Table S1. The complete list for diseases screened in the study

Diseases	**Phenotype MIM number**	**Inheritance**	**Gene**
Parietal foramina 2	609597	AD	ALX4
Parietal foramina 1	168500	AD	MSX2
Parietal foramina with cleidocranial dysplasia	168550	AD	MSX2
Craniosynostosis 2	604757	AD	MSX2
Cardiofaciocutaneous syndrome 1	115150	AD	BRAF
LEOPARD syndrome 3	613707	AD	BRAF
Noonan syndrome 7	613706	AD	BRAF
Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia	613563	AD	CBL
Costello syndrome/Congenital myopathy with excess of muscle spindles	218040	AD	HRAS
Cardiofaciocutaneous syndrome 2	615278	AD	KRAS
Noonan syndrome 3	609942	AD	KRAS
RAS-associated autoimmune leukoproliferative disorder	614470	AD	KRAS
cardiofaciocutaneous syndrome 3	615279	AD	MAP2K1
cardiofaciocutaneous syndrome 4	615280	AD	MAP2K2
Noonan syndrome 6	613224	AD	NRAS
LEOPARD syndrome 1	151100	AD	PTPN11
Metachondromatosis	156250	AD	PTPN11
Noonan syndrome 1	163950	AD	PTPN11
Cardiomyopathy, dilated, 1NN	615916	AD	RAF1
Noonan syndrome 5	611553	AD	RAF1
Noonan syndrome 8	615355	AD	RIT1
Noonan syndrome-like with loose anagen hair 1	607721	AD	SHOC2
Noonan syndrome4	610733	AD	SOS1
Noonan syndrome 9	616559	AD	SOS2
Epileptic encephalopathy, early infantile, 2	300672	XLD	CDKL5
CHARGE syndrome	214800	AD	CHD7
Hypogonadotropic hypogonadism 5 with or without anosmia	612370	AD	CHD7
Metaphyseal chondrodysplasia, Schmid type	156500	AD	COL10A1
Marshall syndrome	154780	AD	COL11A1
Stickler syndrome, type II	604841	AD	COL11A1
Achondrogenesis, type II or hypochondrogenesis	200610	AD	COL2A1
Avascular necrosis of the femoral head	608805	AD	COL2A1
Czech dysplasia	609162	AD	COL2A1
Kniest dysplasia	156550	AD	COL2A1
Legg-Calve-Perthes disease	150600	AD	COL2A1
Osteoarthritis with mild chondrodysplasia	604864	AD	COL2A1
Platyspondylic skeletal dysplasia, Torrance type	151210	AD	COL2A1
SED congenita	183900	AD	COL2A1

SMED Strudwick type	184250	AD	COL2A1
Spondyloepiphyseal dysplasia, Stanescu type	616583	AD	COL2A1
Spondyloperipheral dysplasia	271700	AD	COL2A1
Stickler sydrome, type I, nonsyndromic ocular	609508	AD	COL2A1
Stickler syndrome, type I	108300	AD	COL2A1
Caffey disease	114000	AD	COL1A1
Ehlers-Danlos syndrome, arthrochalasia type, 1	130060	AD	COL1A1
Osteogenesis imperfecta, type I	166200	AD	COL1A1
Osteogenesis imperfecta, type II	166210	AD	COL1A1;COL1A2
Osteogenesis imperfecta, type III	259420	AD	COL1A1;COL1A2
Osteogenesis imperfecta, type IV	166220	AD	COL1A1;COL1A2
Ehlers-Danlos syndrome, arthrochalasia type, 2	617821	AD	COL1A2
Chondrodysplasia punctata, X-linked dominant	302960	XLD	EBP
Capillary malformation-arteriovenous malformation 2	618196	AD	EPHB4
Lymphatic malformation 7	617300	AD	EPHB4
Craniosynostosis 4	600775	AD	ERF
Chitayat syndrome	617180	AD	ERF
Acromicric dysplasia	102370	AD	FBN1
Ectopia lentis, familial	129600	AD	FBN1
Geleophysic dysplasia 2	614185	AD	FBN1
Marfan lipodystrophy syndrome	616914	AD	FBN1
Marfan syndrome	154700	AD	FBN1
MASS syndrome	604308	AD	FBN1
Stiff skin syndrome	184900	AD	FBN1
Weill-Marchesani syndrome 2, dominant	608328	AD	FBN1
Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis	207410	AD	FGFR2
Apert syndrome	101200	AD	FGFR2
Beare-Stevenson cutis gyrata syndrome	123790	AD	FGFR2
Bent bone dysplasia syndrome	614592	AD	FGFR2
Crouzon syndrome	123500	AD	FGFR2
Jackson-Weiss syndrome	123150	AD	FGFR2;FGFR1
LADD syndrome	149730	AD	FGFR2;FGFR3
Pfeiffer syndrome/Craniofacial-skeletal-dermatologic dysplasia	101600	AD	FGFR2;FGFR1
Saethre-Chotzen syndrome/Saethre-Chotzen syndrome with or without eyelid anomalies	101400	AD	FGFR2
achondroplasia	100800	AD	FGFR3
Crouzon syndrome with acanthosis nigricans	612247	AD	FGFR3
hypochondroplasia	146000	AD	FGFR3
Muenke syndrome	602849	AD	FGFR3
SADDAN	616482	AD	FGFR3
thanatophoric dysplasia type I	187600	AD	FGFR3
thanatophoric dysplasia type II	187601	AD	FGFR3

Atelosteogenesis, type I	108720	AD	FLNB
Atelosteogenesis, type III	108721	AD	FLNB
Boomerang dysplasia	112310	AD	FLNB
Larsen syndrome	150250	AD	FLNB
Cornelia de Lange syndrome 1	122470	AD	NIPBL
Cornelia de Lange syndrome 2	300590	XLD	SMC1A
Cornelia de Lange syndrome 3	610759	AD	SMC3
Cornelia de Lange syndrome 4	614701	AD	RAD21
Cornelia de Lange syndrome 5	300882	XLD	HDAC8
Au-Kline syndrome	616580	AD	HNRNPK
Osteogenesis imperfecta, type V	610967	AD	IFITM5
Genitopatellar syndrome	606170	AD	KAT6B
SBBYSS syndrome	603736	AD	KAT6B
Kabuki syndrome 1	147920	AD	KMT2D
Pelger-Huet anomaly	169400	AD	LBR
Cardiomyopathy, dilated, 1A	115200	AD	LMNA
Emery-Dreifuss muscular dystrophy 2, autosomal dominant	181350	AD	LMNA
Heart-hand syndrome, Slovenian type	610140	AD	LMNA
Lipodystrophy, familial partial, type 2	151660	AD	LMNA
Malouf syndrome	212112	AD	LMNA
Muscular dystrophy, congenital	613205	AD	LMNA
Rett syndrome	312750	XLD	MECP2
Neurofibromatosis-Noonan syndrome	601321	AD	NF1
Neurofibromatosis, familial spinal	162210	AD	NF1
Neurofibromatosis, type 1	162200	AD	NF1
Watson syndrome	193520	AD	NF1
Neurofibromatosis, type 2	101000	AD	NF2
Sotos syndrome 1	117550	AD	NSD1
CHILD syndrome	308050	XLD	NSDHL
Polycystic kidney disease 1	173900	AD	PKD1
Polycystic kidney disease 2	613095	AD	PKD2
Acrodysostosis 1, with or without hormone resistance	101800	AD	PRKAR1A
Carney complex, type 1	160980	AD	PRKAR1A
Myxoma, intracardiac	255960	AD	PRKAR1A
Pigmented nodular adrenocortical disease, primary, 1	610489	AD	PRKAR1A
Failure of tooth eruption, primary	125350	AD	PTH1R
Metaphyseal chondrodysplasia, Murk Jansen type	156400	AD	PTH1R
Neurodevelopmental disorder with or without anomalies of the brain, eye, or heart	616975	AD	RERE
Cleidocranial dysplasia	119600	AD	RUNX2
Metaphyseal dysplasia with maxillary hypoplasia with or without brachydactyly	156510	AD	RUNX2
King-Denborough syndrome	145600	AD	RYR1

Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome	175050	AD	SMAD4
Myhre syndrome	139210	AD	SMAD4
Polyposis, juvenile intestinal	174900	AD	SMAD4
Aortic valve disease 2	614823	AD	SMAD6
Cerebrocostomandibular syndrome	117650	AD	SNRPB
Hyper-IgE recurrent infection syndrome	147060	AD	STAT3
Autoimmune disease, multisystem, infantile-onset, 1	615952	AD	STAT3
Cardiac, facial, and digital anomalies with developmental delay	618164	AD	TRAF7
Tuberous sclerosis-1	191100	AD	TSC1
Tuberous sclerosis-2	613254	AD	TSC2
Structural brain anomalies with impaired intellectual development and craniosynostosis	618736	AD	ZIC1
Acampomelic campomelic dysplasia/Campomelic dysplasia/Campomelic dysplasia with autosomal sex reversal	114290	AD	SOX9
Craniosynostosis 1	123100	AD	TWIST1
Robinow-Sorauf syndrome	180750	AD	TWIST1
Sweeney-Cox syndrome	617746	AD	TWIST1
Brachydactyly, type A1	112500	AD	IHH
Craniosynostosis 3	615314	AD	TCF12
Loeys-Dietz syndrome 1	609192	AD	TGFBR1
Loeys-Dietz syndrome 2	610168	AD	TGFBR2
Shprintzen-Goldberg syndrome	182212	AD	SKI
Greig cephalopolysyndactyly syndrome	175700	AD	GLI3
Pallister-Hall syndrome	146510	AD	GLI3
Polydactyly, postaxial, types A1 and B	174200	AD	GLI3
Polydactyly, preaxial, type IV	174700	AD	GLI3
C syndrome	211750	AD	CD96
Bohring-Opitz syndrome	605039	AD	ASXL1
Craniofrontonasal dysplasia	304110	XLD	EFNB1
Hartsfield syndrome	615465	AD	FGFR1
Hypogonadotropic hypogonadism 2 with or without anosmia	147950	AD	FGFR1
Osteoglophonic dysplasia	166250	AD	FGFR1
Trigonocephaly 1	190440	AD	FGFR1
Trigonocephaly 2	614485	AD	FREM1
Fontaine progeroid syndrome	612289	AD	SLC25A24
Hypertelorism, Teebi type	145420	AD	SPECC1L
Opitz GBBB syndrome, type II	145410	AD	SPECC1L

Table S2. The comparison of current and previous clinical studies for non-invasive prenatal screening

Study	PMID	Target diseases	Population studied	Nature of study	Screening method	Sample size	Positive cases	Reference method	Pregnancy outcome follow-up
Norton ME, et al. Am J Obstet Gynecol. 2012	22742782	T21, T18	high risk	multicenter, prospective, observational	chromosome selective sequencing	4,002	119	karyotype, FISH, qPCR	not performed
Nicolaides KH, et al. Am J Obstet Gynecol. 2012	23107079	T21, T18	average risk	single center, retrospective	chromosome selective sequencing	2,049	11	karyotype	newborn examination
Bianchi DW, et al. N Engl J Med. 2014	25099587	T21, T18, T13	average risk	multicenter, prospective, observational	low-depth WGS	1,914	8	karyotype	newborn examination
Norton ME, et al. N Engl J Med. 2015	25830321	T21, T18, T13	average risk	multicenter, prospective, observational	targeted sequencing	18,955	31	karyotype, CMA	newborn examination
Current study		7 aneuploidies, 9 MMS, 155 monogenic diseases	high risk	multicenter, prospective, observational	targeted sequencing	>1000	>50	karyotype, CMA, CNV-seq, Sanger	newborn examination