Fetal long QT syndrome: a systematic review – PROSPERO reg. 10527

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Introduction
Symptomatic fetal long QT syndrome (fLQTS) is often misdiagnosed as knowledge of cardiac phenotypes is scarce. Inappropriate management with QT prolonging medication can be fatal. We performed a systematic review (SR) to describe the clinical presentation and potential genotype-phenotype correlations in fLQTS.

Methods
This SR was performed in MEDLINE and EMBASE up till December 2018. Two reviewers independently screened all studies, assessed eligibility and extracted data. Cohort studies, case series or case reports describing the fLQTS phenotype were included. Information regarding the heart rate, arrhythmias, age of first arrhythmias, QTc times, genotype, and outcome was collected.

Results
A total of 161 full-text articles describing 432 fLQTS cases were included. Sinus bradycardia was seen in 148 (44.6%) cases. Prenatally, the mean atrial rate was 126±69/min and the ventricular rate 108±45/min. Ventricular tachycardia (VT) or atrio-ventricular block (AVB), (predominantly 2:1), was seen in 97 fetuses, of whom 33 (33%) died. The median age of first VT/AVB (n=76) was 27 weeks gestation. The highest risk for arrhythmias was in compound or homozygous variant carriers and probands. T613M, T613K (LQTS2) and R1623Q (LQTS3) were malignant heterozygous genotypes. The longest QTc times were recorded in fetuses with only 2:1AVB (m 639±110 msec).

Conclusions
Sinus bradycardia is a feature of fLQTS. When VT/TdP and/or 2:1AVB is/are present, the mortality is high. Arrhythmias usually present around 27 weeks gestation. Genotype-phenotype correlations have been identified and can aid the choice of anti-arrhythmic therapy.