10	2.2	4044	4.6 (2.4, 8.5)	19.3 (6.4, 40.0)	38	2.2	3865	17.1 (12.4, 23.5)	92.6 (63.8, 129.2)
1 to 2	1	0.7	1158	1.4 (0.2, 9.9)	2.4 (-6.0, 41.9)	9	0.8	1276	12.1 (6.3, 23.2)	64.7 (26.4, 128.0)
2 to 3	1	0.4	826	2.4 (0.3, 16.9)	7.0 (-4.8, 62.4)	2	0.3	419	6.4 (1.6, 25.8)	40.3 (-1.6, 165.0)
Unknown	11	2.8	5796	3.9 (2.2, 7.0)	14.1 (4.6, 29.1)	70	3.3	5857	21.4 (16.9, 27.0)	113.9 (87.6, 145.4)
Cumulative r-hGH dose (mg/kg)										
<25	23	5.6	8986	4.1 (2.7, 6.2)	19.4 (10.0, 32.2)	75	3.9	7126	19.2 (15.3, 24.1)	99.8 (77.3, 126.4)
25-49	10	3.9	9203	2.6 (1.4, 4.8)	6.6 (1.0, 15.8)	41	2.8	5143	14.4 (10.6, 19.6)	74.2 (51.7, 102.6)
50-99	17	3.8	11712	4.4 (2.8, 7.1)	11.2 (5.2, 20.0)	11	1.2	2176	9.1 (5.1, 16.5)	45.0 (19.7, 84.9)
≥100	5	1.3	4654	3.9 (1.6, 9.4)	8.0 (0.7, 22.3)	1	0.2	407	4.2 (0.6, 30.0)	18.8 (-5.2, 131.2)
Unknown	9	2.1	3549	4.3 (2.3, 8.3)	19.5 (5.7, 42.3)	56	2.6	4842	21.2 (16.3, 27.5)	110.2 (81.9, 144.7)
By cause										
Infectious and parasitic disease (A00-B99)	0	0.3	38104	0.0 (., .)	-0.1 (., 0.9)	1	0.2	19693	6.3 (0.9, 44.5)	0.4 (-0.1, 2.7)
Neoplasms (C00-D48)	2	1.8	38104	1.1 (0.3, 4.4)	0.0 (-0.4, 1.4)	135	1.1	19693	128.6 (108.6, 152.2)	68.0 (56.9, 80.6)
Diseases of blood and blood-forming organs (D50-D89)	3	0.1	38104	30.1 (9.7, 93.4)	0.8 (0.1, 2.3)	1	0.1	19693	19.6 (2.8, 139.2)	0.5 (0.0, 2.8)
Endocrine, nutritional & metabolic disease (E00-E90)	4	0.3	38104	13.1 (4.9, 34.8)	1.0 (0.2, 2.6)	1	0.2	19693	6.7 (0.9, 47.5)	0.4 (-0.1, 2.8)
Mental & behavioural disorders (F00-F99)	1	0.2	38104	4.8 (0.7, 34.2)	0.2 (0.0, 1.4)	0	0.2	19693	0.0 (., .)	-0.1 (., 1.8)
Diseases of nervous system, eye & ear (G00-H95)	5	0.7	38104	6.8 (2.8, 16.3)	1.1 (0.2, 2.9)	3	0.4	19693	6.8 (2.2, 21.2)	1.3 (0.1, 4.2)
Diseases of circulatory system (I00-I99)	8	0.7	38104	10.9 (5.5, 21.9)	1.9 (0.7, 3.9)	8	0.4	19693	18.5 (9.2, 36.9)	3.8 (1.5, 7.8)
Diseases of respiratory system (J00-J99)	5	0.4	38104	14.4 (6.0, 34.6)	1.2 (0.3, 3.0)	5	0.2	19693	28.4 (11.8, 68.3)	2.4 (0.7, 5.8)
Diseases of digestive system (K00-K93)	1	0.2	38104	5.5 (0.8, 39.3)	0.2 (0.0, 1.4)	1	0.1	19693	10.3 (1.4, 72.8)	0.5 (0.0, 2.8)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	38104	0.0 (., .)	0.0 (., 1.0)	0	0.0	19693	0.0 (., .)	0.0 (., 1.9)
Diseases of musculoskeletal system & connective tissue (M00-M99)	1	0.1	38104	18.4 (2.6, 130.9)	0.2 (0.0, 1.4)	3	0.0	19693	126.5 (40.8, 392.2)	1.5 (0.3, 4.4)
Diseases of genitourinary system (N00-N99)	0	0.0	38104	0.0 (., .)	0.0 (., 1.0)	3	0.0	19693	169.8 (54.8, 526.5)	1.5 (0.3, 4.4)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	38104	0.0 (., .)	0.0 (., 1.0)	0	0.0	19693	0.0 (., .)	0.0 (., 1.9)
Conditions originating in perinatal period (P00-P96)	0	0.7	38104	0.0 (., .)	-0.2 (., 0.8)	0	0.1	19693	0.0 (., .)	0.0 (., 1.8)
Congenital anomalies (Q00-Q99)	12	0.9	38104	13.5 (7.7, 23.8)	2.9 (1.4, 5.3)	5	0.3	19693	19.7 (8.2, 47.3)	2.4 (0.7, 5.8)
Symptoms, signs & ill-defined conditions (R00-R99)	11	2.2	38104	4.9 (2.7, 8.9)	2.3 (0.9, 4.6)	5	1.0	19693	4.8 (2.0, 11.6)	2.0 (0.3, 5.4)
Accidents and violence (V00-Y98)	11	7.7	38104	1.4 (0.8, 2.6)	0.9 (-0.6, 3.1)	13	6.5	19693	2.0 (1.2, 3.4)	3.3 (0.2, 8.0)
By circulatory cause										
Ischemic heart disease	1	0.1	38104	19.1 (2.7, 135.4)	0.2 (0.0, 1.4)	0	0.0	19693	0.0 (., .)	0.0 (., 1.9)
Cerebrovascular disease	2	0.2	38104	10.1 (2.5, 40.3)	0.5 (0.0, 1.8)	2	0.1	19693	17.8 (4.4, 71.0)	1.0 (0.1, 3.6)
Other circulatory disease	5	0.5	38104	10.4 (4.3, 25.0)	1.2 (0.3, 2.9)	6	0.3	19693	21.6 (9.7, 48.1)	2.9 (1.0, 6.5)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S4a: Comprehensive mortality data for all countries excluding France (risk group 1a and 1b)

	Risk group 1a					Risk group 1b				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	27	27.4	62218	1.0 (0.7, 1.4)	-0.1 (-1.5, 1.9)	19	15.8	34831	1.2 (0.8, 1.9)	0.9 (-1.3, 4.0)
Country										
Belgium	3	3.5	5784	0.8 (0.3, 2.6)	-0.9 (-5.0, 9.0)	1	1.6	2702	0.6 (0.1, 4.4)	-2.3 (-5.9, 14.7)
Switzerland	0	1.4	3590	0.0 (., .)	-3.9 (., 6.4)	0	0.3	897	0.0 (., .)	-3.6 (., 37.5)
Germany	5	4.2	10264	1.2 (0.5, 2.9)	0.8 (-2.5, 7.3)	1	0.9	2318	1.1 (0.2, 7.8)	0.4 (-3.8, 20.1)
Italy	2	3.4	9409	0.6 (0.1, 2.4)	-1.5 (-3.3, 4.1)	2	0.5	1444	3.7 (0.9, 14.7)	10.1 (-2.1, 46.3)
The Netherlands	3	2.1	6512	1.5 (0.5, 4.5)	1.4 (-2.2, 10.3)	1	1.1	3838	0.9 (0.1, 6.4)	-0.3 (-2.8, 11.6)
Sweden	9	7.8	17793	1.2 (0.6, 2.2)	0.7 (-2.1, 5.2)	7	4.8	10766	1.5 (0.7, 3.1)	2.1 (-1.8, 8.9)
UK	5	5.1	8867	1.0 (0.4, 2.4)	-0.1 (-3.9, 7.4)	7	6.5	12867	1.1 (0.5, 2.3)	0.4 (-2.9, 6.1)
Sex										
Male	23	22.5	42111	1.0 (0.7, 1.5)	0.1 (-1.9, 2.9)	13	12.8	23332	1.0 (0.6, 1.7)	0.1 (-2.5, 4.0)
Female	4	4.9	20107	0.8 (0.3, 2.2)	-0.5 (-1.9, 2.7)	6	3.0	11499	2.0 (0.9, 4.5)	2.6 (-0.7, 8.8)
Age started treatment (years)										
0-4	1	3.1	5453	0.3 (0.0, 2.3)	-3.8 (-5.6, 4.5)	4	2.9	4598	1.4 (0.5, 3.7)	2.5 (-3.9, 16.0)
5-9	8	7.7	21680	1.0 (0.5, 2.1)	0.1 (-2.0, 3.7)	5	4.7	13590	1.1 (0.4, 2.5)	0.2 (-2.3, 5.1)
10-14	15	14.2	31449	1.1 (0.6, 1.8)	0.3 (-1.8, 3.3)	9	7.2	15176	1.2 (0.6, 2.4)	1.2 (-2.1, 6.5)
15-19	3	2.4	3636	1.3 (0.4, 3.9)	1.7 (-4.8, 17.6)	1	1.0	1467	1.0 (0.1, 7.2)	0.1 (-6.6, 31.3)
Time since start of treatment (years)										
0-4	4	6.8	20113	0.6 (0.2, 1.6)	-1.4 (-2.8, 1.7)	6	4.0	9965	1.5 (0.7, 3.4)	2.1 (-1.8, 9.1)
5-9	5	7.7	19157	0.6 (0.3, 1.6)	-1.4 (-3.2, 2.1)	6	3.6	9685	1.7 (0.7, 3.7)	2.5 (-1.4, 9.8)
10-14	12	7.0	13583	1.7 (1.0, 3.0)	3.7 (-0.6, 10.3)	1	4.1	8216	0.2 (0.0, 1.7)	-3.7 (-4.9, 1.8)
15-19	4	4.3	7292	0.9 (0.4, 2.5)	-0.4 (-4.4, 8.2)	5	2.9	5126	1.7 (0.7, 4.1)	4.1 (-2.5, 17.1)
20-24	2	1.5	1987	1.4 (0.3, 5.4)	2.7 (-6.2, 29.0)	1	1.2	1695	0.9 (0.1, 6.1)	-1.0 (-6.8, 26.0)
25-29	0	0.1	87	0.0 (., .)	-10.7 (., 416.0)	0	0.1	144	0.0 (., .)	-8.0 (., 248.5)
Attained age (years)										
0-4	0	1.6	340	0.0 (., .)	-46.4 (., 62.2)	0	1.7	282	0.0 (., .)	-58.9 (., 71.8)
5-9	0	0.6	3849	0.0 (., .)	-1.6 (., 8.0)	1	0.4	2853	2.3 (0.3, 16.6)	2.0 (-1.4, 18.0)
10-14	3	2.2	13813	1.4 (0.4, 4.3)	0.6 (-1.1, 4.8)	4	1.2	7463	3.4 (1.3, 9.2)	3.8 (-0.1, 12.2)
15-19	11	8.5	20096	1.3 (0.7, 2.3)	1.2 (-1.5, 5.6)	7	4.0	9883	1.7 (0.8, 3.7)	3.0 (-1.2, 10.5)
20-24	4	8.1	14330	0.5 (0.2, 1.3)	-2.9 (-4.9, 1.5)	3	4.3	7798	0.7 (0.2, 2.1)	-1.7 (-4.8, 5.7)
25-29	4	4.2	6984	0.9 (0.4, 2.5)	-0.3 (-4.5, 8.6)	3	2.6	4384	1.2 (0.4, 3.6)	1.0 (-4.4, 14.1)
30-34	5	1.8	2439	2.8 (1.2, 6.8)	13.2 (-0.6, 40.6)	1	1.3	1786	0.8 (0.1, 5.6)	-1.4 (-6.9, 24.2)
35-39	0	0.4	357	0.0 (., .)	-10.7 (., 92.6)	0	0.4	367	0.0 (., .)	-9.9 (., 90.5)
40-44	0	0.0	11	0.0 (., .)	-19.7 (., 3491.8)	0	0.0	15	0.0 (., .)	-15.8 (., 2432.2)
Duration of treatment (years)										
<2	5	3.4	7014	1.5 (0.6, 3.6)	2.3 (-2.5, 11.8)	7	2.3	4652	3.1 (1.5, 6.5)	10.2 (1.2, 26.2)
2	1	2.8	6067	0.4 (0.1, 2.5)	-3.0 (-4.6, 4.5)	2	1.5	3194	1.3 (0.3, 5.4)	1.6 (-3.9, 18.0)
3	3	3.4	7585	0.9 (0.3, 2.7)	-0.5 (-3.7, 7.1)	2	1.5	3424	1.3 (0.3, 5.2)	1.4 (-3.8, 16.6)
4-5	6	5.2	11800	1.2 (0.5, 2.6)	0.7 (-2.5, 6.7)	1	3.3	7458	0.3 (0.0, 2.1)	-3.1 (-4.4, 3.0)
6-9	4	5.7	13913	0.7 (0.3, 1.9)	-1.2 (-3.3, 3.3)	3	3.9	9778	0.8 (0.2, 2.4)	-0.9 (-3.3, 5.0)
≥10	3	3.1	6164	1.0 (0.3, 3.0)	-0.1 (-4.0, 9.3)	2	2.6	4783	0.8 (0.2, 3.1)	-1.3 (-4.9, 9.7)
Unknown	5	3.9	9675	1.3 (0.5, 3.1)	1.1 (-2.4, 8.0)	2	0.7	1543	2.8 (0.7, 11.2)	8.3 (-3.0, 42.2)
Mean r-hGH dose (µg/kg/d)										
<15	0	0.3	562	0.0 (., .)	-5.7 (., 60.0)	1	0.3	565	3.0 (0.4, 21.5)	11.8 (-5.4, 92.7)
15-19	1	1.2	2251	0.9 (0.1, 6.1)	-0.7 (-5.0, 19.6)	1	0.8	1186	1.3 (0.2, 9.5)	2.1 (-6.1, 40.7)
20-24	1	2.6	5563	0.4 (0.1, 2.7)	-2.8 (-4.6, 5.4)	1	1.5	3151	0.6 (0.1, 4.6)	-1.7 (-4.8, 12.8)

25-29	6	3.8	7674	1.6 (0.7, 3.6)	2.9 (-2.0, 12.1)	3	2.4	5089	1.3 (0.4, 4.0)	1.3 (-3.4, 12.6)
30-34	5	5.8	12560	0.9 (0.4, 2.1)	-0.6 (-3.3, 4.7)	8	4.3	9567	1.8 (0.9, 3.7)	3.8 (-0.9, 12.0)
35-39	1	2.0	4578	0.5 (0.1, 3.5)	-2.3 (-4.4, 7.7)	0	1.0	2553	0.0 (., .)	-4.1 (., 10.4)
40-49	1	1.6	3743	0.6 (0.1, 4.5)	-1.5 (-4.1, 10.7)	0	1.0	2266	0.0 (., .)	-4.4 (., 11.8)
≥50	0	0.8	2034	0.0 (., .)	-4.0 (., 14.1)	2	1.5	3751	1.3 (0.3, 5.3)	1.3 (-3.4, 15.2)
Unknown	12	9.4	23254	1.3 (0.7, 2.3)	1.1 (-1.4, 5.0)	3	3.0	6702	1.0 (0.3, 3.1)	0.1 (-3.5, 8.7)

Birth weight SDS

<-4	0	0.0	80	0.0 (., .)	-3.1 (., 456.9)	2	1.0	2177	2.1 (0.5, 8.5)	4.8 (-3.2, 28.8)
-3 to -4	0	0.2	242	0.0 (., .)	-7.1 (., 145.3)	3	1.6	3428	1.9 (0.6, 5.9)	4.2 (-2.8, 21.0)
-2 to -3	0	0.5	967	0.0 (., .)	-5.3 (., 32.8)	4	3.9	8982	1.0 (0.4, 2.7)	0.1 (-3.2, 7.0)
-1 to -2	5	5.3	11291	0.9 (0.4, 2.2)	-0.3 (-3.3, 5.6)	6	4.0	8795	1.5 (0.7, 3.3)	2.3 (-2.0, 10.3)
0 to -1	7	6.8	15364	1.0 (0.5, 2.2)	0.2 (-2.6, 5.0)	3	3.3	6666	0.9 (0.3, 2.8)	-0.4 (-4.0, 8.2)
0 to 1	3	4.1	8827	0.7 (0.2, 2.3)	-1.2 (-3.9, 5.3)	0	1.2	2667	0.0 (., .)	-4.5 (., 9.3)
1 to 2	1	0.9	1979	1.2 (0.2, 8.4)	0.8 (-4.2, 23.9)	0	0.3	678	0.0 (., .)	-4.9 (., 49.5)
2 to 3	0	0.1	313	0.0 (., .)	-4.4 (., 113.5)	0	0.1	187	0.0 (., .)	-4.4 (., 192.7)
Unknown	11	9.6	23156	1.2 (0.6, 2.1)	0.6 (-1.8, 4.4)	1	0.5	1253	2.1 (0.3, 14.6)	4.1 (-3.7, 40.6)

Cumulative r-hGH dose (mg/kg)

<25	6	6.3	13425	1.0 (0.4, 2.1)	-0.2 (-3.0, 5.1)	7	4.3	8411	1.6 (0.8, 3.4)	3.2 (-1.8, 12.0)
25-49	5	6.2	14004	0.8 (0.3, 1.9)	-0.9 (-3.3, 3.9)	6	3.6	8211	1.7 (0.8, 3.8)	3.0 (-1.6, 11.6)
50-99	4	5.8	12704	0.7 (0.3, 1.8)	-1.4 (-3.7, 3.5)	1	4.3	9563	0.2 (0.0, 1.6)	-3.5 (-4.5, 1.3)
≥100	2	1.9	4091	1.1 (0.3, 4.3)	0.3 (-4.0, 13.1)	3	2.0	4846	1.5 (0.5, 4.7)	2.1 (-2.8, 14.0)
Unknown	10	7.2	17994	1.4 (0.7, 2.6)	1.6 (-1.3, 6.2)	2	1.7	3800	1.2 (0.3, 4.9)	0.9 (-3.7, 14.7)

By cause

Infectious and parasitic disease (A00-B99)	0	0.3	51954	0.0 (., .)	-0.1 (., 0.7)	0	0.2	32513	0.0 (., .)	-0.1 (., 1.1)
Neoplasms (C00-D48)	1	2.9	62218	0.3 (0.0, 2.4)	-0.3 (-0.5, 0.4)	1	1.7	34831	0.6 (0.1, 4.1)	-0.2 (-0.5, 1.1)
Diseases of blood and blood-forming organs (D50-D89)	2	0.1	62218	16.2 (4.1, 64.9)	0.3 (0.0, 1.1)	0	0.1	34831	0.0 (., .)	0.0 (., 1.0)
Endocrine, nutritional & metabolic disease (E00-E90)	0	0.5	62218	0.0 (., .)	-0.1 (., 0.5)	1	0.3	34831	3.1 (0.4, 22.2)	0.2 (-0.1, 1.5)
Mental & behavioural disorders (F00-F99)	0	0.8	62218	0.0 (., .)	-0.1 (., 0.5)	0	0.5	34831	0.0 (., .)	-0.1 (., 0.9)
Diseases of nervous system, eye & ear (G00-H95)	0	1.0	51954	0.0 (., .)	-0.2 (., 0.5)	1	0.7	32513	1.4 (0.2, 9.6)	0.1 (-0.2, 1.5)
Diseases of circulatory system (I00-I99)	3	1.5	62218	2.0 (0.6, 6.2)	0.2 (-0.1, 1.2)	2	0.9	34831	2.2 (0.6, 8.9)	0.3 (-0.2, 1.8)
Diseases of respiratory system (J00-J99)	1	0.5	62218	1.9 (0.3, 13.5)	0.1 (-0.1, 0.8)	1	0.4	34831	2.7 (0.4, 19.2)	0.2 (-0.1, 1.5)
Diseases of digestive system (K00-K93)	1	0.4	62218	2.7 (0.4, 19.5)	0.1 (-0.1, 0.8)	0	0.3	34831	0.0 (., .)	-0.1 (., 1.0)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	62218	0.0 (., .)	0.0 (., 0.6)	0	0.0	34831	0.0 (., .)	0.0 (., 1.1)
Diseases of musculoskeletal system & connective tissue (M00-M99)	0	0.1	62218	0.0 (., .)	0.0 (., 0.6)	0	0.1	34831	0.0 (., .)	0.0 (., 1.0)
Diseases of genitourinary system (N00-N99)	0	0.1	62218	0.0 (., .)	0.0 (., 0.6)	0	0.0	34831	0.0 (., .)	0.0 (., 1.0)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.0	62218	0.0 (., .)	0.0 (., 0.6)	0	0.0	34831	0.0 (., .)	0.0 (., 1.1)
Conditions originating in perinatal period (P00-P96)	0	0.5	62218	0.0 (., .)	-0.1 (., 0.5)	0	0.4	34831	0.0 (., .)	-0.1 (., 0.9)
Congenital anomalies (Q00-Q99)	1	1.1	62218	1.0 (0.1, 6.8)	0.0 (-0.2, 0.7)	2	0.7	34831	2.7 (0.7, 10.8)	0.4 (-0.1, 1.9)
Symptoms, signs & ill-defined conditions (R00-R99)	1	1.2	62218	0.8 (0.1, 5.7)	0.0 (-0.2, 0.7)	1	0.8	34831	1.3 (0.2, 9.5)	0.1 (-0.2, 1.4)
Accidents and violence (V00-Y98)	16	15.9	62218	1.0 (0.6, 1.6)	0.0 (-1.1, 1.6)	10	8.3	34831	1.2 (0.6, 2.2)	0.5 (-1.0, 2.9)

By circulatory cause

Ischemic heart disease	1	0.2	62218	5.1 (0.7, 36.3)	0.1 (0.0, 0.9)	0	0.1	34831	0.0 (., .)	0.0 (., 1.0)
Cerebrovascular disease	1	0.3	62218	3.6 (0.5, 25.5)	0.1 (0.0, 0.9)	0	0.2	34831	0.0 (., .)	0.0 (., 1.0)
Other circulatory disease	0	0.8	51954	0.0 (., .)	-0.2 (., 0.5)	2	0.6	32513	3.6 (0.9, 14.5)	0.4 (-0.1, 2.1)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S4b: Comprehensive mortality data for all countries excluding France (risk group 2 and 3)

	Risk group 2					Risk group 3				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	128	33.3	84215	3.8 (3.2, 4.6)	11.2 (8.7, 14.1)	272	15.9	35699	17.1 (15.2, 19.3)	71.7 (63.0, 81.4)
Country										
Belgium	14	4.5	9876	3.1 (1.9, 5.3)	9.7 (3.2, 19.3)	33	2.1	3862	15.4 (10.9, 21.7)	79.9 (53.3, 114.5)
Switzerland	3	1.1	3369	2.8 (0.9, 8.6)	5.7 (-1.4, 22.8)	10	0.7	1493	14.7 (7.9, 27.3)	62.4 (27.6, 118.6)
Germany	7	3.1	9219	2.3 (1.1, 4.8)	4.2 (-0.3, 12.3)	12	1.0	2181	12.3 (7.0, 21.7)	50.5 (24.0, 91.6)
Italy	2	0.4	1609	5.0 (1.2, 19.9)	9.9 (-1.0, 42.4)	0	0.2	475	0.0 (., .)	-3.2 (., 74.4)
The Netherlands	19	3.5	12197	5.4 (3.4, 8.4)	12.7 (6.5, 21.4)	34	1.5	4470	23.1 (16.5, 32.3)	72.8 (49.4, 103.0)
Sweden	28	5.6	15619	5.0 (3.5, 7.3)	14.4 (8.3, 22.3)	49	2.4	5795	20.4 (15.4, 27.0)	80.4 (58.4, 107.7)
UK	55	15.2	32325	3.6 (2.8, 4.7)	12.3 (8.1, 17.5)	134	8.1	17424	16.6 (14.0, 19.7)	72.3 (59.8, 86.5)
Sex										
Male	58	18.3	30623	3.2 (2.4, 4.1)	13.0 (8.4, 18.5)	159	12.2	21237	13.0 (11.2, 15.2)	69.1 (57.9, 81.7)
Female	70	15.0	53592	4.7 (3.7, 5.9)	10.3 (7.4, 13.7)	113	3.7	14462	30.7 (25.5, 36.9)	75.6 (61.8, 91.4)
Age started treatment (years)										
0-4	17	8.6	13171	2.0 (1.2, 3.2)	6.4 (1.0, 14.2)	16	1.5	1968	10.8 (6.6, 17.7)	73.8 (39.0, 124.5)
5-9	40	9.4	32108	4.3 (3.1, 5.8)	9.5 (6.0, 14.0)	81	4.0	11524	20.4 (16.4, 25.4)	66.8 (52.4, 83.9)
10-14	55	12.3	32976	4.5 (3.4, 5.8)	12.9 (8.8, 18.0)	148	8.5	18946	17.4 (14.8, 20.5)	73.6 (61.6, 87.3)
15-19	16	3.0	5959	5.3 (3.3, 8.7)	21.8 (10.3, 38.6)	27	2.0	3261	13.8 (9.5, 20.1)	76.8 (48.6, 114.5)
Time since start of treatment (years)										
0-4	32	10.7	24591	3.0 (2.1, 4.2)	8.7 (4.5, 14.0)	91	4.0	11401	22.5 (18.3, 27.7)	76.3 (60.7, 94.5)
5-9	24	7.1	23568	3.4 (2.3, 5.0)	7.2 (3.5, 12.1)	86	4.3	10371	20.0 (16.2, 24.7)	78.8 (62.2, 98.3)
10-14	36	7.4	19580	4.8 (3.5, 6.7)	14.6 (9.1, 21.7)	45	4.0	7977	11.3 (8.5, 15.2)	51.4 (36.2, 70.5)
15-19	23	5.4	12027	4.3 (2.8, 6.4)	14.6 (7.6, 24.2)	35	2.4	4360	14.4 (10.3, 20.1)	74.7 (50.3, 106.1)
20-24	12	2.4	4165	5.0 (2.8, 8.8)	23.0 (9.1, 44.5)	15	1.0	1455	14.8 (8.9, 24.5)	96.1 (50.7, 163.0)
25-29	1	0.2	285	4.6 (0.6, 32.7)	27.5 (-6.7, 188.0)	0	0.1	135	0.0 (., .)	-9.3 (., 264.4)
Attained age (years)										
0-4	3	5.6	1076	0.5 (0.2, 1.7)	-24.5 (-46.6, 29.1)	0	1.0	155	0.0 (., .)	-62.3 (., 175.3)
5-9	7	1.1	7457	6.6 (3.1, 13.9)	8.0 (2.4, 17.9)	9	0.3	1718	34.6 (18.0, 66.6)	50.9 (22.4, 98.0)
10-14	13	2.6	17758	5.0 (2.9, 8.6)	5.8 (2.4, 11.0)	53	1.1	7067	47.5 (36.3, 62.2)	73.4 (54.6, 96.5)
15-19	31	8.1	23834	3.8 (2.7, 5.4)	9.6 (5.4, 15.0)	86	4.4	10736	19.5 (15.8, 24.1)	76.0 (60.0, 94.8)
20-24	29	8.0	18916	3.6 (2.5, 5.2)	11.1 (6.0, 17.8)	73	4.7	8828	15.6 (12.4, 19.6)	77.4 (59.5, 98.7)
25-29	32	4.7	10224	6.8 (4.8, 9.6)	26.7 (16.8, 39.6)	30	2.8	4960	10.9 (7.6, 15.5)	54.9 (35.2, 80.8)
30-34	10	2.4	4075	4.2 (2.2, 7.8)	18.7 (5.9, 39.3)	18	1.3	1839	14.1 (8.9, 22.4)	90.9 (51.1, 147.8)
35-39	3	0.7	840	4.3 (1.4, 13.4)	27.5 (-0.9, 96.2)	2	0.4	374	5.3 (1.3, 21.3)	43.4 (-3.6, 183.1)
40-44	0	0.1	35	0.0 (., .)	-13.6 (., 1045.4)	1	0.0	22	31.1 (4.4, 220.5)	435.9 (-3.1, 2494.8)
Duration of treatment (years)										
<2	29	3.3	7647	8.9 (6.2, 12.8)	33.7 (21.1, 50.2)	74	2.1	4379	35.4 (28.2, 44.5)	164.2 (127.9, 207.4)
2	12	2.5	6584	4.8 (2.7, 8.4)	14.4 (5.6, 28.0)	34	2.0	4114	17.0 (12.2, 23.8)	77.8 (52.4, 110.6)
3	15	3.0	7839	5.0 (3.0, 8.2)	15.3 (6.8, 27.7)	32	2.2	4573	14.3 (10.1, 20.3)	65.1 (43.0, 93.9)
4-5	22	5.4	15351	4.0 (2.7, 6.1)	10.8 (5.4, 18.2)	58	3.3	7479	17.7 (13.7, 22.9)	73.2 (54.5, 95.9)
6-9	29	7.3	21764	4.0 (2.8, 5.7)	10.0 (5.6, 15.8)	49	3.4	8657	14.4 (10.9, 19.1)	52.7 (37.9, 70.9)
≥10	8	8.5	15223	0.9 (0.5, 1.9)	-0.3 (-3.3, 4.8)	8	1.4	3103	5.6 (2.8, 11.3)	21.2 (6.6, 46.2)
Unknown	13	3.3	9806	4.0 (2.3, 6.9)	9.9 (3.7, 19.3)	17	1.5	3395	11.5 (7.2, 18.5)	45.7 (24.8, 75.8)
Mean r-hGH dose (µg/kg/d)										
<15	1	0.7	1200	1.4 (0.2, 10.2)	2.5 (-5.6, 40.6)	23	1.1	1999	21.9 (14.6, 33.0)	109.8 (67.7, 167.4)
15-19	6	1.2	2447	4.8 (2.2, 10.7)	19.4 (3.9, 48.3)	30	1.7	3817	17.3 (12.1, 24.7)	74.1 (48.5, 107.7)
20-24	13	2.8	5773	4.6 (2.7, 7.9)	17.6 (7.1, 33.6)	38	3.1	7089	12.1 (8.8, 16.6)	49.2 (33.5, 69.1)

25-29	14	4.1	8542	3.5 (2.0, 5.8)	11.7 (4.2, 22.8)	50	2.8	6399	17.7 (13.4, 23.4)	73.7 (53.6, 98.6)
30-34	18	4.9	11646	3.7 (2.3, 5.9)	11.3 (5.0, 20.2)	50	1.9	4349	26.2 (19.8, 34.5)	110.6 (80.9, 147.2)
35-39	9	3.4	9293	2.7 (1.4, 5.1)	6.1 (0.8, 14.8)	14	0.9	1946	16.2 (9.6, 27.3)	67.5 (34.9, 116.3)
40-49	21	4.7	15213	4.5 (2.9, 6.9)	10.7 (5.5, 18.0)	8	0.6	1395	12.4 (6.2, 24.8)	52.7 (20.1, 108.4)
≥50	6	1.6	4415	3.7 (1.7, 8.2)	9.9 (1.3, 25.9)	7	0.2	460	40.6 (19.4, 85.2)	148.3 (57.4, 309.5)
Unknown	40	9.9	25688	4.0 (3.0, 5.5)	11.7 (7.3, 17.3)	52	3.6	8245	14.7 (11.2, 19.2)	58.8 (42.8, 78.4)

Birth weight SDS

<-4	3	0.8	1535	3.7 (1.2, 11.5)	14.3 (-1.2, 51.9)	2	0.1	166	25.9 (6.5, 103.7)	115.6 (9.9, 429.8)
-3 to -4	6	1.2	2890	5.2 (2.3, 11.5)	16.7 (3.6, 41.2)	1	0.2	315	6.2 (0.9, 43.7)	26.6 (-4.3, 171.7)
-2 to -3	22	3.4	9069	6.5 (4.3, 9.9)	20.5 (11.5, 33.0)	8	0.5	1323	15.3 (7.7, 30.6)	56.5 (22.2, 115.2)
-1 to -2	31	7.0	17487	4.4 (3.1, 6.3)	13.7 (8.0, 21.2)	38	2.0	4353	19.1 (13.9, 26.2)	82.7 (57.2, 115.2)
0 to -1	23	8.2	19760	2.8 (1.9, 4.2)	7.5 (3.2, 13.3)	59	3.6	8110	16.2 (12.5, 20.9)	68.3 (50.9, 89.4)
0 to 1	13	4.6	10682	2.8 (1.6, 4.8)	7.8 (2.2, 16.5)	49	3.0	6580	16.5 (12.5, 21.8)	69.9 (50.6, 93.9)
1 to 2	3	1.2	2760	2.4 (0.8, 7.6)	6.4 (-2.2, 27.3)	20	1.5	3096	13.8 (8.9, 21.4)	59.9 (34.8, 95.1)
2 to 3	3	0.2	498	14.6 (4.7, 45.4)	56.2 (8.3, 172.1)	3	0.2	530	13.1 (4.2, 40.5)	52.3 (7.3, 161.1)
Unknown	24	6.7	19535	3.6 (2.4, 5.3)	8.9 (4.4, 14.9)	92	4.8	11225	19.0 (15.5, 23.3)	77.6 (61.8, 96.2)

Cumulative r-hGH dose (mg/kg)

<25	27	8.0	15147	3.4 (2.3, 4.9)	12.6 (6.5, 20.7)	96	4.8	10920	20.2 (16.5, 24.7)	83.6 (66.9, 103.0)
25-49	30	7.4	18311	4.1 (2.8, 5.8)	12.4 (7.0, 19.4)	79	4.8	10424	16.4 (13.2, 20.5)	71.2 (55.4, 89.8)
50-99	28	7.6	21151	3.7 (2.5, 5.3)	9.6 (5.2, 15.5)	48	3.3	7345	14.8 (11.1, 19.6)	60.9 (43.8, 82.2)
≥100	19	4.2	12460	4.5 (2.9, 7.1)	11.9 (5.8, 20.4)	10	0.6	1425	16.0 (8.6, 29.7)	65.8 (29.3, 124.7)
Unknown	24	6.1	17146	3.9 (2.6, 5.8)	10.4 (5.4, 17.2)	39	2.4	5585	16.0 (11.7, 21.8)	65.5 (45.3, 91.1)

By cause

Infectious and parasitic disease (A00-B99)	0	0.6	74996	0.0 (., .)	-0.1 (., 0.4)	4	0.3	33518	15.4 (5.8, 41.1)	1.1 (0.2, 3.0)
Neoplasms (C00-D48)	12	3.9	84215	3.0 (1.7, 5.4)	1.0 (0.3, 2.0)	199	1.8	35699	110.7 (96.3, 127.2)	55.2 (47.8, 63.5)
Diseases of blood and blood-forming organs (D50-D89)	5	0.2	84215	31.5 (13.1, 75.6)	0.6 (0.2, 1.4)	6	0.1	35699	83.0 (37.3, 184.8)	1.7 (0.6, 3.6)
Endocrine, nutritional & metabolic disease (E00-E90)	14	0.8	84215	18.1 (10.7, 30.5)	1.6 (0.8, 2.7)	3	0.4	35699	8.7 (2.8, 26.9)	0.7 (0.1, 2.4)
Mental & behavioural disorders (F00-F99)	2	1.0	84215	2.1 (0.5, 8.2)	0.1 (-0.1, 0.7)	1	0.6	35699	1.8 (0.3, 12.8)	0.1 (-0.1, 1.4)
Diseases of nervous system, eye & ear (G00-H95)	4	1.6	74996	2.6 (1.0, 6.9)	0.3 (-0.1, 1.2)	9	0.8	33518	11.4 (5.9, 21.9)	2.4 (1.0, 4.9)
Diseases of circulatory system (I00-I99)	25	1.8	84215	13.6 (9.2, 20.1)	2.7 (1.7, 4.2)	11	0.9	35699	11.8 (6.5, 21.3)	2.8 (1.3, 5.3)
Diseases of respiratory system (J00-J99)	6	0.9	84215	6.7 (3.0, 14.9)	0.6 (0.2, 1.4)	8	0.4	35699	21.0 (10.5, 41.9)	2.1 (0.9, 4.3)
Diseases of digestive system (K00-K93)	2	0.6	84215	3.2 (0.8, 12.8)	0.2 (0.0, 0.8)	7	0.3	35699	23.3 (11.1, 48.9)	1.9 (0.7, 4.0)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	84215	0.0 (., .)	0.0 (., 0.4)	0	0.0	35699	0.0 (., .)	0.0 (., 1.0)
Diseases of musculoskeletal system & connective tissue (M00-M99)	4	0.1	84215	30.4 (11.4, 81.0)	0.5 (0.1, 1.2)	1	0.1	35699	17.6 (2.5, 124.8)	0.3 (0.0, 1.5)
Diseases of genitourinary system (N00-N99)	2	0.1	84215	20.2 (5.1, 80.9)	0.2 (0.0, 0.8)	9	0.0	35699	203.7 (106.0, 391.6)	2.5 (1.1, 4.8)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	84215	0.0 (., .)	0.0 (., 0.4)	0	0.0	35699	0.0 (., .)	0.0 (., 1.0)
Conditions originating in perinatal period (P00-P96)	0	1.1	84215	0.0 (., .)	-0.1 (., 0.3)	0	0.2	35699	0.0 (., .)	-0.1 (., 1.0)
Congenital anomalies (Q00-Q99)	21	1.9	84215	11.1 (7.3, 17.1)	2.3 (1.3, 3.6)	5	0.6	35699	8.3 (3.4, 19.8)	1.2 (0.3, 3.1)
Symptoms, signs & ill-defined conditions (R00-R99)	14	1.9	84215	7.5 (4.5, 12.7)	1.4 (0.7, 2.6)	8	0.6	35699	13.4 (6.7, 26.8)	2.1 (0.8, 4.2)
Accidents and violence (V00-Y98)	17	14.8	84215	1.2 (0.7, 1.9)	0.3 (-0.6, 1.5)	1	8.6	35699	0.1 (0.0, 0.8)	-2.1 (-2.4, -0.8)

By circulatory cause

Ischemic heart disease	1	0.2	84215	4.3 (0.6, 30.9)	0.1 (0.0, 0.6)	1	0.1	35699	7.3 (1.0, 51.9)	0.2 (0.0, 1.5)
Cerebrovascular disease	2	0.4	84215	5.0 (1.3, 20.0)	0.2 (0.0, 0.8)	2	0.2	35699	10.7 (2.7, 42.7)	0.5 (0.0, 2.0)
Other circulatory disease	18	1.1	74996	16.9 (10.7, 26.9)	2.3 (1.3, 3.7)	7	0.6	33518	12.4 (5.9, 26.0)	1.9 (0.7, 4.1)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S5a: Comprehensive mortality data for all countries entering risk two years after end of r-hGH treatment (risk group 1a and 1b)

	Risk group 1a					Risk group 1b				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	61	55.6	83197	1.1 (0.9, 1.4)	0.6 (-1.1, 2.7)	37	22.1	38029	1.7 (1.2, 2.3)	3.9 (1.0, 7.6)
Country										
Belgium	2	2.2	3269	0.9 (0.2, 3.6)	-0.7 (-6.1, 15.2)	1	0.9	1489	1.2 (0.2, 8.3)	1.0 (-5.6, 31.7)
Switzerland	0	0.6	1201	0.0 (., .)	-4.7 (., 26.1)	0	0.1	298	0.0 (., .)	-4.4 (., 119.5)
France	46	40.9	55984	1.1 (0.8, 1.5)	0.9 (-1.3, 3.7)	26	12.2	19349	2.1 (1.4, 3.1)	7.1 (2.5, 13.4)
Germany	5	2.1	4343	2.3 (1.0, 5.6)	6.6 (-1.2, 21.9)	0	0.5	1074	0.0 (., .)	-4.7 (., 29.6)
Italy	1	1.2	2925	0.8 (0.1, 5.8)	-0.7 (-4.1, 14.9)	0	0.2	542	0.0 (., .)	-4.3 (., 63.8)
The Netherlands	2	1.1	2912	1.8 (0.5, 7.3)	3.1 (-2.9, 21.1)	0	0.6	1664	0.0 (., .)	-3.5 (., 18.6)
Sweden	2	3.8	6958	0.5 (0.1, 2.1)	-2.6 (-5.1, 4.9)	6	2.9	5284	2.1 (0.9, 4.7)	5.9 (-1.3, 19.3)
UK	3	3.7	5606	0.8 (0.3, 2.5)	-1.2 (-5.4, 9.1)	4	4.7	8330	0.9 (0.3, 2.3)	-0.8 (-4.3, 6.7)
Sex										
Male	50	47.5	55834	1.1 (0.8, 1.4)	0.4 (-1.9, 3.3)	30	17.9	23307	1.7 (1.2, 2.4)	5.2 (1.0, 10.7)
Female	11	8.1	27363	1.4 (0.8, 2.5)	1.1 (-0.9, 4.2)	7	4.2	14722	1.7 (0.8, 3.5)	1.9 (-0.9, 7.0)
Age started treatment (years)										
0-4	3	1.5	3411	2.0 (0.6, 6.1)	4.3 (-2.6, 21.3)	4	1.1	2822	3.7 (1.4, 9.9)	10.4 (0.0, 32.5)
5-9	13	10.4	19588	1.2 (0.7, 2.1)	1.3 (-1.8, 6.0)	6	5.9	12229	1.0 (0.5, 2.3)	0.1 (-3.0, 5.9)
10-14	36	33.8	50259	1.1 (0.8, 1.5)	0.4 (-1.7, 3.2)	21	12.2	19938	1.7 (1.1, 2.6)	4.4 (0.4, 10.0)
15-19	9	9.9	9938	0.9 (0.5, 1.8)	-0.9 (-5.8, 7.3)	6	2.9	3040	2.1 (0.9, 4.6)	10.1 (-2.4, 33.4)
Time since start of treatment (years)										
0-4	0	1.8	3308	0.0 (., .)	-5.4 (., 5.8)	1	0.6	1301	1.8 (0.3, 12.9)	3.5 (-4.0, 38.6)
5-9	15	16.6	26044	0.9 (0.5, 1.5)	-0.6 (-3.1, 3.1)	12	5.8	10938	2.1 (1.2, 3.6)	5.6 (0.3, 13.8)
10-14	26	20.3	30589	1.3 (0.9, 1.9)	1.9 (-1.1, 5.8)	9	8.2	14233	1.1 (0.6, 2.1)	0.6 (-2.9, 6.3)
15-19	16	14.1	19840	1.1 (0.7, 1.9)	1.0 (-2.5, 6.0)	12	5.8	9274	2.1 (1.2, 3.6)	6.7 (0.4, 16.3)
20-24	4	2.8	3331	1.4 (0.5, 3.8)	3.6 (-5.1, 22.3)	3	1.6	2140	1.9 (0.6, 5.8)	6.6 (-4.6, 33.5)
25-29	0	0.1	86	0.0 (., .)	-10.7 (., 420.0)	0	0.1	144	0.0 (., .)	-8.0 (., 248.5)
Attained age (years)										
0-4	0	0.0	3	0.0 (., .)	-71.4 (., 12779.0)	0	0.0	1	0.0 (., .)	-73.4 (., 42802.1)
5-9	0	0.0	141	0.0 (., .)	-1.5 (., 259.9)	0	0.0	166	0.0 (., .)	-1.5 (., 220.4)
10-14	0	0.4	2180	0.0 (., .)	-1.7 (., 15.3)	1	0.3	1650	3.9 (0.5, 27.3)	4.5 (-1.4, 32.2)
15-19	17	8.2	17821	2.1 (1.3, 3.3)	4.9 (1.0, 10.7)	7	3.8	9084	1.9 (0.9, 3.9)	3.6 (-1.0, 11.7)
20-24	17	23.0	32294	0.7 (0.5, 1.2)	-1.9 (-4.1, 1.3)	12	9.0	14380	1.3 (0.8, 2.3)	2.1 (-2.0, 8.3)
25-29	14	15.2	21394	0.9 (0.5, 1.6)	-0.6 (-3.5, 3.9)	11	5.7	8832	1.9 (1.1, 3.5)	6.0 (-0.2, 15.9)
30-34	12	7.5	8422	1.6 (0.9, 2.8)	5.4 (-1.5, 16.0)	6	2.7	3353	2.2 (1.0, 4.9)	9.8 (-1.5, 30.9)
35-39	1	1.2	928	0.8 (0.1, 5.8)	-2.4 (-12.9, 46.9)	0	0.6	548	0.0 (., .)	-11.5 (., 55.8)
40-44	0	0.0	16	0.0 (., .)	-21.1 (., 2341.1)	0	0.0	16	0.0 (., .)	-16.5 (., 2234.0)
Duration of treatment (years)										
<2	17	14.0	20490	1.2 (0.8, 2.0)	1.5 (-2.0, 6.5)	9	4.8	8188	1.9 (1.0, 3.6)	5.2 (-0.8, 15.1)
2	9	12.2	17206	0.7 (0.4, 1.4)	-1.8 (-4.7, 2.9)	6	4.4	7545	1.4 (0.6, 3.1)	2.2 (-2.9, 11.5)
3	14	10.6	15561	1.3 (0.8, 2.2)	2.2 (-1.9, 8.3)	8	3.9	6415	2.0 (1.0, 4.1)	6.4 (-0.7, 18.5)
4-5	10	10.9	16723	0.9 (0.5, 1.7)	-0.5 (-3.6, 4.5)	7	4.6	7818	1.5 (0.7, 3.2)	3.1 (-2.2, 12.6)
6-9	10	6.5	10459	1.5 (0.8, 2.9)	3.4 (-1.6, 11.4)	2	3.5	6205	0.6 (0.1, 2.3)	-2.4 (-5.2, 6.1)
≥10	1	1.5	2613	0.7 (0.1, 4.8)	-1.9 (-5.6, 15.6)	3	0.9	1656	3.5 (1.1, 10.8)	12.9 (-1.5, 47.7)
Unknown	0	0.1	145	0.0 (., .)	-5.8 (., 249.2)	2	0.1	201	16.2 (4.1, 64.8)	93.2 (5.9, 352.7)
Mean r-hGH dose (µg/kg/d)										
<15	3	3.6	4280	0.8 (0.3, 2.6)	-1.4 (-7.0, 12.1)	3	1.5	1785	2.0 (0.6, 6.2)	8.4 (-4.9, 40.7)
15-19	19	16.0	21098	1.2 (0.8, 1.9)	1.4 (-2.1, 6.5)	6	4.8	6848	1.3 (0.6, 2.8)	1.8 (-3.7, 12.1)

20-24	6	10.7	16157	0.6 (0.3, 1.3)	-2.9 (-5.2, 1.5)	8	3.6	6119	2.2 (1.1, 4.5)	7.2 (-0.2, 19.9)
25-29	8	6.6	10568	1.2 (0.6, 2.4)	1.3 (-3.0, 8.7)	2	2.9	5262	0.7 (0.2, 2.7)	-1.8 (-5.1, 8.1)
30-34	2	4.6	8248	0.4 (0.1, 1.7)	-3.1 (-5.3, 3.2)	6	3.0	5793	2.0 (0.9, 4.4)	5.2 (-1.4, 17.4)
35-39	1	1.5	2833	0.7 (0.1, 4.7)	-1.7 (-5.2, 14.4)	0	0.8	1779	0.0 (., .)	-4.7 (., 16.0)
40-49	3	1.1	2181	2.7 (0.9, 8.2)	8.6 (-2.3, 35.0)	0	0.8	1594	0.0 (., .)	-4.8 (., 18.3)
≥50	0	0.7	1353	0.0 (., .)	-5.2 (., 22.0)	6	2.0	4081	3.1 (1.4, 6.9)	9.9 (0.6, 27.2)
Unknown	19	10.9	16482	1.7 (1.1, 2.7)	4.9 (0.4, 11.4)	6	2.8	4768	2.2 (1.0, 4.8)	6.8 (-1.2, 21.6)

Birth weight SDS

<-4	0	0.0	49	0.0 (., .)	-4.0 (., 750.7)	1	0.6	1224	1.6 (0.2, 11.4)	3.1 (-4.9, 40.4)
-3 to -4	0	0.2	187	0.0 (., .)	-8.0 (., 189.1)	4	1.2	2417	3.3 (1.2, 8.8)	11.5 (-0.5, 37.4)
-2 to -3	0	0.5	771	0.0 (., .)	-6.4 (., 41.4)	4	4.8	8297	0.8 (0.3, 2.2)	-1.0 (-4.5, 6.5)
-1 to -2	10	8.7	13959	1.1 (0.6, 2.1)	0.9 (-2.8, 6.9)	13	6.7	11579	1.9 (1.1, 3.3)	5.4 (0.2, 13.4)
0 to -1	16	17.0	25712	0.9 (0.6, 1.5)	-0.4 (-3.1, 3.5)	6	4.7	7445	1.3 (0.6, 2.8)	1.7 (-3.4, 11.2)
0 to 1	6	9.9	14079	0.6 (0.3, 1.4)	-2.7 (-5.4, 2.3)	1	1.7	2548	0.6 (0.1, 4.1)	-2.8 (-6.6, 15.1)
1 to 2	5	2.5	3416	2.0 (0.8, 4.9)	7.5 (-2.4, 27.0)	0	0.4	557	0.0 (., .)	-6.4 (., 59.7)
2 to 3	1	0.8	1041	1.3 (0.2, 9.1)	2.1 (-7.3, 46.0)	1	0.2	234	6.1 (0.9, 43.1)	35.7 (-5.9, 230.9)
Unknown	23	16.1	23983	1.4 (0.9, 2.1)	2.9 (-0.6, 7.7)	7	1.8	3728	4.0 (1.9, 8.4)	14.1 (2.8, 34.0)

Cumulative r-hGH dose (mg/kg)

0-49	34	37.0	53520	0.9 (0.7, 1.3)	-0.6 (-2.5, 2.0)	26	13.9	22964	1.9 (1.3, 2.8)	5.3 (1.4, 10.6)
50-99	7	6.3	10552	1.1 (0.5, 2.3)	0.7 (-3.3, 7.7)	3	4.1	7491	0.7 (0.2, 2.3)	-1.5 (-4.6, 6.2)
≥100	1	1.5	2643	0.7 (0.1, 4.8)	-1.8 (-5.5, 15.5)	2	1.4	2806	1.5 (0.4, 5.8)	2.3 (-4.0, 20.9)
Unknown	19	10.9	16482	1.7 (1.1, 2.7)	4.9 (0.4, 11.4)	6	2.8	4768	2.2 (1.0, 4.8)	6.8 (-1.2, 21.6)

By cause

Infectious and parasitic disease (A00-B99)	1	0.7	78854	1.4 (0.2, 10.1)	0.0 (-0.1, 0.6)	0	0.3	36956	0.0 (., .)	-0.1 (., 0.9)
Neoplasms (C00-D48)	5	5.3	83197	0.9 (0.4, 2.3)	0.0 (-0.4, 0.8)	1	2.3	38029	0.4 (0.1, 3.1)	-0.3 (-0.6, 0.9)
Diseases of blood and blood-forming organs (D50-D89)	0	0.2	83197	0.0 (., .)	0.0 (., 0.4)	1	0.1	38029	11.9 (1.7, 84.3)	0.2 (0.0, 1.4)
Endocrine, nutritional & metabolic disease (E00-E90)	1	0.8	83197	1.3 (0.2, 9.5)	0.0 (-0.1, 0.6)	1	0.4	38029	2.8 (0.4, 19.6)	0.2 (-0.1, 1.4)
Mental & behavioural disorders (F00-F99)	1	1.5	83197	0.7 (0.1, 4.6)	-0.1 (-0.2, 0.5)	0	0.6	38029	0.0 (., .)	-0.2 (., 0.8)
Diseases of nervous system, eye & ear (G00-H95)	2	2.0	78854	1.0 (0.3, 4.1)	0.0 (-0.2, 0.7)	1	0.9	36956	1.1 (0.2, 7.9)	0.0 (-0.2, 1.3)
Diseases of circulatory system (I00-I99)	7	2.7	83197	2.6 (1.2, 5.5)	0.5 (0.0, 1.4)	5	1.2	38029	4.2 (1.7, 10.0)	1.0 (0.1, 2.8)
Diseases of respiratory system (J00-J99)	0	0.8	83197	0.0 (., .)	-0.1 (., 0.3)	1	0.4	38029	2.6 (0.4, 18.2)	0.2 (-0.1, 1.4)
Diseases of digestive system (K00-K93)	1	0.6	83197	1.6 (0.2, 11.0)	0.0 (-0.1, 0.6)	0	0.3	38029	0.0 (., .)	-0.1 (., 0.9)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	83197	0.0 (., .)	0.0 (., 0.4)	0	0.0	38029	0.0 (., .)	0.0 (., 1.0)
Diseases of musculoskeletal system & connective tissue (M00-M99)	0	0.1	83197	0.0 (., .)	0.0 (., 0.4)	0	0.1	38029	0.0 (., .)	0.0 (., 1.0)
Diseases of genitourinary system (N00-N99)	0	0.1	83197	0.0 (., .)	0.0 (., 0.4)	0	0.1	38029	0.0 (., .)	0.0 (., 1.0)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	83197	0.0 (., .)	0.0 (., 0.4)	0	0.0	38029	0.0 (., .)	0.0 (., 1.0)
Conditions originating in perinatal period (P00-P96)	0	0.0	83197	0.0 (., .)	0.0 (., 0.4)	0	0.0	38029	0.0 (., .)	0.0 (., 1.0)
Congenital anomalies (Q00-Q99)	1	0.8	83197	1.2 (0.2, 8.6)	0.0 (-0.1, 0.6)	0	0.4	38029	0.0 (., .)	-0.1 (., 0.9)
Symptoms, signs & ill-defined conditions (R00-R99)	10	4.6	83197	2.2 (1.2, 4.1)	0.7 (0.0, 1.7)	10	1.5	38029	6.7 (3.6, 12.5)	2.2 (0.9, 4.4)
Accidents and violence (V00-Y98)	31	34.7	83197	0.9 (0.6, 1.3)	-0.4 (-1.6, 1.1)	17	13.4	38029	1.3 (0.8, 2.0)	0.9 (-0.9, 3.6)

By circulatory cause

Ischemic heart disease	1	0.38	83197	2.6 (0.4, 18.5)	0.1 (0.0, 0.6)	0	0.19	38029	0.0 (., .)	0.0 (., 0.9)
Cerebrovascular disease	3	0.6	83197	5.0 (1.6, 15.5)	0.3 (0.0, 1.0)	1	0.25	38029	3.9 (0.6, 27.9)	0.2 (-0.1, 1.4)
Other circulatory disease	2	1.6	78854	1.3 (0.3, 5.0)	0.1 (-0.2, 0.7)	4	0.73	36956	5.5 (2.0, 14.5)	0.9 (0.1, 2.6)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone

Table S5b: Comprehensive mortality data for all countries entering risk two years after end of r-hGH treatment (risk group 2 and 3)

	Risk group 2					Risk group 3				
	Obs	Exp	py	SMR (95% CI)	AER (95% CI)	Obs	Exp	py	SMR (95% CI)	AER (95% CI)
Overall	126	25.6	58509	4.9 (4.1, 5.9)	17.2 (13.6, 21.3)	258	16.8	28976	15.4 (13.6, 17.4)	83.2 (72.7, 94.8)
Country										
Belgium	10	2.4	5000	4.3 (2.3, 7.9)	15.3 (4.9, 32.1)	17	1.5	2179	11.6 (7.2, 18.7)	71.3 (38.7, 118.2)
Switzerland	1	0.3	921	3.2 (0.5, 22.9)	7.5 (-3.1, 57.1)	0	0.1	176	0.0 (., .)	-3.8 (., 206.0)
France	40	8.9	19745	4.5 (3.3, 6.1)	15.8 (10.0, 23.1)	98	7.1	10665	13.8 (11.3, 16.8)	85.2 (67.9, 105.3)
Germany	4	1.4	3630	3.0 (1.1, 7.9)	7.3 (-0.7, 24.5)	3	0.3	483	11.7 (3.8, 36.4)	56.9 (7.5, 176.3)
Italy	1	0.1	385	8.8 (1.2, 62.7)	23.1 (-2.3, 141.9)	0	0.1	133	0.0 (., .)	-3.7 (., 274.6)
The Netherlands	9	1.7	5056	5.3 (2.8, 10.2)	14.5 (4.8, 30.4)	15	0.9	2177	17.7 (10.7, 29.3)	65.0 (34.7, 109.8)
Sweden	20	2.2	5023	9.0 (5.8, 14.0)	35.4 (19.9, 57.1)	33	1.4	2838	23.9 (17.0, 33.6)	111.4 (75.2, 158.4)
UK	41	8.7	18749	4.7 (3.5, 6.4)	17.2 (11.1, 25.0)	92	5.6	10326	16.4 (13.4, 20.2)	83.7 (66.4, 103.8)
Sex										
Male	56	13.4	17854	4.2 (3.2, 5.4)	23.9 (16.2, 33.2)	144	13.3	17135	10.8 (9.2, 12.7)	76.3 (63.1, 91.2)
Female	70	12.2	40655	5.7 (4.5, 7.2)	14.2 (10.4, 18.7)	114	3.5	11841	33.0 (27.5, 39.7)	93.4 (76.5, 112.7)
Age started treatment (years)										
0-4	11	1.7	4753	6.4 (3.6, 11.6)	19.6 (8.0, 37.8)	7	0.3	794	20.6 (9.8, 43.3)	83.9 (31.2, 177.4)
5-9	36	7.3	18455	5.0 (3.6, 6.9)	15.6 (9.7, 23.1)	74	4.1	8282	18.1 (14.4, 22.7)	84.4 (65.2, 107.2)
10-14	57	12.8	29078	4.4 (3.4, 5.8)	15.2 (10.4, 21.0)	148	9.7	16549	15.2 (12.9, 17.9)	83.6 (69.7, 99.2)
15-19	22	3.8	6223	5.7 (3.8, 8.7)	29.2 (16.0, 47.4)	29	2.6	3352	11.1 (7.7, 15.9)	78.7 (50.1, 116.4)
Time since start of treatment (years)										
0-4	12	0.6	1600	19.3 (11.0, 34.1)	71.1 (34.9, 127.2)	28	0.5	1150	54.7 (37.7, 79.2)	239.1 (157.4, 347.5)
5-9	24	5.9	14659	4.1 (2.7, 6.1)	12.4 (6.5, 20.4)	86	4.7	8664	18.3 (14.8, 22.7)	93.9 (74.0, 117.2)
10-14	45	9.1	21928	5.0 (3.7, 6.7)	16.4 (10.8, 23.3)	74	6.2	10887	11.9 (9.4, 14.9)	62.2 (47.6, 79.6)
15-19	32	7.2	15653	4.4 (3.1, 6.3)	15.8 (9.4, 24.2)	52	4.0	6452	13.1 (10.0, 17.2)	74.4 (54.0, 99.5)
20-24	12	2.6	4384	4.6 (2.6, 8.0)	21.4 (8.1, 41.8)	18	1.2	1690	14.5 (9.1, 23.0)	99.2 (55.8, 161.0)
25-29	1	0.2	285	4.6 (0.6, 32.7)	27.5 (-6.7, 188.0)	0	0.1	134	0.0 (., .)	-9.2 (., 265.9)
Attained age (years)										
0-4	0	0.0	4	0.0 (., .)	-75.3 (., 10095.4)	0	0.0	0	0.0 (., .)	-60.0 (., 122149.8)
5-9	2	0.0	132	111.3 (27.8, 445.0)	150.7 (17.0, 547.9)	0	0.0	42	0.0 (., .)	-1.3 (., 870.5)
10-14	6	0.2	1031	39.6 (17.8, 88.2)	56.8 (19.9, 125.3)	6	0.1	442	90.8 (40.8, 202.1)	134.2 (48.3, 293.9)
15-19	26	3.8	11975	6.8 (4.7, 10.1)	18.5 (11.0, 28.6)	70	2.4	6008	28.9 (22.9, 36.5)	112.5 (86.8, 143.2)
20-24	31	10.5	24099	3.0 (2.1, 4.2)	8.5 (4.4, 13.9)	102	7.1	11930	14.3 (11.8, 17.3)	79.5 (63.7, 97.8)
25-29	40	6.9	14762	5.8 (4.3, 8.0)	22.5 (14.7, 32.3)	49	4.5	7394	10.8 (8.2, 14.3)	60.1 (42.9, 81.5)
30-34	17	3.4	5554	5.0 (3.1, 8.0)	24.5 (11.7, 42.9)	24	2.0	2658	11.8 (7.9, 17.6)	82.7 (50.2, 126.7)
35-39	4	0.9	917	4.7 (1.8, 12.5)	34.3 (2.6, 102.4)	6	0.5	479	11.4 (5.1, 25.4)	114.4 (35.0, 261.8)
40-44	0	0.1	37	0.0 (., .)	-14.2 (., 986.8)	1	0.0	23	29.0 (4.1, 206.1)	421.8 (-4.0, 2418.9)
Duration of treatment (years)										
<2	30	4.1	8454	7.3 (5.1, 10.4)	30.6 (19.1, 45.8)	66	3.2	5643	20.7 (16.3, 26.3)	111.3 (84.8, 143.2)
2	19	3.3	7145	5.8 (3.7, 9.1)	22.0 (11.4, 36.9)	49	2.7	4599	18.4 (13.9, 24.4)	100.8 (73.0, 135.1)
3	17	3.7	8336	4.6 (2.8, 7.4)	15.9 (7.4, 28.2)	32	3.0	4762	10.9 (7.7, 15.4)	61.0 (39.8, 88.7)
4-5	24	6.0	14467	4.0 (2.7, 5.9)	12.4 (6.5, 20.5)	52	4.0	6836	13.0 (9.9, 17.0)	70.2 (51.0, 93.9)
6-9	28	6.0	14519	4.6 (3.2, 6.7)	15.1 (8.7, 23.7)	48	3.2	5628	15.0 (11.3, 19.9)	79.6 (57.2, 107.4)
≥10	7	2.3	5184	3.1 (1.5, 6.4)	9.1 (1.0, 23.4)	9	0.6	1128	14.9 (7.8, 28.6)	74.5 (31.1, 146.2)
Unknown	1	0.2	405	6.2 (0.9, 44.3)	20.7 (-3.3, 133.7)	2	0.2	381	11.8 (3.0, 47.2)	48.0 (1.9, 185.1)
Mean r-hGH dose (µg/kg/d)										
<15	3	0.9	1296	3.4 (1.1, 10.4)	16.3 (-2.1, 60.8)	30	1.5	2206	20.0 (14.0, 28.6)	129.2 (84.9, 187.3)
15-19	13	2.4	3748	5.4 (3.2, 9.4)	28.3 (12.1, 52.9)	33	2.7	4541	12.3 (8.7, 17.3)	66.8 (44.1, 96.1)

20-24	20	2.8	5196	7.0 (4.5, 10.9)	33.0 (18.0, 54.0)	44	3.9	6576	11.3 (8.4, 15.1)	61.0 (42.7, 83.9)
25-29	17	3.5	6756	4.9 (3.0, 7.8)	20.0 (9.5, 35.1)	43	2.9	5030	15.1 (11.2, 20.4)	79.8 (56.2, 109.5)
30-34	13	3.7	8829	3.5 (2.0, 6.0)	10.5 (3.6, 21.0)	29	1.5	2989	19.7 (13.7, 28.4)	92.1 (60.1, 134.4)
35-39	13	3.4	9393	3.8 (2.2, 6.5)	10.2 (3.7, 20.0)	9	0.7	1259	13.3 (6.9, 25.6)	66.1 (27.3, 130.3)
40-49	19	3.8	11344	5.1 (3.2, 7.9)	13.4 (6.8, 22.8)	6	0.6	1066	10.0 (4.5, 22.3)	50.7 (15.0, 116.9)
≥50	6	1.0	2635	6.2 (2.8, 13.7)	19.1 (4.7, 45.9)	7	0.2	413	36.5 (17.4, 76.6)	164.7 (63.4, 344.3)
Unknown	22	4.1	9312	5.3 (3.5, 8.1)	19.2 (10.4, 31.3)	57	2.9	4897	19.7 (15.2, 25.5)	110.5 (82.2, 144.9)

Birth weight SDS

<-4	3	0.4	826	7.7 (2.5, 24.0)	31.6 (2.8, 101.5)	2	0.1	97	37.0 (9.3, 148.1)	200.0 (19.3, 736.8)
-3 to -4	4	0.8	1946	5.1 (1.9, 13.6)	16.5 (1.6, 48.6)	1	0.1	205	9.6 (1.3, 67.9)	43.7 (-3.9, 266.5)
-2 to -3	19	2.7	7093	7.0 (4.5, 11.0)	23.0 (12.3, 38.0)	9	0.5	936	20.1 (10.5, 38.7)	91.4 (39.2, 177.8)
-1 to -2	31	6.0	14428	5.2 (3.6, 7.3)	17.3 (10.4, 26.3)	31	2.0	3577	15.6 (11.0, 22.2)	81.1 (53.3, 117.5)
0 to -1	28	6.5	14432	4.3 (3.0, 6.3)	14.9 (8.4, 23.5)	63	4.3	7319	14.7 (11.5, 18.9)	80.2 (60.3, 104.3)
0 to 1	15	3.4	7299	4.4 (2.7, 7.3)	15.9 (6.8, 29.2)	51	3.4	5526	15.1 (11.5, 19.9)	86.2 (62.6, 115.2)
1 to 2	3	1.0	1933	2.9 (0.9, 9.0)	10.2 (-2.1, 40.0)	17	1.4	2324	12.2 (7.6, 19.6)	67.1 (36.6, 111.1)
2 to 3	3	0.4	707	7.9 (2.5, 24.4)	37.1 (3.4, 118.7)	2	0.4	536	5.2 (1.3, 20.8)	30.1 (-2.7, 127.7)
Unknown	20	4.4	9847	4.5 (2.9, 7.0)	15.8 (7.9, 26.9)	82	4.8	8457	17.2 (13.9, 21.4)	91.3 (71.5, 114.7)

Cumulative r-hGH dose (mg/kg)

0-49	64	11.1	22895	5.7 (4.5, 7.3)	23.1 (16.7, 30.8)	158	10.4	17761	15.1 (13.0, 17.7)	83.1 (69.8, 98.1)
50-99	26	7.1	17407	3.7 (2.5, 5.4)	10.9 (5.7, 17.8)	33	2.9	5297	11.4 (8.1, 16.1)	56.9 (37.4, 82.0)
≥100	14	3.3	8895	4.3 (2.5, 7.2)	12.1 (4.9, 22.7)	10	0.6	1022	18.1 (9.8, 33.7)	92.5 (41.5, 174.6)
Unknown	22	4.1	9312	5.3 (3.5, 8.1)	19.2 (10.4, 31.3)	57	2.9	4897	19.7 (15.2, 25.5)	110.5 (82.2, 144.9)

By cause

Infectious and parasitic disease (A00-B99)	0	0.4	54879	0.0 (., .)	-0.1 (., 0.6)	4	0.2	28493	17.0 (6.4, 45.3)	1.3 (0.3, 3.5)
Neoplasms (C00-D48)	11	3.4	58509	3.2 (1.8, 5.8)	1.3 (0.4, 2.8)	173	1.8	28976	96.1 (82.8, 111.6)	59.1 (50.5, 68.7)
Diseases of blood and blood-forming organs (D50-D89)	3	0.1	58509	25.7 (8.3, 79.6)	0.5 (0.1, 1.5)	3	0.1	28976	47.0 (15.2, 145.7)	1.0 (0.2, 3.0)
Endocrine, nutritional & metabolic disease (E00-E90)	12	0.6	58509	20.5 (11.6, 36.1)	2.0 (1.0, 3.5)	3	0.3	28976	9.9 (3.2, 30.7)	0.9 (0.1, 2.9)
Mental & behavioural disorders (F00-F99)	2	0.9	58509	2.2 (0.5, 8.6)	0.2 (-0.1, 1.1)	1	0.6	28976	1.7 (0.2, 12.4)	0.1 (-0.2, 1.7)
Diseases of nervous system, eye & ear (G00-H95)	6	1.2	54879	5.2 (2.3, 11.6)	0.9 (0.2, 2.2)	9	0.7	28493	12.5 (6.5, 24.0)	2.9 (1.2, 5.7)
Diseases of circulatory system (I00-I99)	23	1.7	58509	13.8 (9.2, 20.7)	3.6 (2.2, 5.6)	13	1.0	28976	13.5 (7.9, 23.3)	4.2 (2.1, 7.3)
Diseases of respiratory system (J00-J99)	7	0.6	58509	12.0 (5.7, 25.1)	1.1 (0.4, 2.4)	12	0.3	28976	38.1 (21.6, 67.1)	4.0 (2.0, 7.1)
Diseases of digestive system (K00-K93)	1	0.6	58509	1.8 (0.3, 13.0)	0.1 (-0.1, 0.9)	6	0.3	28976	19.9 (8.9, 44.3)	2.0 (0.7, 4.4)
Diseases of skin and subcutaneous tissue (L00-L99)	0	0.0	58509	0.0 (., .)	0.0 (., 0.6)	0	0.0	28976	0.0 (., .)	0.0 (., 1.3)
Diseases of musculoskeletal system & connective tissue (M00-M99)	4	0.1	58509	34.8 (13.1, 92.8)	0.7 (0.2, 1.7)	2	0.1	28976	38.5 (9.6, 153.9)	0.7 (0.1, 2.5)
Diseases of genitourinary system (N00-N99)	1	0.1	58509	13.3 (1.9, 94.7)	0.2 (0.0, 0.9)	8	0.0	28976	201.1 (100.6, 402.1)	2.7 (1.2, 5.4)
Pregnancy, childbirth and the puerperium (O00-O99)	0	0.1	58509	0.0 (., .)	0.0 (., 0.6)	0	0.0	28976	0.0 (., .)	0.0 (., 1.3)
Conditions originating in perinatal period (P00-P96)	0	0.0	58509	0.0 (., .)	0.0 (., 0.6)	0	0.0	28976	0.0 (., .)	0.0 (., 1.3)
Congenital anomalies (Q00-Q99)	19	0.5	58509	35.8 (22.8, 56.1)	3.2 (1.9, 5.0)	6	0.3	28976	20.8 (9.3, 46.3)	2.0 (0.7, 4.4)
Symptoms, signs & ill-defined conditions (R00-R99)	20	1.4	58509	14.3 (9.2, 22.2)	3.2 (1.8, 5.0)	10	1.0	28976	10.3 (5.5, 19.1)	3.1 (1.3, 6.0)
Accidents and violence (V00-Y98)	17	13.7	58509	1.2 (0.8, 2.0)	0.6 (-0.6, 2.3)	8	10.0	28976	0.8 (0.4, 1.6)	-0.7 (-2.3, 2.0)

By circulatory cause

Ischemic heart disease	2	0.23	58509	8.6 (2.2, 34.4)	0.3 (0.0, 1.2)	1	0.16	28976	6.4 (0.9, 45.7)	0.3 (0.0, 1.9)
Cerebrovascular disease	2	0.38	58509	5.2 (1.3, 20.8)	0.3 (0.0, 1.2)	1	0.2	28976	4.9 (0.7, 34.9)	0.3 (-0.1, 1.9)
Other circulatory disease	17	0.98	54879	17.4 (10.8, 28.0)	2.9 (1.6, 4.8)	11	0.59	28493	18.7 (10.3, 33.7)	3.7 (1.7, 6.7)

py = person-years

SMR = Standardized Mortality Ratio

AER = Absolute Excess Risk (per 10,000 person-years)

r-hGH = Recombinant human Growth Hormone