Annex 1: studies 1-16 and variant details.
Thirona Naicker et al. Systematic review on the known variants and genes associated with orofacial clefts in Africa. PAMJ - Clinical Medicine. 2022;9:31756.
https://www.clinical-medicine.panafrican-med-journal.com/content/article/9/31756/full

No	Reference	Study type	Location of patients	Gene	Mutation: cDNA or SNP	Novel / Known	Cleft type	Mutation type	ACMG	CADD Score	Location of testing lab
1	Alade et al. (2020)	Case-control study (candidate gene analysis)	Ghana	IRF6	c.107T>A c.326A>C c.1311A>T	Novel Novel Novel	Syndromic (VWS) Syndromic (VWS) Syndromic (VWS)	Missense Missense Missense	P P VUS	29.3 23.6 25.5	Iowa, USA
2	Mbuyi-Musanzayi et al. (2019)	Family based case-control study (candidate gene, Chromosomal microarray analysis)	Congo	IRF6	chr1:209.872.038-210.246.107	Novel	Syndromic (VWS)	Microdeletion	N/A	N/A	Louvain, Belgium
3	Butali et al. (2019)	Case-control study (GWAS)	Nigeria, Ghana, Ethiopia	near CTNNA2 SULT2A1 8q24 PAX7 VAX1 SOX5P1	rs80004662 rs62529857 rs72728755 rs742071 rs6585429-A rs12543318	Novel Novel Known Known Known Known	Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CL±P) Non-syndromic (CL±P) Non-syndromic (CL±P) Non-syndromic (CL±P)	Intronic variant Intronic variant N/A Intronic variant Intronic variant Intronic variant	B B B B LB B	N/A	Iowa, USA
4	Jaouadi et al. (2018)	Case-parent trios' design (whole exome sequencing)	Tunisia	ALPK3	c.1531_1532delAA; p.Lys511Argfs*12	Novel	Syndromic (Paediatric syndromic cardiomyopathy)	Frameshift Deletion	LP	N/A	Marseille, France
5	Gowans et al. (2018)	Case-control study (candidate gene analysis)	Ghana, Ethiopia, Nigeria	GREM1	c.490C>T c.182G>A	Novel Novel	Non-syndromic (soft palate) Non-syndromic (CL±P)	Missense Missense	VUS VUS	22.9 22.9	Iowa, USA
6.	Eshete et al. (2018)	Case-control study, case-parent trios	Ghana, Ethiopia, Nigeria	GRHL3	c.332delC c.497C>A c.1229A>G c.1282A>C c.1677C>A	Novel Novel Novel Novel Novel	Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CP)	Frameshift Missense Missense Splice site Nonsense	P VUS VUS VUS LP	N/A 23.6 29.1 19.31 40	Iowa, USA

		(candidate gene analysis)									
7	Gowans et al. (2017)	Family-based study (candidate gene and segregation analyses)	Ghana, Ethiopia, Nigeria	IRF6	c.175-2A>C c.194G>T c.205G>A c.379+1G>T c.554A>C c.960G>C c.1060+26C>T Chr1:209979529A>T c.263A>G c.334C>G c.380-116T>A c.749G>A c.748C>T c.945G>T	Novel Novel Novel Novel Novel Novel Novel Known Known Known Known Known Known Known	Non-syndromic (CL±P) Syndromic Non-syndromic (CL±P) Syndromic Non-syndromic (CL±P) Syndromic and non-syndromic Syndromic Syndromic and non-syndromic Non-syndromic (CL±P) Non-syndromic (CL±P) Syndromic and non-syndromic Syndromic Syndromic and non-syndromic Non-syndromic (CL±P)	Splice acceptor variant Missense Missense Splice donor variant Missense Missense Intronic TF binding site variant Missense Missense Intronic Missense Stop-gained Synonymous	P P P VUS LP VUS N/A P B B P P VUS	33 26.2 32 34 21.7 25.7 4.61 17.37 25.8 17.11 2.09 29.3 38 18.74	Iowa, USA
8	Gowans et al. (2016)	Case-control study Family-based study (candidate genes analyses, meta-analyses)	Ghana, Ethiopia, Nigeria	PAX7 8q24 VAX1 MSX1 TULP4 CRISPLD2 NOG1 ARHGAP29 PAX7	Rs742071 Rs987525 Rs7078160 Rs115200552 Rs651333 Rs4783099 Rs17760296 c.967A>G c.1277delAinsTA c.1281+4A>G c.511-107T>C c.341-30T>A c.1227G>A	Known Known Known Known Known Known Known Novel Novel Novel Novel Novel Novel	Non-syndromic (CL±P) N/A Non-syndromic (CL±P) Non-syndromic (CL±P) Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CP) Non-syndromic (CL) Non-syndromic (CL±P) Non-syndromic (CL±P) Non-syndromic (CL±P&CP) Non-syndromic (CL) Non-syndromic (CL)	Intronic variant N/A Intronic variant 3' UTR variant Intron variant 3' UTR variant Intron variant Missense Coding sequence variant Splice region variant/Intronic Intronic Intronic Synonymous	B B B LB B B B VUS LP VUS VUS VUS LB	 3.45 1.12 23.4 23.6 22.6 19.55 5.73 15.66	Iowa, USA
9	Ratbi et al. (2014)	Case-parent trios (candidate gene analysis)	Morocco	IRF6	c.250C>T	Known	Syndromic (PPS)	Missense	P	28.5	Rabat, Morocco
10	Butali et al.	Family-based study	Nigeria,	IRF6	c.196A>T c.551T>A c.1061-2A>G	Novel Novel Known	Syndromic (VWS) Syndromic (VWS) Syndromic (VWS)	Stop-gained Splice site	P VUS P	38 NA 34	Iowa, USA

	(2014)	(candidate gene analysis)	Ethiopia		c.752T>C c.690T>G rs121434227 G>A	Known Novel Known	Syndromic (VWS) Syndromic (VWS) Syndromic (PPS)	Splice acceptor variant Missense Missense Missense	P LP P	31 23.8 32	
11	Butali et al. (2014)	Family-based study (candidate genes analyses)	Nigeria, Ethiopia	ARHGAP29 PAX7 MAFB	c.2864G>A c.2738C>A c.1396G>A c.952+2T>A c.1282G>A c.493C>G	Known Known Known Novel Novel Novel	Non-syndromic (CL±P) Non-syndromic (CL) Non-syndromic (CL) Non-syndromic (CL) Non-syndromic (CL) Non-syndromic (CP)	Missense Stop-gained Missense Splice donor variant Missense Missense	B P VUS P VUS VUS	15.95 39 22.7 28.3 25.1 23.3	Iowa, USA
12	Figueiredo et al. (2014)	Case-control study, Family-based study, Replication study	Congo	8q24	Found no association in Africans	N/A	Non-syndromic (CL±P)	N/A	N/A		Southern California, USA
13	Migliore et al. (2013)	Family-based study (candidate gene analysis)	Cameroon	MID1	c.1142-1285del	Novel	Syndromic	Complex rearrangement	VUS	N/A	Trieste, Italy
14	Weatherley-White et al. (2011)	Cased-control study (candidate loci analyses)	Kenya	8q24	Found no association in Africans	Known	Non-syndromic (CL±P)	N/A	N/A		Colorado, USA
15	Butali et al. (2011)	Case-control study Family-based study (candidate genes analyses)	Nigeria	MSX1	A34G/c.119C>G	Known	Non-syndromic (CL±P)	Missense	B	13.64	Iowa, USA
16	Chaabouni et al. (2005)	Family based Linkage study	Tunisia	TBX22	c.358C>T	Novel	Syndromic (CP and ankyloglossia)	Intergenic variant	LP	25.4	Tunis

ACMG: American college of medical genetics; CADD: combined annotation-dependent depletion; B: benign; LB: likely benign; LP: likely pathogenic; P: pathogenic; VUS: variant of unknown significance