

SUPPLEMENTARY MATERIALS

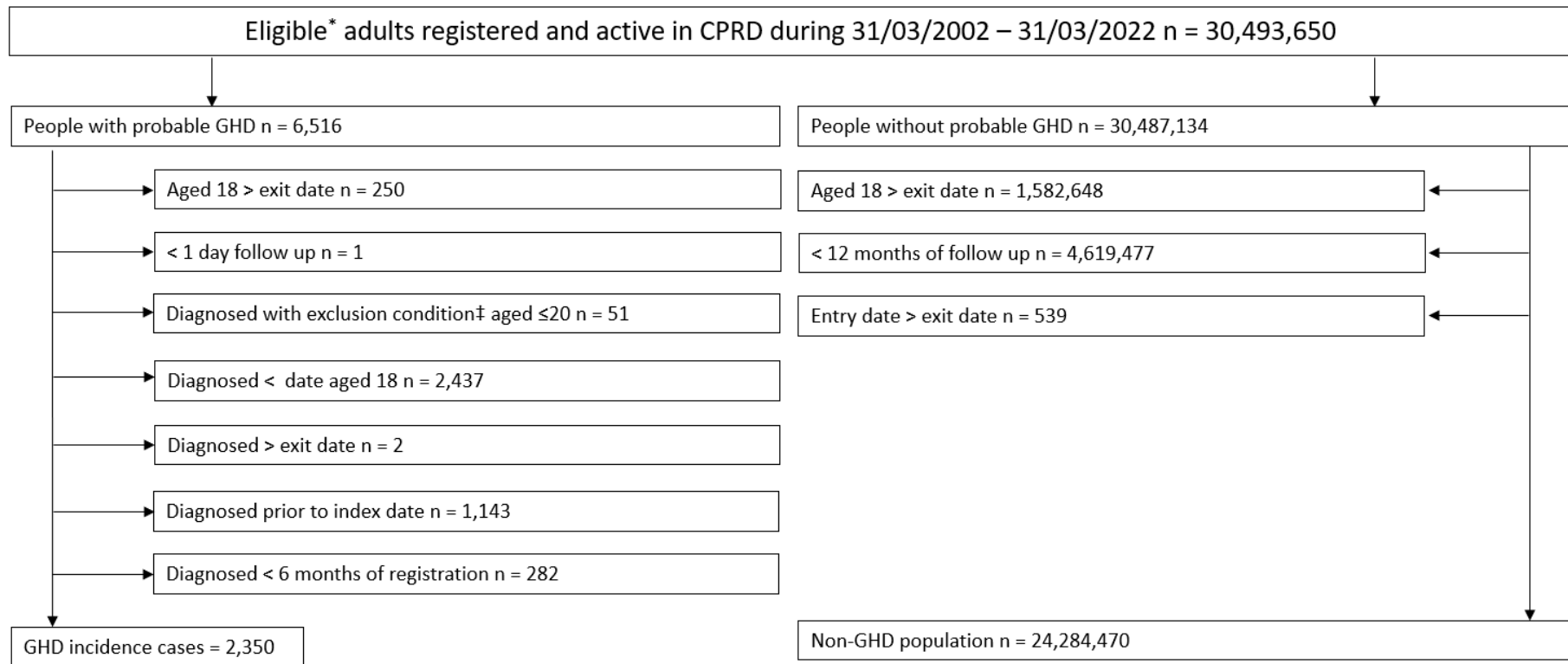
The epidemiology of growth hormone
deficiency in adults:

A population-based study in the UK

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Figure s1: Patient flow diagram for the incidence cohort



* People with missing sex, region, date of birth or Last Collection Date (LCD), or hypopituitarism diagnosis without confirmed GHD are not eligible.

‡ Turner Syndrome, chronic renal insufficiency, children born small for gestational age (SGA) or Prader-Willi syndrome.

Table s1: Regional descriptive statistics for the GHD incident cohort at identification

	Incident GHD cases (%)
n	2,350
Geographical Region n (%)	
North East	50 (2.1)
North West	493 (21.0)
Yorkshire & The Humber	100 (4.3)
East Midlands	44 (1.9)
West Midlands	334 (14.2)
East of England	122 (5.2)
London	267 (11.4)
South Central	436 (18.6)
South West	494 (21.0)
Scotland	10 (0.4)

Table s2: Temporal trend in the incidence of GHD over the twenty-year study period

Year	GHD cases n	Person years	Incidence per 100,000 person years (95% CI)
5	994	95,933,190	1.04 (0.97, 1.10)
10	619	50,613,120	1.22 (1.13, 1.32)
15	403	29,918,030	1.35 (1.22, 1.49)
20	334	17,928,780	1.86 (1.67, 2.07)

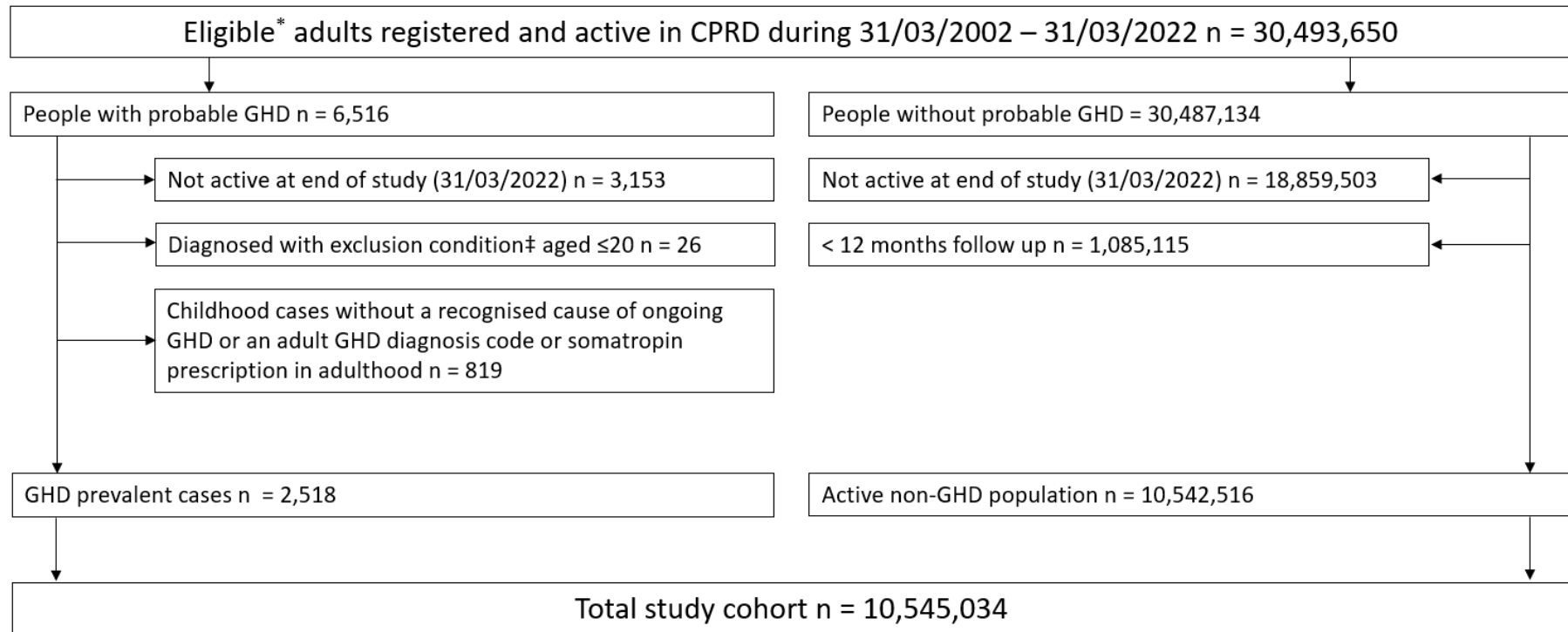
Table s3: Incidence of GHD by demographic and clinical subgroups

Subgroup	GHD cases	Person-years	Incidence rate per 100,000 person-years (95%CI)	Adjusted Incidence Rate Ratio^a (95%CI)
Overall	2,350	194,392,020	1.21 (1.16, 1.26)	
Sex				
Male	1,289	96,796,498	1.33 (1.26, 1.41)	1.0 (reference)
Female	1,061	97,595,522	1.09 (1.02, 1.16)	0.67 (0.62, 0.73)
Age group				
18-19	33	21,234,800	0.16 (0.11, 0.22)	0.30 (0.21, 0.44)
20-29	181	36,992,983	0.49 (0.42, 0.57)	1.0 (reference)
30-39	263	43,076,122	0.61 (0.54, 0.69)	1.17 (0.97, 1.41)
40-49	371	33,455,845	1.11 (1.00, 1.23)	2.03 (1.70, 2.43)
50-59	435	26,556,951	1.64 (1.49, 1.80)	2.88 (2.42, 3.43)
60-69	465	18,004,457	2.58 (2.35, 2.83)	4.23 (3.55, 5.03)
70-79	409	10,405,939	3.93 (3.56, 4.33)	6.36 (5.33, 7.59)
80+	193	4,664,922	4.14 (3.57, 4.76)	7.72 (6.29, 9.48)
Ethnicity				
White	1,844	114,957,258	1.60 (1.53, 1.68)	1.0 (reference)
South Asian	143	6,834,729	2.09 (1.76, 2.47)	1.73 (1.45, 2.07)
Black	135	4,661,766	2.90 (2.43, 3.43)	2.23 (1.85, 2.70)
Other	48	3,106,589	1.55 (1.14, 2.05)	1.23 (0.92, 1.65)
Mixed	23	1,174,635	1.96 (1.24, 2.94)	1.97 (1.31, 2.99)
Not recorded	157	63,657,044	0.25 (0.21, 0.29)	0.16 (0.13, 0.20)
Deprivation				
1 (least deprived)	448	38,989,246	1.15 (1.05, 1.26)	0.89 (0.77, 1.02)
2	500	38,918,622	1.29 (1.18, 1.40)	1.00 (0.88, 1.14)
3	442	37,011,472	1.19 (1.09, 1.31)	0.94 (0.83, 1.08)
4	469	38,382,975	1.22 (1.11, 1.34)	0.98 (0.86, 1.12)
5 (most deprived)	434	35,064,259	1.24 (1.12, 1.36)	1.0 (reference)
Not recorded	57	6,025,447	0.95 (0.72, 1.23)	3.10 (2.22, 4.32)

Geographical region				
North East	50	6,135,920	0.82 (0.61, 1.07)	0.69 (0.51, 0.94)
North West	493	35,647,698	1.38 (1.26, 1.51)	1.22 (1.05, 1.42)
Yorkshire & The Humber	100	6,999,187	1.43 (1.16, 1.74)	1.33 (1.06, 1.67)
East Midlands	44	4,825,702	0.91 (0.66, 1.22)	0.92 (0.67, 1.27)
West Midlands	334	30,621,750	1.09 (0.98, 1.21)	0.92 (0.78, 1.08)
East of England	122	8,338,601	1.46 (1.22, 1.75)	1.29 (1.04, 1.60)
London	267	23,395,151	1.14 (1.01, 1.29)	1.0 (reference)
South Central	436	39,675,843	1.10 (1.00, 1.21)	1.04 (0.89, 1.21)
South West	494	37,951,897	1.30 (1.19, 1.42)	1.24 (1.06, 1.45)
Scotland	10	800,271	1.25 (0.60, 2.30)	2.12 (1.06, 4.25)

^aAdjusted for sex, age at study entry date, deprivation, region, ethnicity.

Figure s2: Patient flow diagram for the prevalence cohort



*People with missing sex, region, date of birth or Last Collection Date (LCD), or a hypopituitarism diagnosis code without confirmed GHD are not eligible.

‡ Turner Syndrome, chronic renal insufficiency, children born small for gestational age (SGA) or Prader-Willi syndrome.

Table s4: Baseline characteristics of the GHD prevalent cohort

	Prevalent GHD cases
n	2,518
Age at identification (median [IQR])	45.0 [22.8, 59.9]
Current age at point prevalence (median [IQR])	56.2 [38.3, 70.3]
Sex n (%)	
Male	1,385 (55.0)
Female	1,133 (45.0)
Age group n (%)	
18-19	55 (2.2)
20-29	313 (12.4)
30-39	334 (13.3)
40-49	324 (12.9)
50-59	404 (16.0)
60-69	455 (18.1)
70-79	414 (16.4)
80+	219 (8.7)
Ethnicity n (%)	
White	1,812 (72.0)
South Asian	154 (6.1)
Black	141 (5.6)
Other	50 (2.0)
Mixed	27 (1.1)
Not recorded	334 (13.3)
Deprivation n (%)	
1 (least deprived)	482 (19.1)
2	483 (19.2)
3	450 (17.9)
4	483 (19.2)
5 (most deprived)	439 (17.4)
Not recorded	181 (7.2)
Geographical Region n (%)	
North East	66 (2.6)
North West	536 (21.3)
Yorkshire & The Humber	99 (3.9)
East Midlands	63 (2.5)
West Midlands	345 (13.7)
East of England	120 (4.8)
London	271 (10.8)
South Central	479 (19.0)
South West	526 (20.9)
Scotland	13 (0.5)

IQR, inter quartile range

Table s5: Point prevalence for identified GHD

	GHD cases	Total	Point prevalence (95% CI)
Overall	2,518	10,545,034	0.024 (0.023, 0.025)
Sex			
Male	1,385	5,296,410	0.026 (0.025, 0.028)
Female	1,133	5,248,624	0.022 (0.020, 0.023)
Age group			
18-19	55	283,808	0.019 (0.015, 0.025)
20-29	313	1,635,952	0.019 (0.017, 0.021)
30-39	334	1,923,251	0.017 (0.016, 0.019)
40-49	324	1,765,161	0.018 (0.016, 0.020)
50-59	404	1,803,372	0.022 (0.020, 0.025)
60-69	455	1,404,707	0.032 (0.030, 0.036)
70-79	414	1,069,568	0.039 (0.035, 0.043)
80+	219	659,215	0.033 (0.029, 0.038)
Ethnicity			
White	1,812	5,635,008	0.032 (0.031, 0.034)
South Asian	154	429,958	0.036 (0.030, 0.042)
Black	141	275,159	0.051 (0.043, 0.061)
Other	50	194,541	0.026 (0.019, 0.034)
Mixed	27	79,323	0.034 (0.023, 0.050)
Not recorded	334	3,931,045	0.008 (0.008, 0.009)
Deprivation			
1 (least deprived)	482	2,057,889	0.023 (0.021, 0.026)
2	483	2,082,135	0.023 (0.021, 0.025)
3	450	2,026,414	0.022 (0.020, 0.024)
4	483	2,163,263	0.022 (0.020, 0.024)
5 (most deprived)	439	1,964,128	0.022 (0.020, 0.025)
Not recorded	181	251,205	0.072 (0.062, 0.084)
Geographical region			
North East	66	327,808	0.020 (0.016, 0.026)
North West	536	1,860,354	0.029 (0.026, 0.031)
Yorkshire & The Humber	99	395,910	0.025 (0.020, 0.031)
East Midlands	63	273,680	0.023 (0.018, 0.030)
West Midlands	345	1,661,550	0.021 (0.019, 0.023)
East of England	120	465,826	0.026 (0.021, 0.031)
London	271	1,236,108	0.022 (0.019, 0.025)
South Central	479	2,084,347	0.023 (0.021, 0.025)
South West	526	2,191,115	0.024 (0.022, 0.026)
Scotland	13	48,336	0.027 (0.015, 0.047)

Figure s3: Time since GHD identification and percentage initiating somatropin treatment

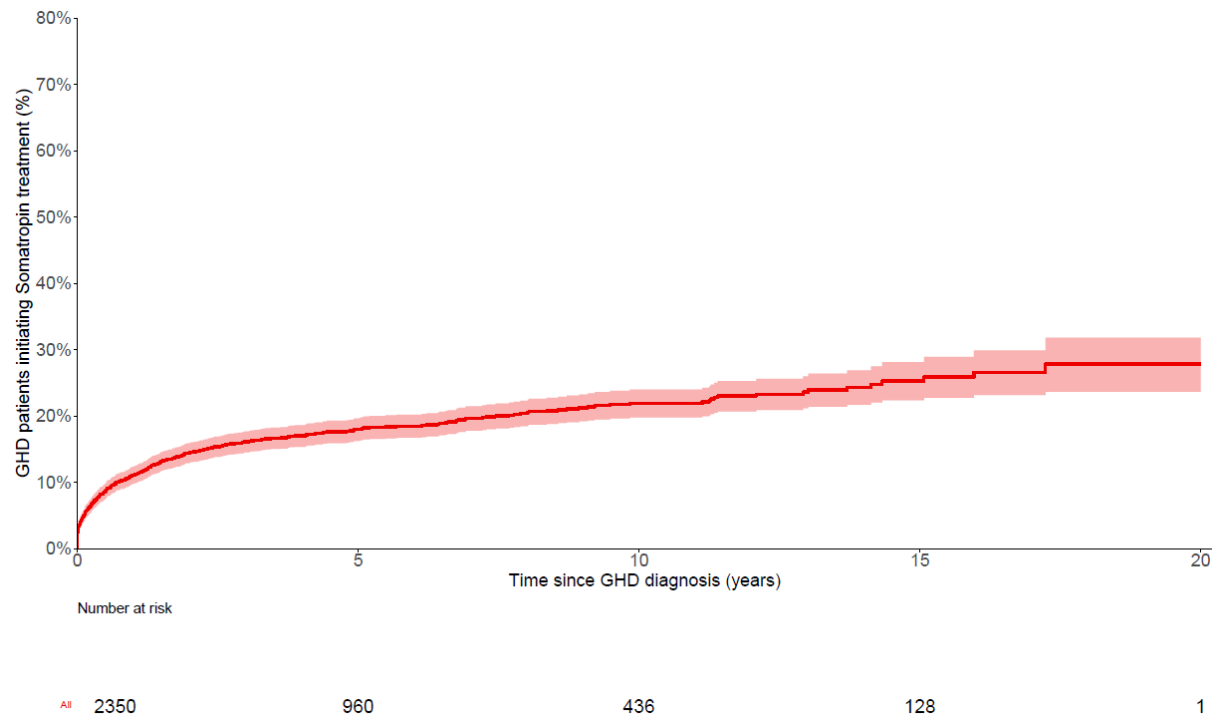


Figure s4: Persistence of GHD somatropin treatment, based on 194 day interval (90th centile) threshold

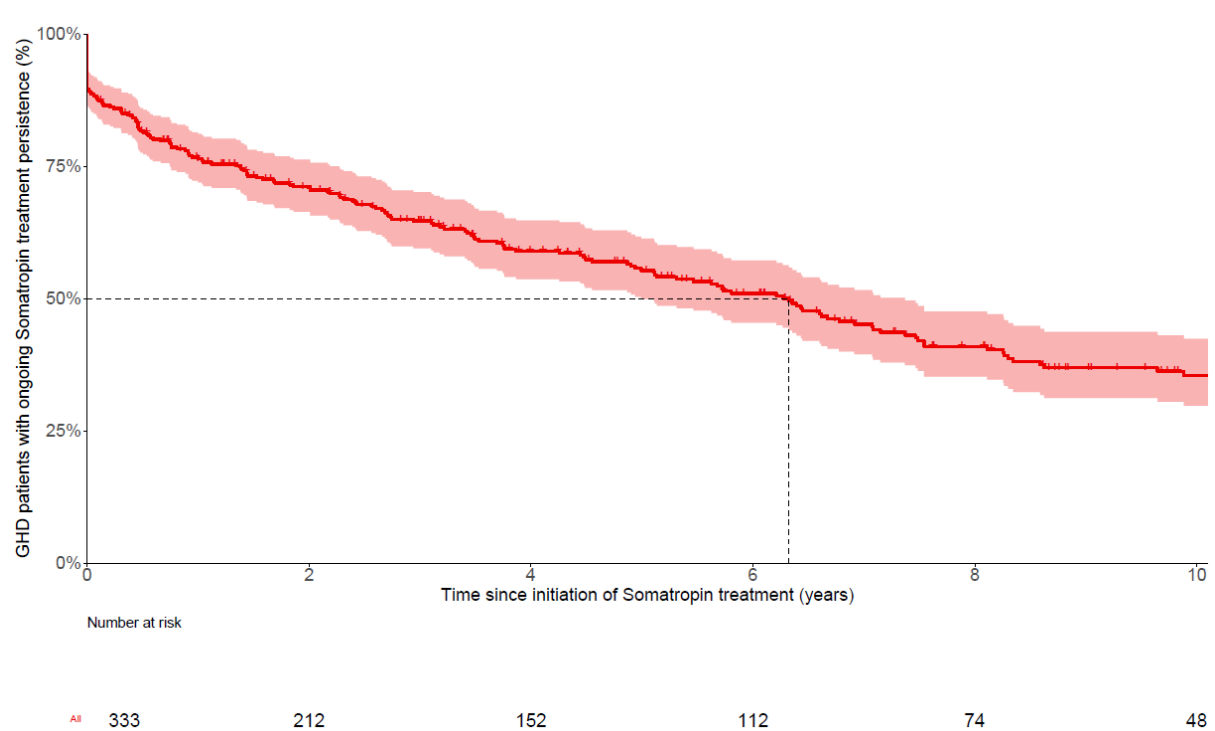


Table s6: Incidence of GHD by demographic and clinical subgroups, using the broader GHD case definition

Subgroup	GHD cases	Person-years	Incidence rate per 100,000 person-years (95%CI)	Adjusted Incidence Rate Ratio^a (95%CI)
Overall	4,202	194,405,121	2.16 (2.10, 2.23)	
Sex				
Male	2,206	96,803,518	2.28 (2.19, 2.38)	1.0 (reference)
Female	1,996	97,601,603	2.05 (1.96, 2.14)	0.74 (0.70, 0.79)
Age group				
18-19	61	21,234,825	0.29 (0.22, 0.37)	0.29 (0.22, 0.38)
20-29	356	36,993,641	0.96 (0.87, 1.07)	1.0 (reference)
30-39	534	43,077,553	1.24 (1.14, 1.35)	1.22 (1.07, 1.40)
40-49	679	33,458,056	2.03 (1.88, 2.19)	1.94 (1.70, 2.20)
50-59	801	26,559,696	3.02 (2.81, 3.23)	2.78 (2.45, 3.15)
60-69	775	18,007,023	4.30 (4.01, 4.62)	3.71 (3.27, 4.22)
70-79	670	10,408,204	6.44 (5.96, 6.94)	5.47 (4.81, 6.24)
80+	326	4,666,124	6.99 (6.25, 7.79)	6.74 (5.79, 7.84)
Ethnicity				
White	3,237	114,967,381	2.82 (2.72, 2.91)	1.0 (reference)
South Asian	258	6,835,524	3.78 (3.33, 4.26)	1.68 (1.47, 1.91)
Black	236	4,662,366	5.06 (4.44, 5.75)	2.06 (1.78, 2.37)
Other	84	3,106,808	2.70 (2.16, 3.35)	1.15 (0.92, 1.43)
Mixed	49	1,174,814	4.17 (3.09, 5.51)	2.25 (1.69, 2.99)
Not recorded	338	63,658,228	0.53 (0.48, 0.59)	0.20 (0.18, 0.23)
Deprivation				
1 (least deprived)	802	38,991,919	2.06 (1.92, 2.20)	0.86 (0.78, 0.95)
2	828	38,920,915	2.13 (1.99, 2.28)	0.89 (0.81, 0.98)
3	791	37,014,082	2.14 (1.99, 2.29)	0.91 (0.82, 1.00)
4	850	38,385,430	2.21 (2.07, 2.37)	0.94 (0.85, 1.04)

5 (most deprived)	823	35,066,966	2.35 (2.19, 2.51)	1.0 (reference)
Not recorded	108	6,025,809	1.79 (1.47, 2.16)	2.73 (2.15, 3.46)
Geographical region				
North East	109	6,136,338	1.78 (1.46, 2.14)	0.94 (0.76, 1.15)
North West	924	35,650,870	2.59 (2.43, 2.76)	1.42 (1.27, 1.59)
Yorkshire & The Humber	162	6,999,626	2.31 (1.97, 2.70)	1.34 (1.12, 1.61)
East Midlands	82	4,826,019	1.70 (1.35, 2.11)	1.07 (0.85, 1.36)
West Midlands	586	30,623,559	1.91 (1.76, 2.08)	1.00 (0.89, 1.14)
East of England	204	8,339,155	2.45 (2.12, 2.81)	1.35 (1.15, 1.60)
London	427	23,396,292	1.83 (1.66, 2.01)	1.0 (reference)
South Central	767	39,678,178	1.93 (1.80, 2.08)	1.14 (1.01, 1.28)
South West	925	37,954,766	2.44 (2.28, 2.60)	1.45 (1.28, 1.63)
Scotland	16	800,318	2.00 (1.14, 3.25)	1.84 (1.07, 3.16)

^aAdjusted for sex, age at study entry date, deprivation, region, ethnicity.

Table s7: Point prevalence for identified GHD, using the broader GHD case definition

	GHD cases	Total	Point prevalence (95% CI)
Overall	4,869	10,547,385	0.046 (0.045, 0.047)
Sex			
Male	2,531	5,297,556	0.048 (0.046, 0.050)
Female	2,338	5,249,829	0.045 (0.043, 0.046)
Age group			
18-19	81	283,834	0.029 (0.023, 0.036)
20-29	489	1,636,128	0.030 (0.027, 0.033)
30-39	620	1,923,537	0.032 (0.030, 0.035)
40-49	688	1,765,525	0.039 (0.036, 0.042)
50-59	832	1,803,800	0.046 (0.043, 0.049)
60-69	932	1,405,184	0.066 (0.062, 0.071)
70-79	790	1,069,944	0.074 (0.069, 0.079)
80+	437	659,433	0.066 (0.060, 0.073)
Ethnicity			
White	3,372	5,636,568	0.060 (0.058, 0.062)
South Asian	309	430,113	0.072 (0.064, 0.080)
Black	279	275,297	0.101 (0.090, 0.114)
Other	103	194,594	0.053 (0.043, 0.064)
Mixed	60	79,356	0.076 (0.058, 0.098)
Not recorded	746	3,931,457	0.019 (0.018, 0.020)
Deprivation			
1 (least deprived)	896	2,058,303	0.044 (0.041, 0.047)
2	891	2,082,543	0.043 (0.040, 0.046)
3	896	2,026,860	0.044 (0.041, 0.047)
4	937	2,163,717	0.043 (0.041, 0.046)
5 (most deprived)	886	1,964,575	0.045 (0.042, 0.048)
Not recorded	363	251,387	0.144 (0.130, 0.160)
Geographical region			
North East	135	327,877	0.041 (0.035, 0.049)
North West	988	1,860,806	0.053 (0.050, 0.057)
Yorkshire & The Humber	198	396,009	0.050 (0.043, 0.058)
East Midlands	113	273,730	0.041 (0.034, 0.050)
West Midlands	661	1,661,866	0.040 (0.037, 0.043)
East of England	234	465,940	0.050 (0.044, 0.057)
London	532	1,236,369	0.043 (0.039, 0.047)
South Central	939	2,084,807	0.045 (0.042, 0.048)
South West	1,050	2,191,639	0.048 (0.045, 0.051)
Scotland	19	48,342	0.039 (0.024, 0.063)