Summary Statistic Harmonisation Flowchart Yes Alleles in correct orientation Version 2.1 - 17th July 2018 - Outcome code 1 Alleles on forward strand allele == alt - Requires harmonisation - Flip alleles Alleles in flipped orientation - Flip effects and EAF Is effect/alt - Outcome code 2 Is effect allele Are effect and allele freq known in sum alt allele Infer strand --maf_palin_th frequencies VCF? - Already harmonised Alleles in correct orientation - Take reverse comp of alleles - Outcome code 3 Does effect allele Alleles on reverse strand complement of - Outcome code 17 - Outcome code 18 alt allele? - Take reverse comp of alleles Alleles in flipped orientation - Flip alleles Arg: --palin_mode - Flip effects and EAF - Outcome code 4 Yes - Already harmonised Alleles in correct orientation - Outcome code 5 Assume forward allele == alt allele? strand - Requires harmonisation - Flip alleles Alleles in flipped orientation - Flip effects and EAF - Outcome code 6 Yes Already harmonised Alleles in correct orientation - Take reverse comp of alleles - Outcome code 7 Matching Does effect allel After filtering, a Is variant Assume reverse single matching variant exists? allele, effect strand complement of VCF? alt allele? allele and build - Requires harmonisation known? - Take reverse comp of alleles Alleles in flipped orientation - Flip alleles - Flip effects and EAF - Outcome code 8 - Cannot harmonise - Cannot harmonise - No records in reference - Multiple records exist (ambiguous) - Outcome code 14 - Outcome code 16 - Outcome code 15 - Will not harmonise Drop palindromic - Outcome code 9 - Already harmonised Alleles in correct orientation - Outcome code 10 Are alleles Alleles on forward strand allele == alt with forward allele? strand? Requires harmonisation - Flip alleles Alleles in flipped orientation - Flip effects and EAF - Outcome code 11 Alleles in correct orientation - Take reverse comp of alleles - Outcome code 12 Does effect allele == reverse Alleles on reverse strand

complement of alt allele?

Alleles in flipped orientation

Requires harmonisation
Take reverse comp of alleles

- Flip effects and EAF - Outcome code 13