Supplemental Information

The supplemental information includes a comprehensive list of genes and loci (Table S1) associated with intellectual disability along with data items, including when available, OMIM reference, associated gene(s), DECIPHER alleles, impact on mortality, and inheritance pattern. Table S2 and Table S3 list the references used in each calculation for the costs of intellectual and physical disability presented in Table 1 and Table 2 respectively in the main manuscript and an excel file (Supplementary Excel file 1) that provides all the data used in the costing analyses and the methods used to calculate the low, middle and upper estimates for each cost category (note this is a separate file to this document). Figure S1 provides a PRISMA flow diagram that details how monogenic diseases associated with intellectual disability were ascertained. A table of contents is provided listing each supplemental resource individually.

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Table S1. The most frequent intellectual disability etiologies

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
KBG syndrome	148050	*ANKRD11*	*99*	Intellectual Disability Syndromic	Autosomal dominant	3
16q24.3 microdeletion syndrome		*ANKRD11*	*99*	Chromosomal	Autosomal dominant	3
Monosomy 22q13	606232	*SHANK3*	*98*	Chromosomal	Autosomal dominant	3
X-linked non-syndromic intellectual disability	300055	*MECP2*	*83*	Intellectual Disability Non-Syndromic	X-linked recessive	3
Rett syndrome	312750	*MECP2*	*83*	Intellectual Disability Syndromic	X-linked dominant	3
Wiedemann-Steiner syndrome	605130	*KMT2A*	*72*	Intellectual Disability Syndromic	Autosomal dominant	3
Coffin-Siris syndrome	135900	*ARID1B*	*67*	Intellectual Disability Syndromic	Autosomal dominant	3
Nicolaides-Baraitser syndrome	601358	*ARID1B*	*67*	Intellectual Disability Syndromic	Autosomal dominant	3
6q25 microdeletion syndrome	612863	*ARID1B*	*67*	Chromosomal	Autosomal dominant	3
Mental retardation, X-linked 102	300958	*DDX3X*	*65*	Intellectual Disability Non-Syndromic	X-linked dominant	3
Mental retardation, autosomal dominant 7	614104	*DYRK1A*	*60*	Intellectual Disability Non-Syndromic	Autosomal dominant	3
Autosomal recessive non-syndromic intellectual disability	249500	*MED13L*	*57*	Intellectual Disability Non-Syndromic	Autosomal recessive	3
Kleefstra syndrome due to a point mutation	610253	*EHMT1*	*55*	Intellectual Disability Syndromic	Autosomal dominant	3
9q34 microdeletion syndrome	610253	*EHMT1*	*55*	Chromosomal	Autosomal dominant	3
Microphthalmia, Lenz type	309800	*NAA10*	*54*	Ophthalmological	X-linked recessive	3

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Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Periventricular nodular heterotopia	300049	*FLNA*	*53*	Central Nervous System	X-linked dominant	3
Frontometaphyseal dysplasia	305620	*FLNA*	*53*	Skeletal Dysplasias	X-linked dominant	3
Osteodysplasty, Melnick-Needles type	309350	*FLNA*	*53*	Skeletal Dysplasias	X-linked dominant	3
Otopalatodigital syndrome type 1	311300	*FLNA*	*53*	Skeletal Dysplasias	X-linked dominant	3
X-linked non-syndromic intellectual disability	309530	*IQSEC2*	*51*	Intellectual Disability Non-Syndromic	X-linked recessive	3
Severe intellectual disability-progressive postnatal microcephaly- midline stereotypic hand movements syndrome	309530	*IQSEC2*	*51*	Intellectual Disability Syndromic	X-linked recessive	3
Alpha-thalassemia - X-linked intellectual disability syndrome	301040	*ATRX*	*50*	Intellectual Disability Syndromic	X-linked recessive	3
Mental retardation hypotonic face syndrome	309580	*ATRX*	*50*	Intellectual Disability Syndromic	X-linked recessive	3
Epileptic encephalopathy, early infantile, 11	613721	*SCN2A*	*50*	Epilepsy Syndromes	Autosomal dominant	2
West syndrome	613721	*SCN2A*	*50*	Epilepsy Syndromes	Autosomal dominant	2
Glass syndrome	612313	*SATB2*	*49*	Intellectual Disability Syndromic	Autosomal dominant	3
2q33.1 microdeletion syndrome	612313	*SATB2*	*49*	Chromosomal	Autosomal dominant	3
Mental retardation, autosomal dominant 23 (Intellectual disability-facial dysmorphism syndrome due to SETD5 haploinsufficiency	615761	*SETD5*	*48*	Intellectual Disability Syndromic	Autosomal dominant	3
Cornelia de Lange syndrome 2	300590	*SMC1A*	*48*	Intellectual Disability Syndromic	X-linked recessive	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Rubinstein-Taybi syndrome due to CREBBP mutations	180849	*CREBBP*	*46*	Intellectual Disability Syndromic	Autosomal dominant	3
Rubinstein-Taybi syndrome due to 16p13.3 microdeletion	610543	*CREBBP*	*46*	Chromosomal	Autosomal dominant	3
Koolen-De Vries syndrome due to a point mutation	610443	*KANSL1*	*46*	Intellectual Disability Syndromic	Autosomal dominant	3
17q21.31 microdeletion syndrome	610443	*KANSL1*	*46*	Chromosomal	Autosomal dominant	3
X-linked intellectual disability, Najm type (MICPCH)	300749	*CASK*	*44*	Intellectual Disability Syndromic	X-linked dominant	3
Early infantile epileptic encephalopathy		*CASK*	*44*	Epilepsy Syndromes	X-linked recessive	3
Duchenne muscular dystrophy	310200	*DMD*	*44*	Neuromuscular	X-linked recessive	3
Helsmoortel-van der Aa syndrome	615873	*ADNP*	*42*	Intellectual Disability Syndromic	Autosomal dominant	3
Smith-Magenis syndrome	182290	*RAI1*	*42*	Intellectual Disability Syndromic	Autosomal dominant	3
17p11.2 microduplication syndrome (Potocki-Lupski syndrome)	610883	*RAI1*	*42*	Chromosomal	Autosomal dominant	3
Mental retardation, autosomal dominant 5	612621	*SYNGAP1*	*40*	Intellectual Disability Non-Syndromic	Autosomal dominant	3
Severe feeding difficulties - failure to thrive - microcephaly due to ASXL3 deficiency (Bainbridge-Ropers syndrome)	615485	*ASXL3*	*39*	Intellectual Disability Syndromic	Autosomal dominant	3
Autosomal dominant non-syndromic intellectual disability		*TCF4*	*39*	Intellectual Disability Non-Syndromic	Autosomal dominant	3

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Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Pitt-Hopkins syndrome	610954	*TCF4*	*39*	Intellectual Disability Syndromic	Autosomal dominant	3
Rubinstein-Taybi syndrome 2 (due to EP300 haploinsufficiency)	613684	*EP300*	*38*	Intellectual Disability Syndromic	Autosomal dominant	3
Mental retardation, autosomal dominant 9	614255	*KIF1A*	*38*	Intellectual Disability Non-Syndromic	Autosomal dominant	3
Neurofibromatosis type 1 due to NF1mutation or intragenic deletion	162200	*NF1*	*38*	Intellectual Disability Syndromic	Autosomal dominant	3
17q11 microdeletion syndrome	613675	*NF1*	*38*	Chromosomal	Autosomal dominant	3
17q11.2 microduplication syndrome	613675	*NF1*	*38*	Chromosomal	Autosomal dominant	3
Beta-propeller protein-associated neurodegeneration	300894	*WDR45*	*38*	Intellectual Disability Syndromic	X-linked dominant	3
Okur-Chung neurodevelopmental syndrome	617062	*CSNK2A1*	*37*	Intellectual Disability Syndromic	Autosomal dominant	3
Mental retardation, autosomal dominant 6	613970	*GRIN2B*	*37*	Intellectual Disability Non-Syndromic	Autosomal dominant	3
X-linked intellectual disability, Turner type	309590	*HUWE1*	*36*	Intellectual Disability Syndromic	X-linked recessive	3
Spinocerebellar ataxia type 29	117360	*ITPR1*	*36*	Cerebellar/Ataxias	Autosomal dominant	3
Mental retardation, autosomal dominant 32	616268	*KAT6A*	*36*	Cardiac	Autosomal dominant	3
intellectual disability - sparse hair - brachydactyly (Nicolaides-Baraitser syndrome)	601358	*SMARCA2*	*36*	Intellectual Disability Syndromic	Autosomal dominant	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Congenital heart defects, dysmorphic facial features, and intellectual developmental disorder	617360	*CDK13*	*35*	Cardiac	Autosomal dominant	3
Cornelia de Lange syndrome 5	300882	*HDAC8*	*35*	Intellectual Disability Syndromic	X-linked recessive	3
Early infantile epileptic encephalopathy, 7	613720	*KCNQ2*	*35*	Epilepsy Syndromes	Autosomal dominant	3
Syndromic X-linked intellectual disability due to JARID1C mutation	300534	*KDM5C*	*35*	Intellectual Disability Syndromic	X-linked recessive	3
Early infantile epileptic encephalopathy, 4	612164	*STXBP1*	*35*	Epilepsy Syndromes	Autosomal dominant	3
Dravet syndrome	612164	*STXBP1*	*35*	Epilepsy Syndromes	Autosomal dominant	3
Epileptic encephalopathy, early infantile, 54	617391	*HNRNPU*	*34*	Epilepsy Syndromes	Autosomal Dominant	3
Desanto-Shinawi syndrome	616708	*WAC*	*33*	Intellectual Disability Syndromic	Autosomal dominant	3
Atypical Rett syndrome	300672	*CDKL5*	*32*	Intellectual Disability Syndromic	X-linked dominant	3
Early infantile epileptic encephalopathy	300672	*CDKL5*	*32*	Epilepsy Syndromes	X-linked dominant	3
West syndrome	300672	*CDKL5*	*32*	Epilepsy Syndromes	X-linked dominant	3
5q14.3 microdeletion syndrome	613443	*MEF2C*	*32*	Chromosomal	Autosomal dominant	3
Sotos syndrome 1	117550	*NSD1*	*32*	Overgrowth	Autosomal dominant	3
5q35 microduplication syndrome	117550	*NSD1*	*32*	Chromosomal	Autosomal dominant	3
CHARGE syndrome	214800	*CHD7*	*31*	Malformations	Autosomal dominant	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
COFS syndrome	214150	*ERCC6*	*31*	Intellectual Disability Syndromic	Autosomal recessive	2
Cockayne syndrome type 1	133540	*ERCC6*	*31*	Neoplastic	Autosomal recessive	2
Verheij Syndrome	615583	*PUF60*	*31*	Malformations	Autosomal dominant	3
Autism spectrum disorder due to AUTS2 deficiency (Mental retardation, autosomal dominant 26)	615834	*AUTS2*	*30*	Intellectual Disability Syndromic	Autosomal dominant	3
Severe intellectual disability-progressive spastic diplegia syndrome	615075	*CTNNB1*	*30*	Intellectual Disability Syndromic	Autosomal dominant	3
Intellectual disability-severe speech delay-mild dysmorphism syndrome	613670	*FOXP1*	*30*	Intellectual Disability Syndromic	Autosomal dominant	3
LEOPARD syndrome 1	151100	*PTPN11*	*29*	Intellectual Disability Syndromic	Autosomal dominant	3
Noonan syndrome 1	163950	*PTPN11*	*29*	Intellectual Disability Syndromic	Autosomal dominant	3
X-linked non-syndromic intellectual disability	300046	*USP9X*	*29*	Intellectual Disability Non-Syndromic	X-linked recessive	3
Autosomal dominant childhood-onset proximal spinal muscular atrophy without contractures	158600	*DYNC1H1*	*28*	Neuromuscular	Autosomal dominant	3
Mandibulofacial dysostosis-microcephaly syndrome	610536	*EFTUD2*	*28*	Craniofacial	Autosomal dominant	3
Kabuki syndrome 2	300867	*KDM6A*	*28*	Intellectual Disability Syndromic	Autosomal dominant	3

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Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
X-linked intellectual disability - cerebellar hypoplasia	300486	*OPHN1*	*28*	Intellectual Disability Non-Syndromic	X-linked recessive	3
Christianson syndrome	300243	*SLC9A6*	*28*	Intellectual Disability Syndromic	X-linked recessive	3
Cohen syndrome	216550	*VPS13B*	*28*	Intellectual Disability Syndromic	Autosomal recessive	3
Marshall-Smith syndrome	602535	*NFIX*	*27*	Overgrowth	Autosomal dominant	3
Sotos syndrome 2	614753	*NFIX*	*27*	Overgrowth	Autosomal dominant	3
Mental retardation, autosomal dominant 35	616355	*PPP2R5D*	*27*	Intellectual Disability Syndromic	Autosomal dominant	3
Intellectual disability with postnatal overgrowth	618430	*TCF20*	*27*	Intellectual Disability Non-Syndromic	Autosomal dominant	3
Mental retardation, autosomal dominant 44	601893	*TRIO*	*27*	Intellectual Disability Syndromic	Autosomal dominant	3
Atypical Rett syndrome	613454	*FOXG1*	*26*	Intellectual Disability Syndromic	Autosomal dominant	3
14q11.2 microduplication syndrome	613457	*FOXG1*	*26*	Chromosomal	Autosomal dominant	3
14q12 microdeletion syndrome	613457	*FOXG1*	*26*	Chromosomal	Autosomal dominant	3
Hypotonia-speech impairment-severe cognitive delay syndrome	615419	*NALCN*	*26*	Intellectual Disability Syndromic	Autosomal dominant/ recessive	3
Intellectual disability - obesity - brain malformations - facial dysmorphism	613192	*TRAPPC9*	*26*	Intellectual Disability Syndromic	Autosomal recessive	3
X-linked non-syndromic intellectual disability (Opitz-Kaveggia syndrome)	305450	*MED12*	*25*	Intellectual Disability Non-Syndromic	X-linked recessive	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
X-linked intellectual disability with marfanoid habitus (Lujan-Fryns syndrome)	309520	*MED12*	*25*	Intellectual Disability Syndromic	X-linked recessive	3
Ohdo syndrome, X-linked	300895	*MED12*	*25*	Intellectual Disability Syndromic	X-linked recessive	3
Myoclonic-atonic epilepsy	616421	*SLC6A1*	*25*	Epilepsy Syndromes	Autosomal dominant	2
Intellectual disability-developmental delay-contractures syndrome	314580	*ZC4H2*	*25*	Intellectual Disability Syndromic	X-linked recessive	3
Tall stature-intellectual disability-facial dysmorphism syndrome (Tatton-Brown-Rahman syndrome)	615879	*DNMT3A*	*24*	Intellectual Disability Syndromic	Autosomal dominant	3
Blepharophimosis-intellectual disability syndrome, SBBYS type	603736	*KAT6B*	*24*	Intellectual Disability Syndromic	Autosomal dominant	3
Genitopatellar syndrome	606170	*KAT6B*	*24*	Skeletal Dysplasias	Autosomal dominant	3
Juvenile myoclonic epilepsy	121201	*KCNQ3*	*24*	Epilepsy Syndromes	Autosomal dominant	3
Benign familial neonatal seizures, 2	121201	*KCNQ3*	*24*	Epilepsy Syndromes	Autosomal dominant	3
Mental retardation, autosomal recessive 65	618109	*KDM5B*	*24*	Intellectual Disability Syndromic	Autosomal recessive	3
White-Sutton syndrome	616364	*POGZ*	*24*	Intellectual Disability Syndromic	Autosomal dominant	2
Dravet syndrome	607208	*SCN1A*	*24*	Epilepsy Syndromes	Autosomal dominant	3
Malignant migrating partial seizures of infancy	604403	*SCN1A*	*24*	Epilepsy Syndromes	Autosomal dominant	3
Mental retardation, autosomal dominant 49	617752	*TRIP12*	*24*	Intellectual Disability Syndromic	Autosomal dominant	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Autosomal dominant non-syndromic intellectual disability	616579	*CHAMP1*	*23*	Intellectual Disability Syndromic	Autosomal dominant	3
Severe intellectual disability-poor language-strabismus-grimacing face-long fingers syndrome	615074	*GATAD2B*	*23*	Intellectual Disability Syndromic	Autosomal dominant	3
Mental retardation, autosomal dominant 31	616158	*PURA*	*23*	Epilepsy Syndromes	Autosomal dominant	3
Schinzel-Giedion syndrome	269150	*SETBP1*	*23*	Intellectual Disability Syndromic	Autosomal dominant	2
Mental retardation, autosomal dominant 41 (Pierpont syndrome)	612376	*TBL1XR1*	*23*	Intellectual Disability Syndromic	Autosomal dominant	3
Mental retardation, X-linked 93	300659	*BRWD3*	*22*	Intellectual Disability Non-Syndromic	X-linked recessive	3
Lennox-Gastaut syndrome (Epileptic encephalopathy, childhood-onset)	615369	*CHD2*	*22*	Epilepsy Syndromes	Autosomal dominant	3
Mental retardation, X-linked 98	300524	*NEXMIF*	*21*	Intellectual Disability Syndromic	X-linked recessive	3
Geleophysic dysplasia 2	614185	*FBN1*	*20*	Skeletal Dysplasias	Autosomal dominant	3
Glaucoma - ectopia - microspherophakia - stiff joints - short stature (Weill-Marchesani syndrome 2, dominant)	608328	*FBN1*	*20*	Ophthalmological	Autosomal dominant	3
Kabuki syndrome 1	147920	*KMT2D*	*20*	Intellectual Disability Syndromic	Autosomal dominant	3
Proteus-like syndrome	158350	*PTEN*	*20*	Intellectual Disability Syndromic	Autosomal dominant	3
Macrocephaly-autism syndrome	605309	*PTEN*	*20*	Intellectual Disability Syndromic	Autosomal dominant	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Bannayan-Riley-Ruvalcaba syndrome	158350	*PTEN*	*20*	Overgrowth	Autosomal dominant	3
Witteveen-Kolk syndrome	613406	*SIN3A*	*20*	Intellectual Disability Syndromic	Autosomal dominant	3
Mental retardation X linked, syndromic 33	300966	*TAF1*	*20*	Intellectual Disability Syndromic	X-linked recessive	3
Baraitser-Winter syndrome 1	243310	*ACTB*	*19*	Craniofacial	Autosomal dominant	3
AHDC1-related intellectual disability-obstructive sleep apnea-mild dysmorphism syndrome (Xia-Gibbs syndrome)	615829	*AHDC1*	*19*	Intellectual Disability Syndromic	Autosomal dominant	3
Early infantile epileptic encephalopathy	614558	*SCN8A*	*19*	Epilepsy Syndromes	Autosomal dominant	3
Myhre syndrome	139210	*SMAD4*	*19*	Intellectual Disability Syndromic	Autosomal dominant	3
Hereditary persistence of fetal hemoglobin-sickle cell disease syndrome (Dias-Logan syndrome)	617101	*BCL11A*	*18*	Haematological	Autosomal recessive	3
Intellectual disability - craniofacial dysmorphism - cryptorchidism	615009	*PACS1*	*18*	Intellectual Disability Syndromic	Autosomal dominant	3
Rolandic epilepsy - speech dyspraxia	245570	*GRIN2A*	*17*	Epilepsy Syndromes	Autosomal dominant	3
Early-onset epileptic encephalopathy and intellectual disability due to GRIN2A mutation	245570	*GRIN2A*	*17*	Epilepsy Syndromes	Autosomal dominant	3
Mowat-Wilson syndrome due to a ZEB2 point mutation	235730	*ZEB2*	*17*	Intellectual Disability Syndromic	Autosomal dominant	3

Disease	OMIM	Gene	DECIPHER Alleles	Body System	Inheritance	Longevity[a]
Mowat-Wilson syndrome due to monosomy 2q22	235730	*ZEB2*	*17*	Chromosomal	Autosomal dominant	3
Joubert syndrome 17	614615	*CPLANE1*	*16*	Central Nervous System	Autosomal recessive	3
Joubert syndrome with orofaciodigital defect	277170	*CPLANE1*	*16*	Central Nervous System	Autosomal recessive	3
Neurodevelopmental disorder with dysmorphic facies and distal limb anomalies	617755	*BPTF*	*15*	Intellectual Disability Syndromic	Autosomal dominant	3

[a] Longevity coded as 1=less than two years of life; 2=death by adolescence; and 3=adult life expectancy.

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Table S2. References for cost analysis in Table 1

	Healthcare Costs				**Social Costs**							**Total Costs**
Age/Severity Group	**Hospital Services Costs**	**Community Services Costs**	**Treatment/ Aids/ Adaptations Costs**	**Total Healthcare Costs**	**Accomm-odation Costs**	**Education Costs**	**Daytime Activities Costs**	**Income Support**	**Carer Costs**	**Loss of Productivity**	**Total Social Costs**	**(Healthcare and Social Costs)**
Children 0-3 mild	L[1] M[1] U[1]	L[2] M[2] U[2]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[2,4,5] M[2,4] U[2,4]	L[2] M[4] U[4]	L[4] M[4] U[4]	L[2,6] M[6] U[2,4,6]	L[2,6] M[2,6] U[2,6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children 0-3 moderate	L[1] M[1] U[1]	L[2] M[2] U[2]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[2,4,5] M[2,4] U[2,4]	L[2] M[4] U[4]	L[4] M[4] U[4]	L[6] M[2,4,6] U[2,6]	L[2,6] M[2,6] U[2,6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children 0-3 severe/profound	L[1] M[1] U[1]	L[2] M[2] U[2]	L[2,7] M[2,7] U[2,7]	Sum of previous 3 columns	L[2,4,5] M[2,4] U[2,4]	L[2] M[4] U[4]	L[4] M[4] U[4]	L[2,6] M[2,4,6] U[6]	L[2,6] M[2,6] U[2,6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children **4**-11 mild	L[2,8] M[1,8] U[1]	L[8] M[2,8] U[2]	L[2,3] M[2,3,8] U[3,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[2,4] M[2,4] U[4]	L[4] M[4] U[4]	L[6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children **4**-11 moderate	L[2,8] M[1,8] U[1]	L[8] M[2,8] U[2]	L[2,3] M[2,3,8] U[3,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[2,4] M[2,4] U[4]	L[4] M[4] U[4]	L[6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children **4**-11 severe/profound	L[2,8] M[1,8] U[1]	L[8] M[2,8] U[2]	L[2,7] M[2,7,8] U[7,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[2,4] M[2,4] U[4]	L[4] M[4] U[4]	L[2,6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Children 12-17 mild	L[2,8] M[1,8] U[1]	L[8] M[2,8] U[2]	L[2,3] M[2,3,8] U[3,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[4] M[2,4,9] U[2]	L[4] M[4,9] U[4]	L[6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2,9] M[2,4,9] U[4,9]	Sum of previous **6** columns	Sum of total HC and SC
Children 12-17 moderate	L[2,8] M[1,8] U[1]	L[8] M[2,8] U[2]	L[2,3] M[2,3,8] U[3,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[4] M[2,4,9] U[2]	L[4] M[4,9] U[4]	L[6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2,9] M[2,4,9] U[4,9]	Sum of previous **6** columns	Sum of total HC and SC
Children 12-17 severe/profound	L[2,8] M[1,8] U[1]	L[9] M[9] U[9]	L[2,7] M[2,7,8] U[7,8]	Sum of previous 3 columns	L[2,4,5] M[4,5] U[2,4]	L[4] M[2,4,9] U[2]	L[4] M[4,9] U[4]	L[2,6] M[2,4,6] U[4,6]	L[2,6] M[2,6] U[6]	L[2,9] M[2,4,9] U[4,9]	Sum of previous **6** columns	Sum of total HC and SC
Young adult 18-29 mild	L[2] M[1,2,4] U[4]	L[2] M[3,10] U[11]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[4] M[5,12] U[2,5]	L[6] M[2,4,6] U[2]	L[2,4] M[2,4,13] U[4,13]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[6] U[3,6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Young adult 18-29 moderate	L[2] M[1,2,4] U[4]	L[2] M[3,10] U[11]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[4] M[5,12] U[2,5]	L[6] M[2,4,6] U[2]	L[2,4] M[2,4,13] U[4,13]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[3,6] U[6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC

	Healthcare Costs				**Social Costs**							**Total Costs**
Age/Severity Group	**Hospital Services Costs**	**Community Services Costs**	**Treatment/ Aids/ Adaptations Costs**	**Total Healthcare Costs**	**Accomm-odation Costs**	**Education Costs**	**Daytime Activities Costs**	**Income Support**	**Carer Costs**	**Loss of Productivity**	**Total Social Costs**	**(Healthcare and Social Costs)**
Young adult 18-29 severe/profound	L[2] M[1,2,4] U[4]	L[7,14] M[7,14,15] U[7,15]	L[2,7] M[2,7] U[2,7]	Sum of previous 3 columns	L[4] M[2,5] U[5,12]	L[6] M[2,4,6] U[2]	L[2,4] M[2,4,13] U[4,13]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[3,6] U[6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Adult 30-59 mild	L[2] M[1,2,4] U[4]	L[2] M[3,10] U[11]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[10,16] M[10,16,17] U[2,5]	L[a] M[a] U[a]	L[10] M[10,11,17] U[3]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[6] U[3,6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Adult 30-59 moderate	L[2] M[1,2,4] U[4]	L[2] M[3,10] U[11]	L[2,3] M[2,3] U[2,3]	Sum of previous 3 columns	L[10,16] M[10,16,17] U[2,5]	L[a] M[a] U[a]	L[10] M[10,11,17] U[3]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[3,6] U[6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Adult 30-59 severe/profound	L[2] M[1,2,4] U[4]	L[7,14] M[7,14,15] U[7,15]	L[2,7] M[2,7] U[2,7]	Sum of previous 3 columns	L[14] M[7,16,17] U[2,5]	L[a] M[a] U[a]	L[17] M[7,14] U[7]	L[6] M[2,4,6] U[2,4,6]	L[3,6] M[3,6] U[6]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Elderly adult >60 mild	L[18] M[18] U[18]	L[18] M[18] U[18]	L[3,18] M[3,18] U[3,18]	Sum of previous 3 columns	L[10,16] M[10,16,17] U[2,5]	L[a] M[a] U[a]	L[18] M[18] U[18]	L[6] M[2,4,6] U[2,4,6]	L[3,6,18] M[6,18] U[3,6,18]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Elderly adult >60 moderate	L[18] M[18] U[18]	L[18] M[18] U[18]	L[3,18] M[3,18] U[3,18]	Sum of previous 3 columns	L[10,16] M[10,16,17] U[2,5]	L[a] M[a] U[a]	L[18] M[18] U[18]	L[6] M[2,4,6] U[2,4,6]	L[3,6,18] M[3,6,18] U[6,18]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC
Elderly adult >60 severe/profound	L[18] M[18] U[18]	L[18] M[18] U[18]	L[7,18] M[7,18] U[7,18]	Sum of previous 3 columns	L[14] M[7,16,17] U[2,5]	L[a] M[a] U[a]	L[18] M[18] U[18]	L[6] M[2,4,6] U[2,4,6]	L[3,6,18] M[3,6,18] U[6,18]	L[4] M[2,4] U[4]	Sum of previous **6** columns	Sum of total HC and SC

Health costs (HC); Lower boundary (L); Middle boundary (M); Not applicable (NA); Social costs (SC); Upper boundary (U)

References 2, 4, and 6 have been bolded to highlight where costs estimates have been specifically reported to be in excess (i.e. related to only the costs associated with disability).

Note reference 5 is the source used to adjust costs based on the proportion of individuals reported to receive those services and is not a source of cost data.

[a]Assume $0 cost as any education for (elderly) adults would be provided through daytime activities

Doble B, *et al. J Med Genet* 2020; 57:479–486. doi: 10.1136/jmedgenet-2019-106445

Table S3. References for cost analysis in Table 2

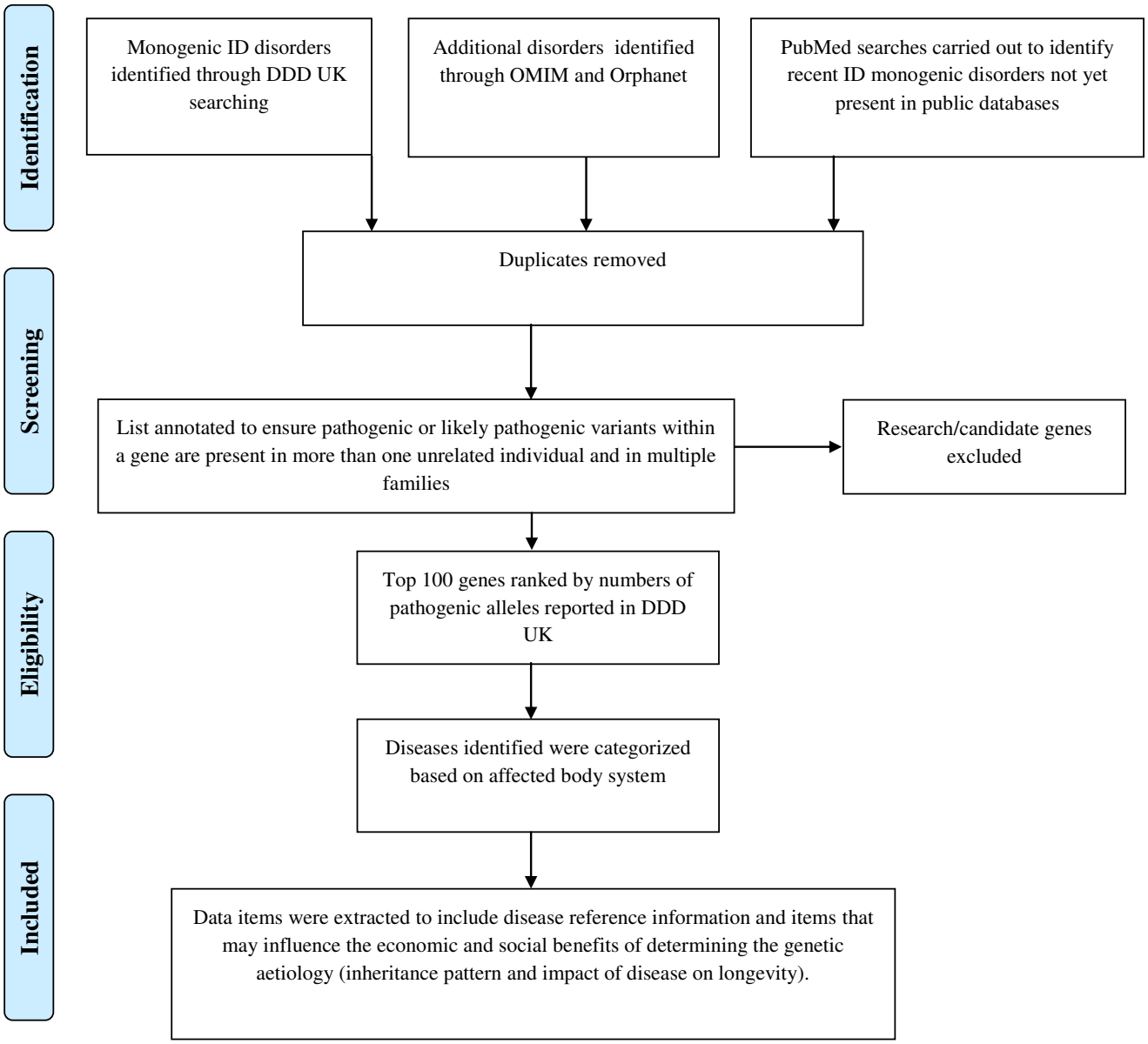
	Healthcare Costs				Social Costs							Total Costs
Age/Severity Group	**Hospital Services Costs**	**Community Services Costs**	**Treatment/ Aids/ Adaptations Costs**	**Total Healthcare Costs**	**Accomm-odation Costs**	**Education Costs**	**Daytime Activities Costs**	**Income Support**	**Carer Costs**	**Loss of Productivity**	**Total Social Costs**	**(Healthcare and Social Costs)**
Children 0-17 severe at home	L[19] M[20] U[19]	L[19] M[19] U[19]	L[19] M[19,20] U[19]	Sum of previous 3 columns	L[a] M[a] U[a]	L[19] M[19] U[19]	L[a] M[a] U[a]	L[21] M[21] U[21]	L[19,21] M[19,21] U[19,21]	L[21] M[21] U[21]	Sum of previous 6 columns	Sum of total HC and SC
Children 0-17 severe in hospital	L[19] M[19] U[19]	L[19] M[19] U[19]	L[19] M[19] U[19]	Sum of previous 3 columns	L[a] M[a] U[a]	L[19] M[19] U[19]	L[a] M[a] U[a]	L[21] M[21] U[21]	L[19,21] M[19,21] U[19,21]	L[21] M[21] U[21]	Sum of previous 6 columns	Sum of total HC and SC
Young adults 18-29 employed	L[22] M[22] U[22]	L[22] M[23] U[23]	L[24,25] M[24-26] U[24,25]	Sum of previous 3 columns	L[22] M[22] U[22,25]	L[a] M[a] U[a]	L[a] M[22] U[22]	L[22,27] M[22,27] U[22,27]	L[a] M[24] U[24,25]	L[27] M[27] U[27]	Sum of previous 6 columns	Sum of total HC and SC
Young adults 18-29 unemployed	L[22] M[22] U[22]	L[22] M[23] U[23]	L[24,25] M[24-26] U[24,25]	Sum of previous 3 columns	L[22] M[22] U[22,25]	L[a] M[22] U[22]	L[22] M[22] U[22]	L[27] M[27] U[27]	L[a] M[24] U[24,25]	L[27] M[21,27] U[21,27]	Sum of previous 6 columns	Sum of total HC and SC
Adults 30-60 employed	L[26] M[26] U[26]	L[a] M[25] U[24]	L[24,25] M[24-26] U[24,25]	Sum of previous 3 columns	L[22] M[22] U[22,25]	L[a] M[a] U[a]	L[a] M[22] U[22]	L[22,27] M[22,27] U[22,27]	L[a] M[24] U[24,25]	L[27] M[27] U[27]	Sum of previous 6 columns	Sum of total HC and SC
Adults 30-60 unemployed	L[26] M[26] U[26]	L[a] M[25] U[24]	L[24,25] M[24-26] U[24,25]	Sum of previous 3 columns	L[22] M[22] U[22,25]	L[a] M[a] U[a]	L[22] M[22] U[22]	L[27] M[27] U[27]	L[a] M[24] U[24,25]	L[27] M[21,27] U[21,27]	Sum of previous 6 columns	Sum of total HC and SC

Health costs (HC); Lower boundary (L); Middle boundary (M); Social costs (SC); Upper boundary (U)

References 19, 20, 22, and 24 have been bolded to highlight where costs estimates have been specifically reported to be in excess (i.e. related to only the costs associated with disability)

[a]Assume $0 costs

Figure S1. PRISMA flow diagram illustrating how a list of monogenic diseases associated with intellectual disability (ID) was ascertained



REFERENCES

1. Sacco P, Capkun-Niggli G, Zhang X, Jose R. The economic burden of fragile x syndrome: healthcare resource utilization in the United States. *American health & drug benefits.* 2013;6(2):73-83.
2. Knapp M, Romeo R, Beecham J. Economic cost of autism in the UK. *Autism : the international journal of research and practice.* 2009;13(3):317-336.
3. Romeo R, Knapp M, Morrison J, et al. Cost estimation of a health-check intervention for adults with intellectual disabilities in the UK. *Journal of intellectual disability research : JIDR.* 2009;53(5):426-439.
4. Buescher AV, Cidav Z, Knapp M, Mandell DS. Costs of autism spectrum disorders in the United Kingdom and the United States. *JAMA pediatrics.* 2014;168(8):721-728.
5. Australian Institute of Health and Welfare. *Disability support services: services provided under the National Disability Agreement. Bulletin no. 122. Cat. no. AUS 182.* Canberra: AIHW; 2014.
6. Doran CM, Einfeld SL, Madden RH, et al. How much does intellectual disability really cost? First estimates for Australia. *Journal of Intellectual & Developmental Disability.* 2012;37(1):42-49.
7. Emerson E, Robertson J, Gregory N, et al. The quality and costs of community-based residential supports and residential campuses for people with severe and complex disabilities. *Journal of Intellectual & Developmental Disability.* 2000;25(4):263-279.
8. Flanders SC, Engelhart L, Pandina GJ, McCracken JT. Direct health care costs for children with pervasive developmental disorders: 1996-2002. *Administration and policy in mental health.* 2007;34(3):213-220.
9. Barron DA, Molosankwe I, Romeo R, Hassiotis A. Urban adolescents with intellectual disability and challenging behaviour: costs and characteristics during transition to adult services. *Health & social care in the community.* 2013;21(3):283-292.
10. Felce D, Perry J, Romeo R, et al. Outcomes and costs of community living: semi-independent living and fully staffed group homes. *American journal of mental retardation : AJMR.* 2008;113(2):87-101.
11. Robertson J, Emerson E, Hatton C, et al. Longitudinal analysis of the impact and cost of person-centered planning for people with intellectual disabilities in England. *American journal of mental retardation : AJMR.* 2006;111(6):400-416.
12. McGill P, Poynter J. High cost residential placements for adults with intellectual disabilities. *Journal of applied research in intellectual disabilities : JARID.* 2012;25(6):584-587.
13. Kang T, Harrington C. Variation in types of service use and expenditures for individuals with developmental disabilities. *Disability and health journal.* 2008;1(1):30-41.
14. Knapp M, Comas-Herrera A, Astin J, Beecham J, Pendaries C. Intellectual disability, challenging behaviour and cost in care accommodation: what are the links? *Health & social care in the community.* 2005;13(4):297-306.
15. Felce D, Lowe K, Perry J, et al. Service support to people in Wales with severe intellectual disability and the most severe challenging behaviours: processes, outcomes and costs. *Journal of intellectual disability research : JIDR.* 1998;42 (Pt 5):390-408.

16. Stancliffe RJ, Keane S. Outcomes and costs of community living: A matched comparison of group homes and semi-independent living. *Journal of Intellectual and Developmental Disability.* 2000;25(4):281-305.
17. Hallam A, Knapp M, Jarbrink K, et al. Costs of village community, residential campus and dispersed housing provision for people with intellectual disability. *Journal of intellectual disability research : JIDR.* 2002;46(Pt 5):394-404.
18. Strydom A, Romeo R, Perez-Achiaga N, et al. Service use and cost of mental disorder in older adults with intellectual disability. *The British journal of psychiatry : the journal of mental science.* 2010;196(2):133-138.
19. Noyes J, Godfrey C, Beecham J. Resource use and service costs for ventilator-dependent children and young people in the UK. *Health & social care in the community.* 2006;14(6):508-522.
20. Kancherla V, Amendah DD, Grosse SD, Yeargin-Allsopp M, Van Naarden Braun K. Medical expenditures attributable to cerebral palsy and intellectual disability among Medicaid-enrolled children. *Research in Developmental Disabilities.* 2012;33(3):832-840.
21. Revill P, Ryan P, McNamara A, Normand C. A cost and outcomes analysis of alternative models of care for young children with severe disabilities in Ireland. *ALTER - European Journal of Disability Research / Revue Européenne de Recherche sur le Handicap.* 2013;7(4):260-274.
22. Beecham J, O'Neill T, Goodman R. Supporting young adults with hemiplegia: services and costs. *Health & social care in the community.* 2001;9(1):51-59.
23. Bent N, Tennant A, Swift T, Posnett J, Scuffham P, Chamberlain MA. Team approach versus ad hoc health services for young people with physical disabilities: a retrospective cohort study. *Lancet.* 2002;360(9342):1280-1286.
24. Walsh J CP. *Cost of Disability Survey Stages 2 and 3 – Demonstration of Relationship: Severity of Disability vs Cost.* Canberra, ACT: Department of Family and Community Services, AGPS; 1999.
25. Hughes D PF. *A Survey of the Unavoidable Cost of Disability Among 200 People with Quadriplegia.* Sydney: The Australian Quadriplegic Association; 1999.
26. Pumkam C, Probst JC, Bennett KJ, Hardin J, Xirasagar S. Health care expenditures among working-age adults with physical disabilities: variations by disability spans. *Disability and health journal.* 2013;6(4):287-296.
27. Knapp M, Perkins M, Beecham J, Dhanasiri S, Rustin C. Transition pathways for young people with complex disabilities: exploring the economic consequences. *Child: Care, Health and Development.* 2008;34(4):512-520.