Conclusions  
HARP and SinMod methods show a high level of agreement for assessment of global mid-ventricular transmural circumferential strain, with good reproducibility for both individual methods. Agreement is much lower for segmental measurements; poor reproducibility for segmental measurements using both techniques probably reflect user variability in identification of right ventricular septal insertion points and contour tracing.

AETIOLOGICAL ROLE OF FOLATE DEFICIENCY IN CONGENITAL HEART DISEASE: EVIDENCE FROM MENDELIAN RANDOMISATION AND META-ANALYSIS  
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Background  
The existence of a causal relationship between lower levels of plasma folate and congenital heart disease (CHD) remains contentious. Randomised trials of this question are not possible, in view of the known protective effect of folate against neural tube defects (NTDs). Folate fortification of flour is known to reduce the incidence of NTDs, but it is not known whether there is any effect on CHD. Clarifying the relationship between folate and CHD could potentially inform the practice of folate fortification. We present a genetic approach using “Mendelian randomisation” to determining the causality of folate in CHD risk.

Methods  
We compared genotype frequencies at the methylene tetrahydrofolate reductase (MTHFR) C677T single nucleotide polymorphism (SNP) in 1186 CHD cases and 4168 controls. The TT genotype at MTHFR C677T is known to be associated with lower activity of MTHFR and plasma folate, and higher levels of plasma homocysteine. The effect of TT genotype on plasma folate levels is greater in conditions of folate deficiency. Thus, if lower plasma folate had a causal effect on CHD risk, a higher frequency of TT genotype among CHD cases than among healthy controls would be anticipated, and this would be expected to be more marked in conditions of folate deficiency. We placed our results in the context of a meta-analysis of all previously published studies of this question (to September 2010), which together included 1883 cases and 3069 controls in 25 studies. Thus, the combined analyses included 3069 CHD cases and 7271 controls. We used random-effects models to combine the data. We conducted sensitivity analyses to examine folate fortification of flour as a potential source of heterogeneity.

Results  
The primary genotyping data in 1186 cases and 4168 controls revealed a trend towards increased risk with the TT genotype, but this did not reach statistical significance (OR 1.15 [95% CI 0.94 to 1.40]). Combination of our primary data with previous studies, however, revealed association in the larger dataset (OR 1.45 [95% CI 1.12 to 1.89]; p=0.005). The population attributable fraction for the TT genotype was 5% of CHD. There was no evidence of publication bias among the contributing studies. We discovered folate fortification status to be a significant source of heterogeneity. Studies conducted in countries with mandatory folate fortification showed no effect of C677T genotype on CHD risk (OR 0.96 [95% CI 0.64 to 1.44]), whereas studies conducted in countries without mandatory fortification showed a significant effect of genotype (OR 1.63 [95% CI 1.19 to 2.25]). These ORs were significantly different from each other (p=0.032).

Conclusions  
We demonstrate genetic evidence in favour of a causal relationship between plasma folate and CHD. The absence of a genetic association in some countries practicing folate fortification suggests that fortification largely abrogates the risk of CHD attributable to folate deficiency.