

Supplementary Materials

Table S1. The search strategies used in the different databases. The asterisk * in a search strategy is used as a wildcard character to represent various word endings or variations.

Database (Number of searched studies)	Search strategy
Embase.com (1878)	<p>((('metastatic melanoma'/exp OR (metastasis/de AND melanoma/de) OR ((metasta* NEAR/6 melanoma*)):ab,ti) AND ('primary melanoma'/de OR ('primary tumor'/de AND melanoma/exp) OR ((primary NEAR/6 melanoma*)):Ab,ti) OR ((melanoma* AND (primary NEAR/6 metasta*)):Ab,ti) OR ((melanoma* AND (primary AND metasta*)):ti)) AND ('mutation'/exp OR 'copy number variation'/de OR 'mutational analysis'/exp OR 'DNA sequence'/de OR 'mutational analysis'/de OR 'gene sequence'/de OR 'DNA fragment'/de OR 'genomic DNA'/de OR 'polymerase chain reaction'/exp OR 'sequence analysis'/exp OR 'molecular pathology'/de OR 'genotyping technique'/exp OR 'nucleotide sequence'/de OR 'promoter region'/de OR 'molecular fingerprinting'/exp OR 'tumor-related gene'/exp OR 'clonal variation'/de OR 'genetic association'/de OR 'molecular genetics'/de OR (sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) NEAR/3 (alterat* OR characteri* OR fragment* OR associat*)) OR (dna NEAR/3 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtqcr OR (mutation* NEAR/6 (analy* OR profil*)) OR (molecul* NEAR/3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* NEAR/3 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/3 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/3 variation*) OR clonalit*):ab,ti) NOT ('cancer of unknown primary site'/mj OR (unknown* NEAR/3 primar*):ti) NOT ([Conference Abstract]/lim AND [1800-2020]/py) OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim) AND [english]/lim NOT ([animals]/lim NOT [humans]/lim)</p>
Medline ALL Ovid (1451)	<p>((((Neoplasm Metastasis / AND Melanoma /) OR ((metasta* ADJ6 melanoma*)):ab,ti.) AND (((primary ADJ6 melanoma*)):ab,ti.) OR ((melanoma* AND (primary ADJ6 metasta*)):ab,ti.) OR ((melanoma* AND (primary AND metasta*)):ti.)) AND (Mutation/ OR DNA Copy Number Variations/ OR DNA Mutational Analysis/ OR Base Sequence/ OR Polymerase Chain Reaction/ OR exp Sequence Analysis/ OR Pathology, Molecular/ OR Genotyping Techniques/ OR Promoter Regions, Genetic/ OR DNA Fingerprinting/ OR Genetic Association Studies/ OR Molecular Biology/ OR (sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) ADJ3 (alterat* OR characteri* OR fragment* OR</p>

Database (Number of searched studies)		Search strategy
		<p>associat*)) OR (dna ADJ3 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtPCR OR (mutation* ADJ6 (analy* OR profil*)) OR (molecul* ADJ3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* ADJ3 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) ADJ3 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal ADJ3 variation*) OR clonalit*).ab,ti.) NOT (*Neoplasms, Unknown Primary/ OR (unknown* ADJ3 primar*).ti.) AND english.la. NOT (exp animals/ NOT humans/)</p>
Web of Science	(1632)	<p>TS=((((metasta* NEAR/5 melanoma*)) AND (((primary NEAR/5 melanoma*)) OR ((melanoma* AND (primary NEAR/5 metast*)) AND ((sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) NEAR/2 (alterat* OR characteri* OR fragment* OR associat*)) OR (dna NEAR/2 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtPCR OR (mutation* NEAR/5 (analy* OR profil*)) OR (molecul* NEAR/2 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* NEAR/2 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/2 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/2 variation*) OR clonalit*))) NOT ti=((unknown* NEAR/2 primar*)) and DT=(article) AND LA=(english)</p>
Cochrane CENTRAL Register of Trials	(356)	<p>(((((metasta* NEAR/6 melanoma*)):ab,ti) AND (((primary NEAR/6 melanoma*)):Ab,ti) OR ((melanoma* AND (primary NEAR/6 metast*)):Ab,ti) OR ((melanoma* AND (primary AND metast*)):ti)) AND ((sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) NEAR/3 (alterat* OR characteri* OR fragment* OR associat*)) OR (dna NEAR/3 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtPCR OR (mutation* NEAR/6 (analy* OR profil*)) OR (molecul* NEAR/3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* NEAR/3 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/3 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/3 variation*) OR clonalit*)):ab,ti) NOT ((unknown* NEAR/3 primar*)):ti)</p>

The following information was used in g:Profiler as input data:

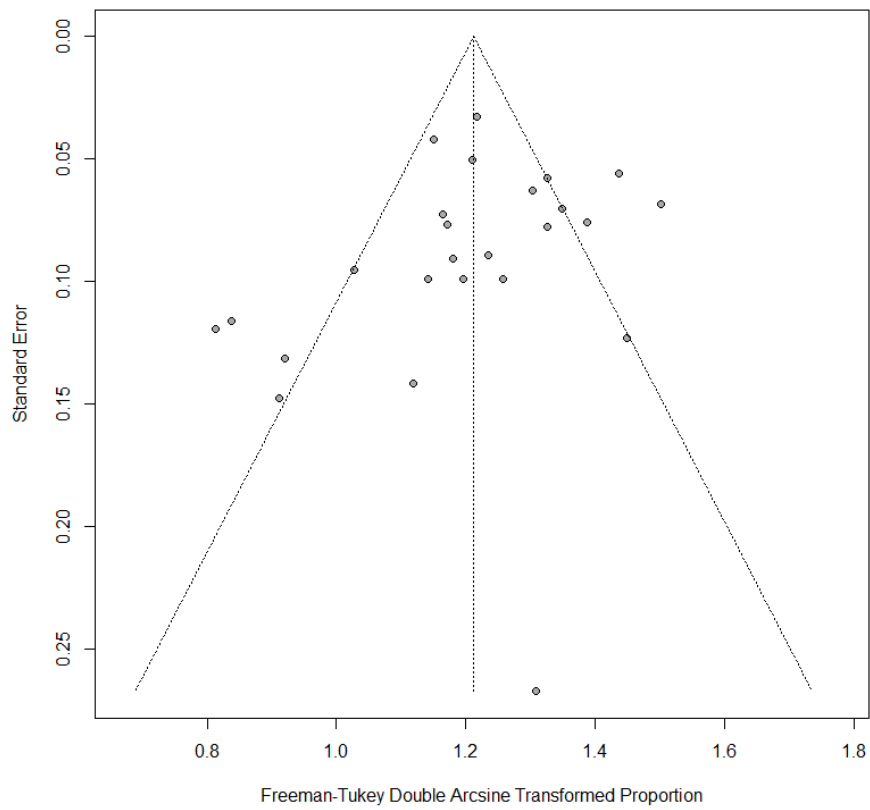
Gene list: *CDK4* *MAP2K1* *RB1* *CTNNB1* *HNFA1* *RAC1* *CDKN2A*
 PIK3CA *TP53* *EPHB6* *TERT* *CDKN2A* *PIK3CA* *TP53* *MAP2K1*
 PTEN *CTNNB1* *HNFA1* *TP53* *MAP2K1* *PTEN* *RAC1*
 BRAF *NRAS* *KIT*

Data sources: GO biological process



Figure S1. Pathways analysis using g:profier.

(A)



(B)

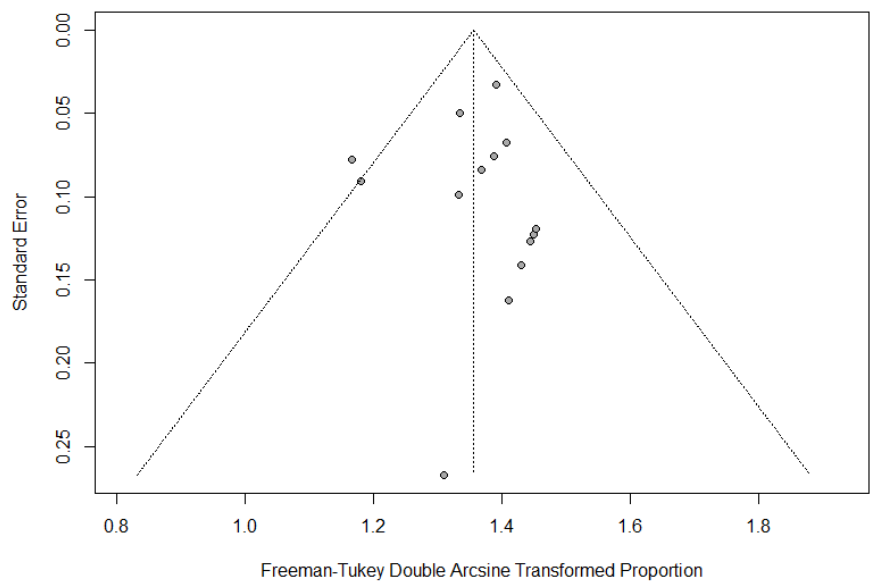


Figure S2. Study effects and publication bias were assessed using funnel plots and the Egger's test. (A) BRAF studies and (B) NRAS studies.