

**Appendix 3 Excluded studies and studies with high risk of bias /Bilaga 3 Exkluderade studier  
 och studier av låg kvalitet**

Excluded studies, page 1–24

Systematic reviews page 24–26

Studies with high risk of bias, page 26–30

<b>Excluded studies</b>	
The Observatory. Genetic Testing. MLO: Medical Laboratory Observer, 2013; 45 (1): 6-6.	Not relevant study design: comment
Agatisa PK, Mercer MB, Leek AC, Smith MB, Philipson E, Farrell RM. A first look at women's perspectives on noninvasive prenatal testing to detect sex chromosome aneuploidies and microdeletion syndromes. Prenat Diagn, 2015; 35 (7): 692-8.	Not relevant PICO: intervention
Alesi V, Bertoli M, Sinibaldi L, Novelli A. The clinical utility and indications of chromosomal microarray analysis in prenatal diagnosis. Bjog, 2013; 120 (1): 119-20.	Not relevant study design: comment
Armengol L, Nevado J, Serra-Juhe C, Plaja A, Mediano C, Garcia-Santiago FA, et al. Clinical utility of chromosomal microarray analysis in invasive prenatal diagnosis. Hum Genet, 2012; 131 (3): 513-23.	Micrarray platform not specified
Avent ND. Refining noninvasive prenatal diagnosis with single-molecule next-generation sequencing. Clin Chem, 2012; 58 (4): 657-8.	Not relevant study design : editorial
Bao B, Wang Y, Hu H, Yao H, Li Y, Tang S, et al. Karyotypic and molecular genetic changes associated with fetal cardiovascular abnormalities: results of a retrospective 4-year ultrasonic diagnosis study. Int J Biol Sci, 2013; 9 (5): 463-71.	Not relevant PICO: Population less than 20 patients
Bayindir B, Dehaspe L, Brison N, Brady P, Ardui S, Kammoun M, et al. Noninvasive prenatal testing using a novel analysis pipeline to screen for all autosomal fetal aneuploidies improves pregnancy management. Eur J Hum Genet, 2015.	Targeted prenatal genetic testing for a specific aberration
Benachi A, Letourneau A, Kleinfinger P, Senat MV, Gautier E, Favre R, et al. Cell-free DNA analysis in maternal plasma in cases of fetal abnormalities detected on ultrasound examination. Obstet Gynecol, 2015; 125 (6): 1330-7.	Not relevant PICO: outcome
Bi W, Breman A, Shaw CA, Stankiewicz P, Gambin T, Lu X, et al. Detection of >/=1Mb microdeletions and microduplications in a single cell using custom oligonucleotide arrays. Prenatal Diagnosis 2012; 32 (1): 10-20.	Not relevant PICO: population
Bianchi DW, Platt LD, Goldberg JD, Abuhamad AZ, Sehnert AJ, Rava RP. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. Obstet Gynecol, 2012; 119 (5): 890-901.	Not relevant PICO: intervention

Bianchi DW, Prosen T, Platt LD, Goldberg JD, Abuhamad AZ, Rava RP, et al. Massively parallel sequencing of maternal plasma DNA in 113 cases of fetal nuchal cystic hygroma. <i>Obstet Gynecol</i> , 2013; 121 (5): 1057-62.	Not relevant PICO: intervention
Bianchi DW, Wilkins-Haug L. Integration of noninvasive DNA testing for aneuploidy into prenatal care: what has happened since the rubber met the road? <i>Clin Chem</i> , 2014; 60 (1): 78-87.	Not relevant study design
Bianchi DW, Parsa S, Bhatt S, Halks-Miller M, Kurtzman K, Sehnert AJ, et al. Fetal sex chromosome testing by maternal plasma DNA sequencing: clinical laboratory experience and biology. <i>Obstet Gynecol</i> , 2015; 125 (2): 375-82.	Not relevant PICO: intervention
Biesecker LG, Green RC. Diagnostic clinical genome and exome sequencing. <i>New England Journal of Medicine</i> , 2014; 370 (25): 2418-25.	Not relevant study design: comment
Blackburn HL, Schroeder B, Turner C, Shriver CD, Ellsworth DL, Ellsworth RE. Management of Incidental Findings in the Era of Next-generation Sequencing. <i>Curr Genomics</i> , 2015; 16 (3): 159-74.	Not relevant study design
Bouffard C, Viville S, Knoppers BM. Genetic diagnosis of embryos: clear explanation, not rhetoric, is needed. <i>CMAJ: Canadian Medical Association Journal</i> , 2009; 181 (6-7): 387-91.	Not relevant study design
Bovolenta M, Rimessi P, Dolcini B, Ravani A, Ferlini A, Gualandi F. Prenatal diagnosis of Duchenne muscular dystrophy by comparative genomic hybridization. <i>Clin Genet</i> , 2010; 77 (5): 503-6.	Not relevant study design case report
Brady PD, Devriendt K, Deprest J, Vermeesch JR. Array-based approaches in prenatal diagnosis. <i>Methods Mol Biol</i> 2012; 838:151-71.	Not relevant study design
Brady PD, Vermeesch JR. Genomic microarrays: a technology overview. <i>Prenat Diagn</i> , 2012; 32 (4): 336-43.	Not relevant study design
Burnell L, Verchere C, Pugash D, Loock C, Robertson S, Lehman A, et al. Additional post-natal diagnoses following antenatal diagnosis of isolated cleft lip +/- Palate. <i>Archives of Disease in Childhood: Fetal and Neonatal Edition</i> , 2014; 99 (4): F286-F90.	Not relevant PICO: intervention
Bustamante-Aragones A, Rodriguez de Alba M, Perlado S, Trujillo-Tiebas MJ, Arranz JP, Diaz-Recasens J, et al. Non-invasive prenatal diagnosis of single-gene disorders from maternal blood. <i>Gene</i> 2012; 504 (1): 144-9.	Not relevant study design
Callaway JL, Huang S, Karampetsou E, Crolla JA. Perspective on the technical challenges involved in the implementation of array-CGH in prenatal diagnostic testing. <i>Mol Biotechnol</i> 2014; 56 (4): 312-8.	Not relevant PICO: outcome

<p>Canton AP, Costa SS, Rodrigues TC, Bertola DR, Malaquias AC, Correa FA, et al. Genome-wide screening of copy number variants in children born small for gestational age reveals several candidate genes involved in growth pathways. <i>Eur J Endocrinol</i> 2014; 171 (2): 253-62.</p>	<p>Not relevant PICO: population</p>
<p>Carss KJ, Hillman SC, Parthiban V, McMullan DJ, Maher ER, Kilby MD, et al. Exome sequencing improves genetic diagnosis of structural fetal abnormalities revealed by ultrasound. <i>Hum Mol Genet</i>, 2014; 23 (12): 3269-77.</p>	<p>Not relevant PICO: intervention</p>
<p>Cavalli P, Cavallari U, Novelli A. Array CGH in routine prenatal diagnosis practice. <i>Prenat Diagn</i> 2012; 32 (7): 708-9; author reply 11-2.</p>	<p>Not relevant study design letter</p>
<p>Chan K, Yam I, Leung KY, Tang M, Chan TK, Chan V. Detection of paternal alleles in maternal plasma for non-invasive prenatal diagnosis of beta-thalassemia: a feasibility study in southern Chinese. <i>Eur J Obstet Gynecol Reprod Biol</i>, 2010; 150 (1): 28-33.</p>	<p>Targeted prenatal genetic testing for a specific aberration</p>
<p>Char D. Preventive Genomic Sequencing and Care of the Individual Patient. <i>American Journal of Bioethics</i>, 2015; 15 (7): 32-3.</p>	<p>Not relevant study design</p>
<p>Chen CP, Chang SD, Chueh HY, Su YN, Su JW, Chern SR, et al. Rapid positive confirmation of trisomy 21 mosaicism at amniocentesis by interphase FISH, QF-PCR and aCGH on uncultured amniocytes. <i>Taiwan J Obstet Gynecol</i>, 2012; 51 (3): 475-80.</p>	<p>Not relevant study design case study</p>
<p>Chen CP, Su YN, Chern SR, Chen YT, Su JW, Pan CW, et al. Prenatal diagnosis of trisomy 8 mosaicism. <i>Taiwan J Obstet Gynecol</i>, 2012; 51 (4): 666-8.</p>	<p>Not relevant study design: case report</p>
<p>Chen CP, Su YN, Chern SR, Tsai FJ, Hsu CY, Lee CC, et al. Prenatal diagnosis of a 4.9-Mb deletion of 10q11.21 --&gt; q11.23 by array comparative genomic hybridization. <i>Taiwan J Obstet Gynecol</i>, 2010; 49 (1): 117-9.</p>	<p>Not relevant study design: case study</p>
<p>Chen CP, Su YN, Chern SR, Wu PS, Su JW, Town DD, et al. Prenatal diagnosis of an interstitial deletion of 10q (10q11.21 -&gt; q21.1): array comparative genomic hybridization characterization and literature review. <i>Taiwan J Obstet Gynecol</i>, 2012; 51 (4): 672-6.</p>	<p>Not relevant study design: case report</p>
<p>Chen CP, Su YN, Hsu CY, Tsai FJ, Chien SC, Chern SR, et al. Abnormally flat facial profile on two- and three-dimensional ultrasound and array comparative genomic hybridization for the diagnosis of Pallister-Killian syndrome. <i>Taiwan J Obstet Gynecol</i>, 2010; 49 (1): 124-8.</p>	<p>Not relevant study design: case study</p>

Chen CP,Su YN,Tsai FJ,Chern SR,Hsu CY,Huang MC, et al. Rapid genome-wide aneuploidy diagnosis using uncultured amniocytes and array comparative genomic hybridization in pregnancy with abnormal ultrasound findings detected in late second and third trimesters. <i>Taiwan J Obstet Gynecol</i> , 2010; 49 (1): 120-3.	Not relevant study design: case study
Chen CP,Wu PC,Lin CJ,Su YN,Chern SR,Tsai FJ, et al. Balanced reciprocal translocations detected at amniocentesis. <i>Taiwan J Obstet Gynecol</i> , 2010; 49 (4): 455-67.	Not relevant PICO: intervention
Chen M,Yang YS,Shih JC,Lin WH,Lee DJ,Lin YS, et al. Microdeletions/duplications involving TBX1 gene in fetuses with conotruncal heart defects which are negative for 22q11.2 deletion on fluorescence in-situ hybridization. <i>Ultrasound Obstet Gynecol</i> 2014; 43 (4): 396-403.	Not relevant PICO: population less than 20 patients
Chen S,Ge H,Wang X,Pan X,Yao X,Li X, et al. Haplotype-assisted accurate non-invasive fetal whole genome recovery through maternal plasma sequencing. <i>Genome Med</i> , 2013; 5 (2): 18.	Not relevant study design: case study
Chen S,Lau TK,Zhang C,Xu C,Xu Z,Hu P, et al. A method for noninvasive detection of fetal large deletions/duplications by low coverage massively parallel sequencing. <i>Prenat Diagn</i> , 2013; 33 (6): 584-90.	Not relevant PICO: intervention
Chen X,Zhao KX, Zhao C. [The development and importance of molecular diagnosis in hereditary retinal diseases]. <i>Zhonghua Yan Ke Za Zhi</i> 2013; 49 (6): 484-7.	Language
Chitty LS,Mason S,Barrett AN,McKay F,Lench N,Daley R, et al. Non-invasive prenatal diagnosis of achondroplasia and thanatophoric dysplasia: next generation sequencing allows for a safer, more accurate and comprehensive approach. <i>Prenat Diagn</i> , 2015.	Targeted prenatal genetic testing for a specific aberration
Chiu RW,Chan KC,Gao Y,Lau VY,Zheng W,Leung TY, et al. Noninvasive prenatal diagnosis of fetal chromosomal aneuploidy by massively parallel genomic sequencing of DNA in maternal plasma. <i>Proc Natl Acad Sci U S A</i> , 2008; 105 (51): 20458-63.	Not relevant PICO: outcome
Choy KW,Kwok YK,Cheng YK,Wong KM,Wong HK,Leung KO, et al. Diagnostic accuracy of the BACs-on-Beads assay versus karyotyping for prenatal detection of chromosomal abnormalities: a retrospective consecutive case series. <i>Bjog</i> 2014; 121 (10): 1245-52.	Not relevant PICO: intervention
Choy KW,Tsang PT,Leung TY,Wang CC,Lau TK,Author A, et al. The application of microarray based comparative genomic	Not relevant study design

hybridization in prenatal diagnosis. <i>Fetal and Maternal Medicine Review</i> , 2008; 19 (2): 119-33.	
Cohen K, Tzika A, Wood H, Berri S, Roberts P, Mason G, et al. Diagnosis of fetal submicroscopic chromosomal abnormalities in failed array CGH samples: copy number by sequencing as an alternative to microarrays for invasive fetal testing. <i>Ultrasound Obstet Gynecol</i> , 2015; 45 (4): 394-401.	Not relevant PICO: Control
Comas C, Echevarria M, Rodriguez MA, Prats P, Rodriguez I, Serra B. Initial experience with non-invasive prenatal testing of cell-free DNA for major chromosomal anomalies in a clinical setting. <i>J Matern Fetal Neonatal Med</i> , 2015; 28 (10): 1196-201.	Not relevant PICO: intervention
Coppinger J, Alliman S, Lamb AN, Torchia BS, Bejjani BA, Shaffer LG. Whole-genome microarray analysis in prenatal specimens identifies clinically significant chromosome alterations without increase in results of unclear significance compared to targeted microarray. <i>Prenat Diagn</i> , 2009; 29 (12): 1156-66.	Data also part of a later publication
Coromilas A, Wynn J, Haverfield E, Chung WK. Nonspecific phenotype of Noonan syndrome diagnosed by whole exome sequencing. <i>Clin Case Rep</i> , 2015; 3 (4): 237-9.	Not relevant study design: case report
Costain G, McDonald-McGinn DM, Bassett AS. Prenatal genetic testing with chromosomal microarray analysis identifies major risk variants for schizophrenia and other later-onset disorders. <i>Am J Psychiatry</i> , 2013; 170 (12): 1498.	Not relevant study design
Dan S, Chen F, Choy KW, Jiang F, Lin J, Xuan Z, et al. Prenatal detection of aneuploidy and imbalanced chromosomal arrangements by massively parallel sequencing. <i>PLoS One</i> , 2012; 7 (2): e27835.	Not relevant PICO: intervention
D'Angelo G, Di Rienzo T, Ojetti V. Microarray analysis in gastric cancer: a review. <i>World J Gastroenterol</i> 2014; 20 (34): 11972-6.	Not relevant PICO: population
Dar Pe, Curnow KJ, Gross SJ, Hall MP, Stosic M, Demko Z, et al. Clinical experience and follow-up with large scale single-nucleotide polymorphism-based noninvasive prenatal aneuploidy testing. <i>American Journal of Obstetrics and Gynecology</i> , 2014; 211 (5): 527.e1-27.e17.	Not relevant PICO: intervention
Darilek S, Ward P, Pursley A, Plunkett K, Furman P, Magoulas P, et al. Pre- and postnatal genetic testing by array-comparative genomic hybridization: genetic counseling perspectives. <i>Genet Med</i> , 2008; 10 (1): 13-8.	Not relevant study design
Davies N. Prenatal screening with microarray technology. <i>MLO: Medical Laboratory Observer</i> , 2015; 47 (5): 8-12.	Not relevant study design

de Jong A,Dondorp WJ,Krumeich A,Boonekamp J,van Lith JM, de Wert GM. The scope of prenatal diagnosis for women at increased risk for aneuploidies: views and preferences of professionals and potential users. <i>J Community Genet</i> , 2013; 4 (1): 125-35.	Not relevant PICO: population
Deshpande M,Harper J,Holloway M,Palmer R, Wang R. Evaluation of array comparative genomic hybridization for genetic analysis of chorionic villus sampling from pregnancy loss in comparison to karyotyping and multiplex ligation-dependent probe amplification. <i>Genet Test Mol Biomarkers</i> , 2010; 14 (3): 421-4.	Not relevant PICO: population
Dickinson JE,Harcourt E, Murch A. The selective use of rapid aneuploidy screening in prenatal diagnosis. <i>Australian &amp; New Zealand Journal of Obstetrics &amp; Gynaecology</i> , 2009; 49 (1): 28-33.	Not relevant PICO: intervention
Dondorp WJ,Page-Christiaens GC, de Wert GM. Genomic futures of prenatal screening: ethical reflection. <i>Clin Genet</i> , 2015.	Not relevant study design
Donnelly JC,Wapner RJ,Simpson JL,Author A,Department o,Obstetrics, et al. Can microarray analysis reveal additional abnormalities in prenatal diagnosis? <i>Expert Review of Obstetrics and Gynecology</i> , 2013; 8 (3): 193-95.	Not relevant study design
Drury S,Williams H,Trump N,Boustred C,Lench N,Scott RH, et al. Exome sequencing for prenatal diagnosis of fetuses with sonographic abnormalities. <i>Prenat Diagn</i> , 2015.	Not relevant PICO: intervention
Dugo N,Padula F,Mobili L,Brizzi C,D'Emidio L,Cignini P, et al. Six consecutive false positive cases from cell-free fetal DNA testing in a single referring centre. <i>J Prenat Med</i> , 2014; 8 (1-2): 31-5.	Not relevant PICO: intervention
Dugoff L. Application of genomic technology in prenatal diagnosis. <i>N Engl J Med</i> 2012; 367 (23): 2249-51.	Not relevant study design : editorial
Duncan A, Langlois S. Use of array genomic hybridization technology in prenatal diagnosis in Canada. <i>J Obstet Gynaecol Can</i> , 2011; 33 (12): 1256-9.	Not relevant study design
Dupont C,Grati FR,Choy KW,Jaillard S,Toutain J,Maurin ML, et al. Prenatal diagnosis of 24 cases of microduplication 22q11.2: an investigation of phenotype-genotype correlations. <i>Prenat Diagn</i> 2014.	Not relevant PICO: Population less than 20 patients
Eng CM,Yang Y, Plon SE. Genetic diagnosis through whole-exome sequencing... <i>N Engl J Med</i> . 2014 Mar 13;370(11):1067–8; <i>N Engl J Med</i> . 2013 Oct 17;369(16):1502–11; <i>N Engl J Med</i> . 2014 Mar 13;370(11):1067. <i>New England Journal of Medicine</i> , 2014; 370 (11): 1068–68.	Not relevant study design: letter

<p>Faas BH, van der Burgt I, Kooper AJ, Pfundt R, Hehir-Kwa JY, Smits AP, et al. Identification of clinically significant, submicroscopic chromosome alterations and UPD in fetuses with ultrasound anomalies using genome-wide 250k SNP array analysis. <i>J Med Genet</i>, 2010; 47 (9): 586–94.</p>	<p>Not relevant PICO: population</p>
<p>Fan HC, Gu W, Wang J, Blumenfeld YJ, El-Sayed YY, Quake SR. Non-invasive prenatal measurement of the fetal genome. <i>Nature</i> 2012; 487 (7407): 320–4.</p>	<p>Not relevant PICO: intervention</p>
<p>Fan HC, Quake SR. Sensitivity of noninvasive prenatal detection of fetal aneuploidy from maternal plasma using shotgun sequencing is limited only by counting statistics. <i>PLoS One</i>, 2010; 5 (5): e10439.</p>	<p>Not relevant PICO: intervention</p>
<p>Faucett A, Savage M. Chromosomal microarray testing. <i>JAAPA: Journal of the American Academy of Physician Assistants</i> (Haymarket Media, Inc.), 2012; 25 (1): 65–66.</p>	<p>Not relevant study design</p>
<p>Filges I, Kang A, Hench J, Wenzel F, Bruder E, Miny P, et al. Fetal polydactyly: a study of 24 cases ascertained by prenatal sonography. <i>J Ultrasound Med</i>, 2011; 30 (7): 1021–9.</p>	<p>Not relevant study design : case series</p>
<p>Fiorentino F. Re: Use of prenatal chromosomal microarray: prospective cohort study and systematic review and meta-analysis. S. C. Hillman, D. J. McMullan, G. Hall, F. S. Togneri, N. James, E. J. Maher, C. H. Meller, D. Williams, R. J. Wapner, E. R. Maher and M. D. Kilby. <i>Ultrasound obstet gynecol</i> 2013; 41: 610–620. <i>Ultrasound Obstet Gynecol</i>, 2013; 41 (6): 608.</p>	<p>Not relevant study design: comment</p>
<p>Fiorentino F, Biricik A, Bono S, Spizzichino L, Cotroneo E, Cottone G, et al. Development and validation of a next-generation sequencing-based protocol for 24-chromosome aneuploidy screening of embryos. <i>Fertil Steril</i>, 2014; 101 (5): 1375–82.</p>	<p>Not relevant PICO: intervention</p>
<p>Fiorentino F, Caiazzo F, Napolitano S, Spizzichino L, Bono S, Sessa M, et al. Introducing array comparative genomic hybridization into routine prenatal diagnosis practice: a prospective study on over 1000 consecutive clinical cases. <i>Prenat Diagn</i>, 2011; 31 (13): 1270–82.</p>	<p>Data also part of a later publication</p>
<p>Fisher A, Bonner C, Biankin AV, Juraskova I. Factors influencing intention to undergo whole genome screening in future healthcare: A single-blind parallel-group randomised trial. <i>Preventive Medicine</i>, 2012; 55 (5): 514–20.</p>	<p>Not relevant study design</p>
<p>Foglieni B, Galbiati S, Ferrari M, Cremonesi L. A fast microelectronic array for screening and prenatal diagnosis of beta-thalassemia. <i>Methods Mol Biol</i>, 2008; 444:169–82.</p>	<p>Targeted prenatal genetic testing for a specific aberration</p>
<p>Futch T, Spinosa J, Bhatt S, de Feo E, Rava RP, Sehnert AJ. Initial clinical laboratory experience in noninvasive prenatal testing</p>	<p>Not relevant PICO: intervention</p>

for fetal aneuploidy from maternal plasma DNA samples. <i>Prenat Diagn</i> , 2013; 33 (6): 569–74.	
Galbiati S,Brisci A,Damin F,Gentilin B,Curcio C,Restagno G, et al. Fetal DNA in maternal plasma: a noninvasive tool for prenatal diagnosis of beta-thalassemia. <i>Expert Opin Biol Ther</i> 2012; 12 Suppl 1S181–7.	Not relevant PICO: intervention
Garcia-Herrero S,Campos-Galindo I,Martinez-Conejero JA,Serra V,Olmo I,Lara C, et al. BACs-on-Beads technology: a reliable test for rapid detection of aneuploidies and microdeletions in prenatal diagnosis. <i>Biomed Res Int</i> 2014; 2014590298.	Not relevant PICO: intervention
Gekas J,Sergi C, Kamnasaran D. Molecular prenatal diagnosis of a sporadic alobar holoprosencephalic fetus: genotype-phenotype correlations. <i>J Prenat Med</i> , 2012; 6 (3): 36–9.	Not relevant study design: case study
Gil MM,Quezada MS,Revello R,Akolekar R, Nicolaidides KH. Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis. <i>Ultrasound Obstet Gynecol</i> , 2015; 45 (3): 249–66.	Not relevant study design
Giorlandino C,Mesoraca A,Bizzoco D,Dello Russo C,Cima A,Di Giacomo G, et al. Introducing the next generation sequencing in genomic amnio and villous sampling. The so called "Next Generation Prenatal Diagnosis" (NGPD). <i>J Prenat Med</i> , 2014; 8 (1–2): 1–10.	Not relevant study design
Grati FR,Ferreira JC, Bajaj K. Noninvasive prenatal screening for fetal trisomies 21, 18, 13 and the common sex chromosome aneuploidies from maternal blood using massively parallel genomic sequencing of DNA. <i>Am J Obstet Gynecol</i> , 2014; 211 (6): 711–12.	Not relevant study design
Grati FR,Vialard F, Gross S. BACs-on-Beads (BoBs) assay for the genetic evaluation of prenatal samples and products of conception. <i>Methods Mol Biol</i> 2015; 1227259–78.	Not relevant PICO: intervention
Gruchy N,Lebrun M,Herlicoviez M,Alliet J,Gourdier D,Kottler ML, et al. Supernumerary marker chromosomes management in prenatal diagnosis. <i>Am J Med Genet A</i> , 2008; 146a (21): 2770–6.	Not relevant PICO: intervention
Gu H,Li H,Zhang L,Luan H,Huang T,Wang L, et al. Diagnostic role of microRNA expression profile in the serum of pregnant women with fetuses with neural tube defects. <i>J Neurochem</i> , 2012; 122 (3): 641–9.	Not relevant PICO: intervention



<p>Guerra C,Rendeiro P,Pereira E,Rosmaninho A,Nogueira R,Pereira S, et al. Microarray for skeletal dysplasias: thanatophoric dysplasia diagnosed in utero using microarray technology. <i>Ultrasound Obstet Gynecol</i>, 2013; 41 (1): 95–6.</p>	<p>Not relevant PICO: Population less than 20 patients</p>
<p>Guex N,Iseli C,Syngelaki A,Deluen C,Pescia G,Nicolaides KH, et al. A robust second-generation genome-wide test for fetal aneuploidy based on shotgun sequencing cell-free DNA in maternal blood. <i>Prenat Diagn</i>, 2013; 33 (7): 707–10.</p>	<p>Not relevant PICO: intervention</p>
<p>Hall GK,Mackie FL,Hamilton S,Evans A,McMullan DJ,Williams D, et al. Chromosomal microarray analysis allows prenatal detection of low level mosaic autosomal aneuploidy. <i>Prenat Diagn</i>, 2014; 34 (5): 505–7.</p>	<p>Not relevant PICO: Population less than 20 patients</p>
<p>Helgeson J,Wardrop J,Boomer T,Almasri E,Paxton WB,Saldivar JS, et al. Clinical outcome of subchromosomal events detected by whole-genome noninvasive prenatal testing. <i>Prenat Diagn</i>, 2015.</p>	<p>Not relevant PICO: intervention</p>
<p>Hill M,Twiss P,Verhoef TI,Drury S,McKay F,Mason S, et al. Non-invasive prenatal diagnosis for cystic fibrosis: detection of paternal mutations, exploration of patient preferences and cost analysis. <i>Prenat Diagn</i>, 2015.</p>	<p>Not relevant PICO: intervention</p>
<p>Hillman S,McMullan D,Maher E, Kilby M. Clinical utility of array comparative genomic hybridisation for prenatal diagnosis: a cohort study of 3171 pregnancies... <i>BJOG</i>. 2012 Apr;119(5):614–25. <i>BJOG: An International Journal of Obstetrics &amp; Gynaecology</i>, 2012; 119 (10): 1281–82.</p>	<p>Not relevant study design : editorial</p>
<p>Hillman SC,Barton PM,Roberts TE,Maher ER,McMullan DM, Kilby MD. BAC chromosomal microarray for prenatal detection of chromosome anomalies in fetal ultrasound anomalies: an economic evaluation. <i>Fetal Diagn Ther</i> 2014; 36 (1): 49–58.</p>	<p>Not relevant PICO: outcome</p>
<p>Hillman SC,McMullan DJ,Maher ER, Kilby MD. Clinical utility of array comparative genomic hybridisation for prenatal diagnosis: a cohort study of 3171 pregnancies. <i>Bjog</i>, 2012; 119 (10): 1281–2; author reply 82.</p>	<p>Not relevant study design: letter</p>
<p>Hillman SC,McMullan DJ,Maher ER, Kilby MD. Meeting the challenge of interpreting high-resolution single nucleotide polymorphism array data: does increased diagnostic power outweigh the dilemma of rare variants. <i>Bjog</i> 2013; 120 (10): 1296.</p>	<p>Not relevant study design</p>
<p>Hillman SC,McMullan DJ,Silcock L,Maher ER, Kilby MD. How does altering the resolution of chromosomal microarray analysis in the prenatal setting affect the rates of pathological and uncertain findings? <i>J Matern Fetal Neonatal Med</i>, 2014; 27 (7): 649–57.</p>	<p>Data also part of a later publication included in the systematic report</p>

Hillman SC, McMullan DJ, Williams D, Maher ER, Kilby MD. Microarray comparative genomic hybridization in prenatal diagnosis: a review. <i>Ultrasound Obstet Gynecol</i> 2012; 40 (4): 385–91.	Not relevant study design
Holm S, Ploug T. Patient Choice and Preventive Genomic Sequencing—More Trouble Upstream. <i>American Journal of Bioethics</i> , 2015; 15 (7): 24–6.	Not relevant study design
Hooks J, Wolfberg AJ, Wang ET, Struble CA, Zahn J, Juneau K, et al. Non-invasive risk assessment of fetal sex chromosome aneuploidy through directed analysis and incorporation of fetal fraction. <i>Prenat Diagn</i> , 2014; 34 (5): 496–9.	Not relevant PICO: intervention
Hua R, Barrett AN, Tan TZ, Huang Z, Mahyuddin AP, Ponnusamy S, et al. Detection of aneuploidy from single fetal nucleated red blood cells using whole genome sequencing. <i>Prenat Diagn</i> , 2014.	Not relevant PICO: intervention
Hui L. Re: Non-invasive prenatal testing for fetal chromosomal abnormalities by low-coverage whole-genome sequencing of maternal plasma DNA: review of 1982 consecutive cases in a single center. T. K. Lau, S. W. Cheung, P. S. S. Lo, A. N. Pursley, M. K. Chan, F. Jiang, H. Zhang, W. Wang, L. F. J. Jong, O. K. C. Yuen, H. Y. C. Chan, W. S. K. Chan and K. W. Choy. <i>Ultrasound Obstet Gynecol</i> 2014; 43: 254–264. <i>Ultrasound Obstet Gynecol</i> , 2014; 43 (3): 245.	Not relevant study design
Jacob HJ. Next-generation sequencing for clinical diagnostics. <i>New England Journal of Medicine</i> , 2013; 369 (16): 1557–58.	Not relevant study design: comment
Jacob HJ. Genetic diagnosis through whole-exome sequencing... <i>N Engl J Med</i> . 2013 Oct 17; 369(16):1557–8; <i>N Engl J Med</i> . 2014 Mar 13; 370(11):1068. <i>New England Journal of Medicine</i> , 2014; 370 (11): 1069–69.	Not relevant study design: comment
Jensen TJ, Kim SK, van den Boom D, Deciu C, Ehrich M. Noninvasive detection of a balanced fetal translocation from maternal plasma. <i>Clin Chem</i> , 2014; 60 (10): 1298–305.	Not relevant study design: case study
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Maarse W,Rozendaal AM,Pajkrt E,Vermeij-Keers C,Mink van der Molen AB, van den Boogaard MJ. A systematic review of associated structural and chromosomal defects in oral clefts: when is prenatal genetic analysis indicated? <i>J Med Genet</i> , 2012; 49 (8): 490–8.	Not relevant PICO: population
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Macera MJ,Sobrinho A,Levy B,Jobanputra V,Aggarwal V,Mills A, et al. Prenatal diagnosis of chromothripsis, with nine breaks characterized by karyotyping, FISH, microarray and whole-genome sequencing. <i>Prenat Diagn</i> , 2015; 35 (3): 299–301.	Not relevant study design: case report
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Meng M, Huo R, Han MY, Chi FL, Dai P, He L, et al. Detection of common deafness mutation by maternal plasma cell-free DNA. <i>Eur Rev Med Pharmacol Sci</i> 2014; 18 (10): 1544–8.	Targeted prenatal genetic testing for a specific aberration
Mennuti MT, Chandrasekaran S, Khalek N, Dugoff L. Cell-free DNA Screening and Sex Chromosome Abnormalities. <i>Prenat Diagn</i> , 2015.	Not relevant study design
Mercier S, Dubourg C, Belleguic M, Pasquier L, Loget P, Lucas J, et al. Genetic counseling and "molecular" prenatal diagnosis of holoprosencephaly (HPE). <i>Am J Med Genet C Semin Med Genet</i> , 2010; 154c (1): 191–6.	Not relevant PICO: Intervention, I - Karyotype compared to MRI
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<p>Nicolaides KH,Syngelaki A,del Mar Gil M,Quezada MS, Zinevich Y. Prenatal detection of fetal triploidy from cell-free DNA testing in maternal blood. <i>Fetal Diagn Ther</i>, 2014; 35 (3): 212–7.</p>	<p>Not relevant PICO: intervention</p>
<p>Nicolaides KH,Syngelaki A,Gil M,Atanasova V, Markova D. Validation of targeted sequencing of single-nucleotide polymorphisms for non-invasive prenatal detection of aneuploidy of chromosomes 13, 18, 21, X, and Y. <i>Prenat Diagn</i>, 2013; 33 (6): 575–9.</p>	<p>Not relevant PICO: intervention</p>
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<p>Palomaki GE,Kloza EM,Lambert-Messerlian GM,Haddow JE,Neveux LM,Ehrich M, et al. DNA sequencing of maternal plasma to detect Down syndrome: an international clinical validation study. <i>Genet Med</i>, 2011; 13 (11): 913–20.</p>	<p>Not relevant PICO: outcome</p>
<p>Papasavva T,van Ijcken WF,Kockx CE,van den Hout MC,Kountouris P,Kythreotis L, et al. Next generation sequencing of SNPs for non-invasive prenatal diagnosis: challenges and feasibility as illustrated by an application to beta-thalassaemia. <i>Eur J Hum Genet</i>, 2013; 21 (12): 1403–10.</p>	<p>Not relevant PICO: intervention</p>



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Phadke S. Cytogenetic microarray in prenatal and postnatal diagnosis. <i>Mol Cytogenet</i> 2014; 7 (Suppl 1 Proceedings of the International Conference on Human): I32.	Not relevant study design: conference abstract
Pieters JJ, Kooper AJ, Eggink AJ, Verhaak CM, Otten BJ, Braat DD, et al. Parents' perspectives on the unforeseen finding of a fetal sex chromosomal aneuploidy. <i>Prenat Diagn</i> , 2011; 31 (3): 286–92.	Not relevant study design
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Pietropolli A, Vicario R, Peconi C, Zampatti S, Quitadamo MC, Capogna MV, et al. Transabdominal coelocentesis as early source of fetal DNA for chromosomal and molecular diagnosis. <i>J Matern Fetal Neonatal Med</i> 2014; 27 (16): 1656–60.	Not relevant PICO: outcome
Pooh RK. Sonogenetics in fetal neurology. <i>Semin Fetal Neonatal Med</i> 2012; 17 (6): 353–9.	Not relevant PICO: Population less than 20 patients
Porreco RP, Garite TJ, Maurel K, Marusiak B, Ehrich M, van den Boom D, et al. Noninvasive prenatal screening for fetal trisomies 21, 18, 13 and the common sex chromosome aneuploidies from maternal blood using massively parallel genomic sequencing of DNA. <i>Am J Obstet Gynecol</i> , 2014; 211 (4): 365.e1–12.	Not relevant PICO: intervention
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Rad S, Turner AL, Ratousi D, Aghajanian P, Williams J, 3rd, Esakoff TF. Predictors for choosing array-comparative genomic hybridization for prenatal diagnosis. <i>Obstet Gynecol</i> 2014; 123 Suppl 1100s–1s.	Not relevant study design: conference abstract
Rajcan-Separovic E. Chromosome microarrays in human reproduction. <i>Hum Reprod Update</i> , 2012; 18 (5): 555–67.	Not relevant study design

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Regier DA,Peacock SJ,Pataky R,van der Hoek K,Jarvik GP,Hoch J, et al. Societal preferences for the return of incidental findings from clinical genomic sequencing: a discrete-choice experiment. <i>CMAJ: Canadian Medical Association Journal</i> , 2015; 187 (6): E190-7.	Not relevant PICO: Population
Rembouskos G,Passamonti U,De Robertis V,Tempesta A,Campobasso G,Volpe G, et al. Aberrant right subclavian artery (ARSA) in unselected population at first and second trimester ultrasonography. <i>Prenat Diagn</i> , 2012; 32 (10): 968–75.	Not relevant PICO: Population less than 20 patients
Rieneck K,Bak M,Jonson L,Clausen FB,Krog GR,Tommerup N, et al. Next-generation sequencing: proof of concept for antenatal prediction of the fetal Kell blood group phenotype from cell-free fetal DNA in maternal plasma. <i>Transfusion</i> , 2013; 53 (11 Suppl 2): 2892–8.	Not relevant PICO: intervention
Robinson WP,Penaherrera MS,Jiang R,Avila L,Sloan J,McFadden DE, et al. Assessing the role of placental trisomy in preeclampsia and intrauterine growth restriction. <i>Prenat Diagn</i> , 2010; 30 (1): 1–8.	Not relevant PICO: outcome
Rosen JM. Genetic diagnosis through whole-exome sequencing... <i>N Engl J Med</i> . 2013 Oct 17;369(16):1557–8. <i>New England Journal of Medicine</i> , 2014; 370 (11): 1068–68.	Not relevant study design : editorial
Rosenfeld JA,Morton SA,Hummel C,Sulpizio SG,McDaniel LD,Schultz RA, et al. Experience Using a Rapid Assay for Aneuploidy and Microdeletion/Microduplication Detection in over 2,900 Prenatal Specimens. <i>Fetal Diagn Ther</i> , 2014; 36 (3): 231–41.	Not relevant PICO: intervention
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Sago H, Sekizawa A. Nationwide demonstration project of next-generation sequencing of cell-free DNA in maternal plasma in Japan: one-year experience. <i>Prenat Diagn</i> , 2014.	Not relevant PICO outcome
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Samango-Sprouse C,Banjevic M,Ryan A,Sigurjonsson S,Zimmermann B,Hill M, et al. SNP-based non-invasive prenatal testing detects sex chromosome aneuploidies with high accuracy. <i>Prenatal Diagnosis</i> , 2013; 33 (7): 643–49.	Not relevant PICO: intervention
Sayres LC,Allyse M, Cho MK. Integrating stakeholder perspectives into the translation of cell-free fetal DNA testing for aneuploidy. <i>Genome Med</i> , 2012; 4 (6): 49.	Not relevant study design
Schou KV,Kirchhoff M,Nygaard U,Jorgensen C, Sundberg K. Increased nuchal translucency with normal karyotype: a follow-up study of 100 cases supplemented with CGH and MLPA analyses. <i>Ultrasound Obstet Gynecol</i> , 2009; 34 (6): 618–22.	Not relevant PICO: intervention
Schulz-Hanke I. [Prenatal diagnosis - how powerful is DNA microarray compared to karyotyping?]. <i>Z Geburtshilfe Neonatol</i> , 2013; 217 (1): 3–4.	Not relevant study design
Sehnert AJ,Rhees B,Comstock D,de Feo E,Heilek G,Burke J, et al. Optimal detection of fetal chromosomal abnormalities by massively parallel DNA sequencing of cell-free fetal DNA from maternal blood. <i>Clin Chem</i> , 2011; 57 (7): 1042–9.	Not relevant PICO: intervention
Shaffer LG,Dabell MP,Rosenfeld JA,Neill NJ,Ballif BC,Coppinger J, et al. Referral patterns for microarray testing in prenatal diagnosis. <i>Prenatal Diagnosis</i> , 2012; 32 (4): 344–50.	Not relevant PICO: control and outcome unclear
Shaw SW,Hsiao CH,Chen CY,Ren Y,Tian F,Tsai C, et al. Noninvasive prenatal testing for whole fetal chromosomal aneuploidies: a multicenter prospective cohort trial in Taiwan. <i>Fetal Diagn Ther</i> , 2014; 35 (1): 13–7.	Not relevant PICO: intervention
Shen GS,Zhang S, He PY. [Application of gene array chip in diagnosis of cytogenetics of recurrent spontaneous abortion]. <i>Zhonghua Fu Chan Ke Za Zhi</i> 2013; 48 (7): 515–8.	Language
Sheth F,Rahman M,Liehr T,Desai M,Patel B,Modi C, et al. Prenatal screening of cytogenetic anomalies - a Western Indian experience. <i>BMC Pregnancy Childbirth</i> , 2015; 1590.	Not relevant PICO: Outcome
Shi X,Zhang Z,Cram DS, Liu C. Feasibility of noninvasive prenatal testing for common fetal aneuploidies in an early gestational window. <i>Clin Chim Acta</i> , 2015; 43924–8.	Not relevant PICO: intervention
Sillence KA,Madgett TE,Roberts LA,Overton TG,Avent ND,Author A, et al. Non-invasive screening tools for down's syndrome: A review. <i>Diagnostics</i> , 2013; 3 (2): 291–314.	Not relevant study design
Song Y,Huang S,Zhou X,Jiang Y,Qi Q,Bian X, et al. Non-invasive prenatal testing for fetal aneuploidies in the first trimester of pregnancy. <i>Ultrasound Obstet Gynecol</i> , 2015; 45 (1): 55–60.	Not relevant PICO: intervention

<p>Song Y,Liu C,Qi H,Zhang Y,Bian X, Liu J. Noninvasive prenatal testing of fetal aneuploidies by massively parallel sequencing in a prospective Chinese population. <i>Prenat Diagn</i>, 2013; 33 (7): 700–6.</p>	<p>Not relevant PICO: intervention</p>
<p>Srebniak MI,Mout L, Van Opstal D, Galjaard RJ. 0.5 Mb array as a first-line prenatal cytogenetic test in cases without ultrasound abnormalities and its implementation in clinical practice. <i>Hum Mutat</i>, 2013; 34 (9): 1298–303.</p>	<p>Not relevant PICO: control</p>
<p>Srebniak MI, Van Opstal D, Joosten M, Diderich KE, de Vries FA, Riedijk S, et al. Whole-genome array as a first-line cytogenetic test in prenatal diagnosis. <i>Ultrasound Obstet Gynecol</i>, 2015; 45 (4): 363–72.</p>	<p>Not relevant study design</p>
<p>Srinivasan A, Bianchi DW, Huang H, Sehnert AJ, Rava RP. Noninvasive detection of fetal subchromosome abnormalities via deep sequencing of maternal plasma. <i>Am J Hum Genet</i>, 2013; 92 (2): 167–76.</p>	<p>Not relevant PICO: intervention</p>
<p>Straver R, Sistermans EA, Holstege H, Visser A, Oudejans CB, Reinders MJ. WISECONDOR: detection of fetal aberrations from shallow sequencing maternal plasma based on a within-sample comparison scheme. <i>Nucleic Acids Res</i>, 2014; 42 (5): e31.</p>	<p>Not relevant PICO: intervention</p>
<p>Sun LH, Li L, Wang XW, Zhu YZ, Chai YC, Li XH, et al. [Prenatal screening and diagnosis of genetic deafness by microarray]. <i>Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi</i> 2012; 47 (12): 991–5.</p>	<p>Language</p>
<p>Tabor HK, Murray JC, Gammill HS, Kitzman JO, Snyder MW, Ventura M, et al. Non-invasive fetal genome sequencing: opportunities and challenges. <i>Am J Med Genet A</i> 2012; 158a (10): 2382–4.</p>	<p>Not relevant study design</p>
<p>Talkowski ME, Ordulu Z, Pillalamarri V, Benson CB, Blumenthal I, Connolly S, et al. Clinical diagnosis by whole-genome sequencing of a prenatal sample. <i>N Engl J Med</i>, 2012; 367 (23): 2226–32.</p>	<p>Not relevant study design: case study</p>
<p>Thung DT, Beulen L, Hehir-Kwa J, Faas BH, Author A, Radboud University Medical Center N, et al. Implementation of whole genome massively parallel sequencing for noninvasive prenatal testing in laboratories. <i>Expert Review of Molecular Diagnostics</i>, 2015; 15 (1): 111–24.</p>	<p>Not relevant study design</p>
<p>Timbs AT, Rugless MJ, Gallienne AE, Haywood AM, Henderson SJ, Old JM. Prenatal diagnosis of hemoglobinopathies by pyrosequencing: a more sensitive and rapid approach to fetal genotyping. <i>Hemoglobin</i>, 2012; 36 (2): 144–50.</p>	<p>Targeted prenatal genetic testing for a specific aberration</p>

Timor-Tritsch IE, Kapp S, Berg R, Bejjani BA, Adams SA, Monteagudo A, et al. Greig cephalopolysyndactyly syndrome: diagnosis based on prenatal sonographic features coupled with comparative genomic hybridization. <i>J Ultrasound Med</i> , 2009; 28 (12): 1735–42.	Not relevant study design: case report
Valduga M, Philippe C, Bach Segura P, Thiebaugeorges O, Miton A, Beri M, et al. A retrospective study by oligonucleotide array-CGH analysis in 50 fetuses with multiple malformations. <i>Prenat Diagn</i> , 2010; 30 (4): 333–41.	Not relevant PICO: population
van der Zwaag PA, Jongbloed JDH, van Tintelen JP. Genetic diagnosis through whole-exome sequencing... <i>N Engl J Med</i> . 2013 Oct 17; 369(16):1502–11. <i>New England Journal of Medicine</i> , 2014; 370 (11): 1067–67.	Not relevant study design: letter
Vanakker O, Vilain C, Janssens K, Van der Aa N, Smits G, Bandelier C, et al. Implementation of genomic arrays in prenatal diagnosis: the Belgian approach to meet the challenges. <i>Eur J Med Genet</i> 2014; 57 (4): 151–6.	Not relevant study design
Wang JC, Sahoo T, Schonberg S, Kopita KA, Ross L, Patek K, et al. Discordant noninvasive prenatal testing and cytogenetic results: a study of 109 consecutive cases. <i>Genet Med</i> , 2014.	Not relevant PICO: intervention
Wang Y, Chen Y, Tian F, Zhang J, Song Z, Wu Y, et al. Maternal mosaicism is a significant contributor to discordant sex chromosomal aneuploidies associated with noninvasive prenatal testing. <i>Clin Chem</i> , 2014; 60 (1): 251–9.	Not relevant PICO: intervention
Wapner RJ, Babiarez JE, Levy B, Stosic M, Zimmermann B, Sigurjonsson S, et al. Expanding the scope of non-invasive prenatal testing: Detection of fetal microdeletion syndromes. <i>Am J Obstet Gynecol</i> , 2014.	Not relevant PICO: intervention
Warren JE, Turok DK, Maxwell TM, Brothman AR, Silver RM. Array comparative genomic hybridization for genetic evaluation of fetal loss between 10 and 20 weeks of gestation. <i>Obstet Gynecol</i> , 2009; 114 (5): 1093–102.	Not relevant PICO: Population
Wegner RD, Stumm M, Hofmann W. Non-invasive prenatal diagnosis using massively parallel sequencing - first experience in Germany. <i>Mol Cytogenet</i> , 2014; 7 (Suppl 1 Proceedings of the International Conference on Human): I14.	Not relevant study design
Wen S, Wei F, He Y, Xu W, Xie R, Zhang X, et al. [Application of noninvasive fetal trisomy testing based on massively parallel sequencing for the detection of chromosomal deletions and duplications]. <i>Zhonghua Yi Xue Yi Chuan Xue Za Zhi</i> 2014; 31 (5): 557–60.	Language
Wenstrom KD. Microarray analysis: elegant, accurate, and expensive. <i>Obstet Gynecol</i> 2014; 124 (2 Pt 1): 199–201.	Not relevant study design : editorial

Westerfield LE,Stover SR,Mathur VS,Nassef SA,Carter TG,Yang Y, et al. Reproductive genetic counseling challenges associated with diagnostic exome sequencing in a large academic private reproductive genetic counseling practice. <i>Prenat Diagn</i> , 2015.	Not relevant study design
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Vialard F,Molina Gomes D,Leroy B,Quarello E,Escalona A,Le Sciellour C, et al. Array comparative genomic hybridization in prenatal diagnosis: another experience. <i>Fetal Diagn Ther</i> , 2009; 25 (2): 277–84.	Not relevant PICO
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Vlatkovic IB,Hafner T,Miskovic B,Vicic A,Poljak B, Stipoljev F. Prenatal diagnosis of sex chromosome aneuploidies and disorders of sex development - a retrospective analysis of 11-year data. <i>Journal of Perinatal Medicine</i> , 2014; 42 (4): 529–34.	Not relevant PICO: intervention
Voelkerding KV, Lyon E. Digital fetal aneuploidy diagnosis by next-generation sequencing. <i>Clin Chem</i> , 2010; 56 (3): 336–8.	Not relevant study design: editorial
Xie W,Tan Y,Li X,Lin G,Jiang H,Chen F, et al. Rapid detection of aneuploidies on a benchtop sequencing platform. <i>Prenat Diagn</i> 2013; 33 (3): 232–7.	Not relevant PICO: Population
Xu HB,Yang H,Liu G, Chen H. Systematic review of accuracy of prenatal diagnosis for abnormal chromosome diseases by microarray technology. <i>Genet Mol Res</i> , 2014; 13 (4): 9115–21.	Not relevant PICO: intervention.
Xu Z,Geng Q,Luo F,Xu F,Li P, Xie J. Multiplex ligation-dependent probe amplification and array comparative genomic hybridization analyses for prenatal diagnosis of cytogenomic abnormalities. <i>Mol Cytogenet</i> , 2014; 7 (1): 84.	Not relevant PICO: Population less than 20 patients
Yakut S,Cetin Z,Simsek M,Mendicioglu, Il,Toru HS,Karauzum SB, et al. Rare Structural Chromosomal Abnormalities in Prenatal Diagnosis; Clinical and Cytogenetic Findings on 10125 Prenatal Cases. <i>Turk Patoloji Derg</i> , 2014.	Not relevant PICO: outcome
Yao H,Jiang F,Hu H,Gao Y,Zhu Z,Zhang H, et al. Detection of fetal sex chromosome aneuploidy by massively parallel sequencing of maternal plasma DNA: initial experience in a Chinese hospital. <i>Ultrasound Obstet Gynecol</i> , 2014; 44 (1): 17–24.	Not relevant PICO: intervention

Yatsenko SA,Peters DG,Saller DN,Chu T,Clemens M, Rajkovic A. Maternal cell-free DNA-based screening for fetal microdeletion and the importance of careful diagnostic follow-up. <i>Genet Med</i> , 2015.	Not relevant study design: case report
Yilmaz Z,Sahin FI,Bulakbasi T,Yuregir OO,Tarim E, Yanik F. Ethical considerations regarding parental decisions for termination following prenatal diagnosis of sex chromosome abnormalities. <i>Genet Couns</i> , 2008; 19 (3): 345–52.	Not relevant study design:
Yohe S,Hauge A,Bunjer K,Kemmer T,Bower M,Schomaker M, et al. Clinical Validation of Targeted Next-Generation Sequencing for Inherited Disorders. <i>Archives of Pathology &amp; Laboratory Medicine</i> , 2015; 139 (2): 204–10.	Not relevant PICO: intervention
Yoo SK,Chan Lim B,Byeun J,Hwang H,Joong Kim K,Seung Hwang Y, et al. Noninvasive Prenatal Diagnosis of Duchenne Muscular Dystrophy: Comprehensive Genetic Diagnosis in Carrier, Proband, and Fetus. <i>Clin Chem</i> , 2015.	Targeted prenatal genetic testing for a specific aberration
Yu SC,Jiang P,Choy KW,Chan KC,Won HS,Leung WC, et al. Noninvasive prenatal molecular karyotyping from maternal plasma. <i>PLoS One</i> , 2013; 8 (4): e60968.	Not relevant PICO: intervention
Yu SCY,Chan KCA,Zheng YWL,Jiang P,Liao GJW,Sun H, et al. Size-based molecular diagnostics using plasma DNA for noninvasive prenatal testing. <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 2014; 111 (23): 8583–88.	Not relevant PICO: intervention
Yuan Y,Jiang F,Hua S,Du B,Hao Y,Ye L, et al. Feasibility study of semiconductor sequencing for noninvasive prenatal detection of fetal aneuploidy. <i>Clin Chem</i> , 2013; 59 (5): 846–9.	Not relevant PICO: outcome
Zhang J,Hu P,Luo C, Ji Q,Zhou J,Liu A, et al. [Application of multiplex ligation-dependent probe amplification for rapid detection of aneuploidies and structural chromosomal abnormalities in prenatal diagnosis]. <i>Zhonghua Yi Xue Yi Chuan Xue Za Zhi</i> , 2014; 31 (1): 11–5.	Language
Zhu R,Zhu X,Yang Y,Duan H,Zhang Y,Wu X, et al. [Application of different technologies for distinguishing true and pseudo mosaicisms during prenatal diagnosis]. <i>Zhonghua Yi Xue Yi Chuan Xue Za Zhi</i> , 2014; 31 (5): 636–40.	Language
Zilina O,Teek R,Tammur P,Kuuse K,Yakoreva M,Vaidla E, et al. Chromosomal microarray analysis as a first-tier clinical diagnostic test: Estonian experience. <i>Mol Genet Genomic Med</i> , 2014; 2 (2): 166–75.	Not relevant PICO

<p>Zimmermann B, Hill M, Gemelos G, Demko Z, Banjevic M, Baner J, et al. Noninvasive prenatal aneuploidy testing of chromosomes 13, 18, 21, X, and Y, using targeted sequencing of polymorphic loci. <i>Prenatal Diagnosis</i>, 2012; 32 (13): 1233–41.</p>	<p>Not relevant PICO: intervention</p>
<p>Zwijnenburg PJG, Lakeman P, Pfundt R, Klein Wassink-Ruiter JS, Kerstjens-Frederikse WS, Van Ravenswaaij-Arts CMA, et al. Detection of submicroscopic chromosomal abnormalities using microarray analysis: The value and pitfalls in prenatal and postnatal diagnosis ORIGINAL (NON-ENGLISH) TITLE Detectie van submicroscopische chromosomale afwijkingen door middel van array-diagnostiek: De meerwaarde en de valkuilen in de prenatale en postnatale diagnostiek. <i>Tijdschrift voor Kindergeneeskunde</i>, 2014; 82 (1): 3–18.</p>	<p>Language</p>
<p><b>Systematic reviews</b></p>	
<p>Callaway JL, Shaffer LG, Chitty LS, Rosenfeld JA, Crolla JA. The clinical utility of microarray technologies applied to prenatal cytogenetics in the presence of a normal conventional karyotype: a review of the literature. <i>Prenat Diagn</i>, 2013; 33 (12): 1119–23.</p>	<p>Systematic review Differences in inclusion/exclusion criteria: includes studies published before 2008 and studies were they uses custom made microarrays. Includes studies with a high risk of bias in the meta-analysis. High risk of bias: Not presenting a clear PICO. The full search is not presented. Only one database is used for the literature search. No quality assessment of the included studies. Pooling of data was done in spite of heterogeneity issues.</p>
<p>Grande M, Jansen FA, Blumenfeld YJ, Fisher A, Odibo AO, Haak MC, et al. Genomic microarray in fetuses with increased nuchal translucency and normal karyotype - a systematic review and meta-analysis. <i>Ultrasound Obstet Gynecol</i>, 2015.</p>	<p>Systematic review Differences in inclusion/exclusion criteria: includes studies were they used custom made microarrays. Uses a cutoff of &gt;5Mb for aberrations to be considered detectable by the karyotype. Studies with fewer than 15 cases were excluded from the meta-analysis.</p>



	<p>Includes studies with a high risk of bias in the meta-analysis.  Moderate risk of bias:  The quality assessment is not presented for each of the included studies separately.</p>
<p>Hillman SC, Pretlove S, Coomarasamy A, McMullan DJ, Davison EV, Maher ER, et al. Additional information from array comparative genomic hybridization technology over conventional karyotyping in prenatal diagnosis: a systematic review and meta-analysis (Provisional abstract). <i>Ultrasound in Obstetrics and Gynecology</i>, 2011; 37 (1): 6–14.</p>	<p>Systematic review  Differences in inclusion exclusion criteria: includes studies published before 2008 and studies were they uses custom made microarrays.  Combines pathogenic CNV:s and VOUS in the meta-analysis. Includes studies with a high risk of bias in the meta-analysis.  High risk of bias:  The full search is not presented. The quality assessment is not presented for each of the included studies separately. Pooling of data was done in spite of heterogeneity issues.</p>
<p>Hillman SC, McMullan DJ, Hall G, Togneri FS, James N, Maher EJ, et al. Use of prenatal chromosomal microarray: prospective cohort study and systematic review and meta-analysis. <i>Ultrasound Obstet Gynecol</i> 2013;41:610–20.</p>	<p>Differences in inclusion exclusion criteria: includes studies published before 2008 and studies were they uses custom made microarrays.  Includes studies with a high risk of bias in the meta-analysis.  High risk of bias:  The full search is not presented. The quality assessment is not presented for each of the included studies separately. Pooling of data was done in spite of heterogeneity issues.</p>
<p>Jansen FA, Blumenfeld YJ, Fisher A, Cobben JM, Odibo AO, Borrell A, et al. Array Comparative Genomic Hybridization and Fetal Congenital Heart Defects - A systematic review and meta-analysis. <i>Ultrasound Obstet Gynecol</i>, 2014.</p>	<p>Systematic review  Differences in inclusion exclusion criteria: includes studies were they uses custom made microarrays or were the platform was not stated.  Includes studies with a high risk of bias in the meta-analysis.  Low risk of bias</p>

<p>Saldarriaga W,Garcia-Perdomo HA,Arango-Pineda J, Fonseca J. Karyotype versus genomic hybridization for the prenatal diagnosis of chromosomal abnormalities: a metaanalysis. Am J Obstet Gynecol, 2014.</p>	<p>Systematic review Differences in inclusion exclusion criteria: Uses CNV:s identified with microarray plus abnormal karyotype as the true positives. Includes studies were they uses custom made microarrays or were the microarray platform was not specified. Includes studies with a high risk of bias in the meta-analysis. High risk of bias: Pooling of data was done in spite of heterogeneity issues.</p>
<p>Wit MC,Srebniak MI,Govaerts LC,Opstal D,Galjaard RJ, Go AT. Additional value of prenatal genomic array testing in fetuses with isolated structural ultrasound abnormalities and a normal karyotype: a systematic review of the literature (Provisional abstract). Ultrasound in Obstetrics and Gynecology, 2014; 43 (2): 139–46.</p>	<p>Systematic review Differences in inclusion exclusion criteria: Includes studies were they uses custom made microarrays or were the microarray platform was not specified. Includes studies with a high risk of bias in the meta-analysis. High risk of bias: Limitation in search, no mesh terms used. The quality assessment is not presented. The software and the algorithm used for the pooling of the data is not presented, nor the weight of the different studies.</p>

<b>Studies with high risk of bias/ Studier med låg kvalitet</b>
<p>Ahn JW,Bint S,Irving MD,Kyle PM,Akolekar R,Mohammed SN, et al. A new direction for prenatal chromosome microarray testing: software-targeting for detection of clinically significant chromosome imbalance without equivocal findings. PeerJ, 2014; 2e354.</p>
<p>Bernhardt BA,Soucier D,Hanson K,Savage MS,Jackson L, Wapner RJ. Women's experiences receiving abnormal prenatal chromosomal microarray testing results. Genet Med, 2013; 15 (2): 139–45.</p>

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- Carey L, Scott F, Murphy K, Mansfield N, Barahona P, Leigh D, et al. Prenatal diagnosis of chromosomal mosaicism in over 1600 cases using array comparative genomic hybridization as a first line test. *Prenat Diagn*, 2014; 34 (5): 478–86.
- D'Amours G, Kibar Z, Mathonnet G, Fetni R, Tihy F, Desilets V, et al. Whole-genome array CGH identifies pathogenic copy number variations in fetuses with major malformations and a normal karyotype. *Clin Genet*, 2012; 81 (2): 128–41.
- Evangelidou P, Alexandrou A, Moutafi M, Ioannides M, Antoniou P, Koumbaris G, et al. Implementation of high resolution whole genome array CGH in the prenatal clinical setting: advantages, challenges, and review of the literature. *Biomed Res Int*, 2013; 2013346762.
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- Filges I, Kang A, Klug V, Wenzel F, Heinemann K, Tercanli S, et al. Array comparative genomic hybridization in prenatal diagnosis of first trimester pregnancies at high risk for chromosomal anomalies. *Mol Cytogenet*, 2012; 5 (1): 38.
- Ganesamoorthy D, Bruno DL, McGillivray G, Norris F, White SM, Adroub S, et al. Meeting the challenge of interpreting high-resolution single nucleotide polymorphism array data in prenatal diagnosis: does increased diagnostic power outweigh the dilemma of rare variants? *Bjog*, 2013; 120 (5): 594–606.
- Gruchy N, Decamp M, Richard N, Jeanne-Pasquier C, Benoist G, Mittre H, et al. Array CGH analysis in high-risk pregnancies: comparing DNA from cultured cells and cell-free fetal DNA. *Prenat Diagn*, 2012; 32 (4): 383–8.
- Held KR, Zahn S, Author A, Mvz genteQ GmbH Lf, Humangenetik FHG, Correspondence A, et al. Microarray-based comparative genomic hybridization for prenatal diagnosis: Indications and clinical evaluation ORIGINAL (NON-ENGLISH) TITLE Pranataler Array: Indikationen, Bewertung. *Medizinische Genetik*, 2014; 26 (4): 398–404.

Huang J,Poon LC,Akolekar R,Choy KW,Leung TY, Nicolaides KH. Is high fetal nuchal translucency associated with submicroscopic chromosomal abnormalities on array CGH? *Ultrasound in Obstetrics & Gynecology*, 2014; 43 (6): 620–24.

Kleeman L,Bianchi DW,Shaffer LG,Rorem E,Cowan J,Craig SD, et al. Use of array comparative genomic hybridization for prenatal diagnosis of fetuses with sonographic anomalies and normal metaphase karyotype. *Prenat Diagn*, 2009; 29 (13): 1213–7.

Klugman S,Suskin B,Spencer BL,Dar P,Bajaj K,Powers J, et al. Clinical utility of chromosomal microarray analysis in prenatal diagnosis: report of first 6 months in clinical practice. *J Matern Fetal Neonatal Med*, 2014; 27 (13): 1333–8.

Konialis C, Pangalos C. Dilemmas in Prenatal Chromosomal Diagnosis Revealed Through a Single Center's 30 Years' Experience and 90,000 Cases. *Fetal Diagn Ther*, 2015.

Lee CN,Lin SY,Lin CH,Shih JC,Lin TH, Su YN. Clinical utility of array comparative genomic hybridisation for prenatal diagnosis: a cohort study of 3171 pregnancies. *Bjog*, 2012; 119 (5): 614–25.

Leung TY,Vogel I,Lau TK,Chong W,Hyett JA,Petersen OB, et al. Identification of submicroscopic chromosomal aberrations in fetuses with increased nuchal translucency and apparently normal karyotype. *Ultrasound Obstet Gynecol*, 2011; 38 (3): 314–9.

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Srebniak M, Boter M, Oudesluijs G, Joosten M, Govaerts L, Van Opstal D, et al. Application of SNP array for rapid prenatal diagnosis: implementation, genetic counselling and diagnostic flow. <i>Eur J Hum Genet</i> , 2011; 19 (12): 1230–7.
Srebniak MI, Boter M, Oudesluijs GO, Cohen-Overbeek T, Govaerts LC, Diderich KE, et al. Genomic SNP array as a gold standard for prenatal diagnosis of foetal ultrasound abnormalities. <i>Mol Cytogenet</i> , 2012; 5 (1): 14.
Tyreman M, Abbott KM, Willatt LR, Nash R, Lees C, Whittaker J, et al. High resolution array analysis: diagnosing pregnancies with abnormal ultrasound findings. <i>J Med Genet</i> , 2009; 46 (8): 531–41.
van der Steen SL, Diderich KE, Riedijk SR, Verhagen-Visser J, Govaerts LC, Joosten M, et al. Pregnant couples at increased risk for common aneuploidies choose maximal information from invasive genetic testing. <i>Clin Genet</i> , 2014.
Van den Veyver IB, Patel A, Shaw CA, Pursley AN, Kang SH, Simovich MJ, et al. Clinical use of array comparative genomic hybridization (aCGH) for prenatal diagnosis in 300 cases. <i>Prenat Diagn</i> , 2009; 29 (1): 29–39.
Van Opstal D, de Vries F, Govaerts L, Boter M, Lont D, van Veen S, et al. Benefits and burdens of using a SNP array in pregnancies at increased risk for the common aneuploidies. <i>Hum Mutat</i> , 2015; 36 (3): 319–26.
Walser SA, Kellom KS, Palmer SC, Bernhardt BA. Comparing genetic counselor's and patient's perceptions of needs in prenatal chromosomal microarray testing. <i>Prenat Diagn</i> , 2015.
Yatsenko SA, Davis S, Hendrix NW, Surti U, Emery S, Canavan T, et al. Application of chromosomal microarray in the evaluation of abnormal prenatal findings. <i>Clin Genet</i> , 2013; 84 (1): 47–54.