

## Background

Women with LQTS types 1 and 2 exhibit a pronounced increase in risk for arrhythmic events after the onset of adolescence. We aimed to develop a novel prediction model of risk estimates for cardiac events (CE) and life-threatening events (LTE) in this population.

## Methods

The model was derived from the Rochester LQTS Registry, with 767 confirmed LQT1 (n=404) and LQT2 (n=363) women with a single mutation. Cox regression was used to develop a risk-prediction model from age 15 to 60 years for 1) cardiac events (defined as syncope, aborted cardiac arrest [ACA], LQTS-related sudden cardiac death [SCD]); and 2) life-threatening events (defined as ACA, SCD, or appropriate ICD shocks).

## Results

For the 767 patients the cumulative follow-up time was 22,243 patient-years, during which 323 patients (42%) experienced cardiac events. We identified three risk-groups based on genotype, mutation-location, and QTc thresholds for each group, adjusting for prior syncope and time-dependent beta-blocker therapy. The 10-year predicted risk of cardiac events ranged from 15% in the low-risk group, 29% in the intermediate risk-group, to 51% in the high-risk group. Consistent results were shown for the endpoint of life-threatening events, with corresponding 10-year projected event rates ranging from 2%, 5%, to 14%. C-statistics for the prediction model for the two respective endpoints were 0.68 (0.65-0.71) and 0.71 (0.66-0.76).

## Conclusions

This is the first risk-prediction model that provides absolute risk estimates for cardiac events and life-threatening events for women with congenital long QT syndrome based on genotype-phenotype data. The projected risk estimates can be used to guide sex-specific management in congenital LQTS.

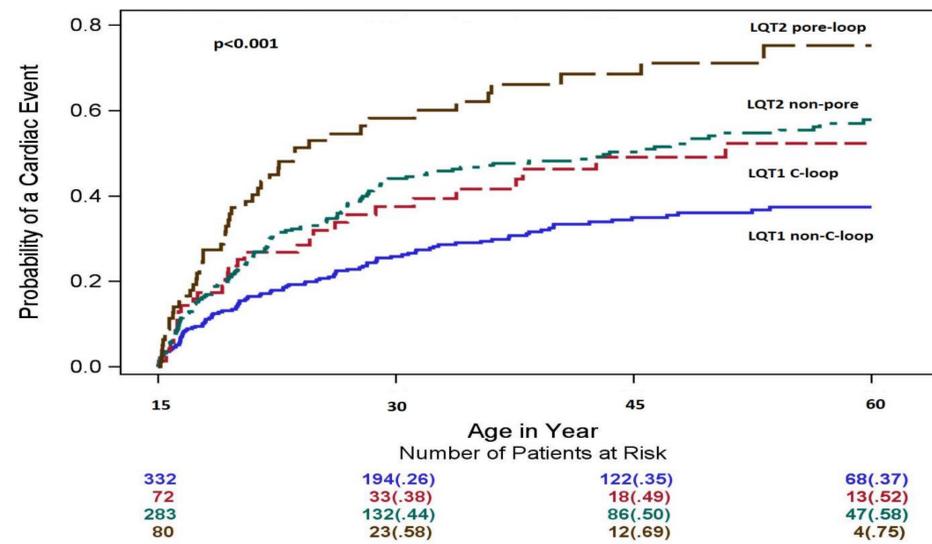


Figure 1: KM estimates of a first CE from age 15 through 60 years by genotype and mutation-location

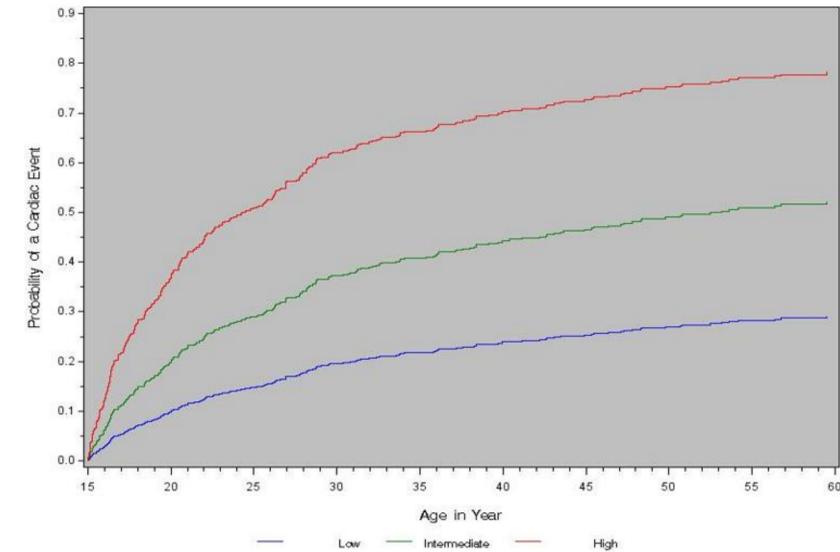


Figure 3: Risk-adjusted prediction of CE from age 15 to 60 years

Figure 2. Risk-groups in LQTS women<sup>a</sup>

<sup>a</sup>All findings are further adjusted for time-dependent beta-blocker therapy and a history of syncope prior to age 15 years.

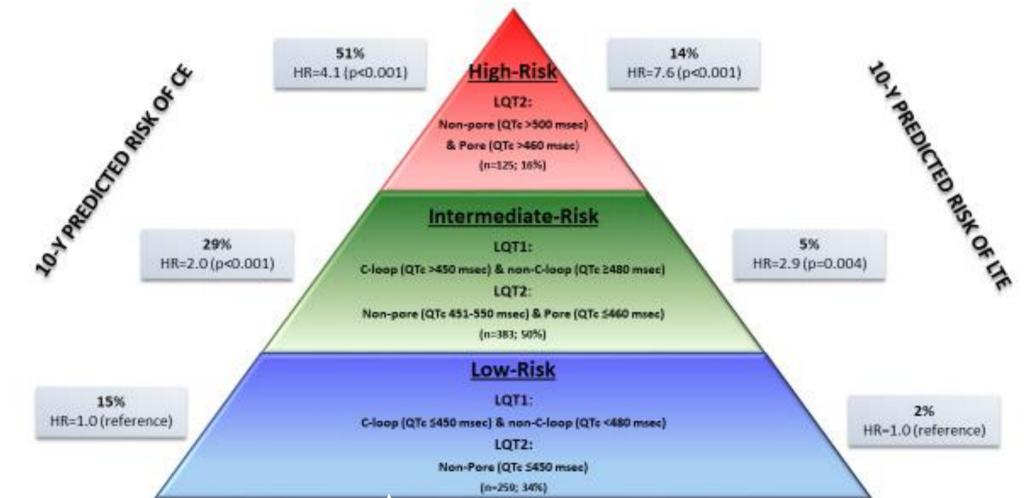


Figure 4: 10-year predicted (p) risk of outcomes with the corresponding observed (o) Kaplan-Meier rates\*

A. Endpoint: Cardiac events

B. Endpoint: Life-threatening events

