Title Page

Title of Project: Dissemination and Implementation of QT Risk Clinical Decision Support.

Principal Investigator: Daniel C Malone, PhD, FAMCP

Other Team Members:

Corneliu Antonescu, MD
Craig Heise, MD
James Tisdale, PharmD,
Raymond Woosley, MD, PhD
Sheila Gephart, RN, PhD
Tyler Gallo, PharmD
Kissy Black
Malinda Tan, PharmD
Maria Wright
John Bennett
Gisele Dee, MS

Inclusive Dates of Project: 04/01/2019 – 03/31/2022

Federal Officer: Edwin Lomotan, MD

Acknowledgment of Agency Support: The project described was supported by grant number R18 HS026662 from the Agency for Healthcare Research and Quality (AHRQ). Thank you to AHRQ for their support. The contents of this report are solely the responsibility of the authors and do not represent the official views of AHRQ.

Grant Award Number: R18 HS026662

Structured Abstract

Purpose: The major goals were to: 1) adapt and disseminate cardiac QT corrected (QTc) risk score (RS) clinical decision support (CDS) advisory; 2) educate clinicians about torsades de pointes (TdP) and associated risk factors; and 3) evaluate the QTc-RS CDS advisory implementation across 30 hospitals.

Scope: Develop a user-centered design CDS advisory for risk of prolonged QTc and torsades de pointes (TdP) based on a validated QTc-RS, develop and deliver educational materials, and evaluate the effectiveness of the advisory.

Methods: A user-centered process was conducted to design and evaluate the CDS. The advisory was implemented in 30 facilities and data were collected on clinician response as well as pre-post implementation mortality.

Results: Over an 8-month period, 7794 QTc-RS advisories were issued. Antibiotics were the most frequent trigger of the advisory (33.1%). At least one action was taken within the advisory window for 2700 (34.6%) of the advisories. The most frequent action taken was ordering an ECG (20.3%). Incoming medication orders were cancelled in 10.2%. Implementation of the advisory was associated with lower inpatient mortality compared to the pre-implementation (OR=0.61, 95%CI:0.49-0.76).

Key Words: clinical decision support, torsades de pointes, prolonged QTc

Purpose

Torsades de Pointes (TdP), is a life-threatening arrhythmia associated with the prolongation of the heart rate-corrected QT (QTc) interval on the electrocardiogram (ECG). Specifically, TdP is polymorphic ventricular tachycardia preceded by QTc prolongation and usually manifesting as short bursts of ventricular contractions between 160 and 250 beats per minute that occur in rapid succession. Further, every 10 millisecond (ms) increase in the QTc interval increases the risk of TdP by 5 to 7%. TdP particularly manifests in hospitalized patients with multiple risk factors including heart failure, female sex, advanced age, and electrolyte abnormalities. In fact, up to 28% of the patients admitted to cardiac care units have QTc > 500 ms, the threshold for highest risk of TdP. Unfortunately, the risk of TdP is often not evaluated or addressed by clinicians due to the complexity of the precipitating factors. Nonetheless, a QTc-RS clinical decision support (CDS) algorithm can estimate the patient's risk for QTc prolongation and assist in mitigating the risk of TdP. This proposal describes a health information technology research project that disseminated and implemented a QTc-RS in a non-profit network of 30 facilities located in six western states that serve rural and urban communities. The specific aims of the project were:

Aim 1: Adapt, implement, and disseminate a QTc-RS CDS in rural and urban facilities across varying acuity levels within inpatient care facilities;

Aim 2: Develop and deliver an educational program on QTc interval prolongation, Torsades de Pointes, and the QTc-RS CDS to health professionals practicing in inpatient environments;

Aim 3: Evaluate the effectiveness of a QTc-RS CDS with respect to process changes within facilities, patient focused clinical outcomes, and end-user satisfaction.

Scope

The primary scope of activities of this grant are outlined below under each specific aim.

Aim 1: Adapt, implement, and disseminate a QTc-RS CDS in rural and urban facilities across varying acuity levels within inpatient care facilities.
Problem: Many patients receive medications with known risk of prolonged QTc and are therefore at risk for TdP in inpatient settings. *Solution:* Using a user-centered design approach that incorporates provider input, we developed a CDS advisory called a QTc-RS that calculates a score predictive of prolonged QTc. We conducted an evaluation of the advisory with physicians and then implemented and disseminated the CDS in 30 facilities.

Aim 2: Develop and deliver an educational program on QTc interval prolongation, Torsades de Pointes, and the QTc-RS CDS to health professionals practicing in inpatient environments
Problem: There is a serious deficiency in the understanding held by healthcare providers regarding the clinical importance of medication-induced QT prolongation. Surveys have found that over 20% of physicians do not know what the QT interval is and why it should be considered when prescribing drugs. More importantly, an alarming 67% of physicians cannot recognize a prolonged QT or accurately measure the QT interval. *Solution:* We created an educational program that was accredited for continuing medical education and delivered this program in-person at 11 hospitals (broadcasted live to 4 other facilities) prior to the outbreak of COVID-19. We also developed enduring educational materials and have them available for any individual to review on the CredibleMeds.org website.

Aim 3: Evaluate the effectiveness of a QTc-RS CDS with respect to process changes within facilities, patient focused clinical outcomes, and end-user satisfaction.
Problem: Many CDS programs often fail to achieve their objectives because they are too sensitive and provide too many alerts to busy clinicians, creating alert fatigue. Also, most CDS are not directly actionable and require clinicians to interrupt their workflow to address the CDS. *Solution:* A QTc-RS clinical decision support advisory incorporating a validated risk score was implemented using patient information obtained from electronic medical records. The QTc-RS was automatically calculated in the background each time an order for

medication with known risk of TdP was initiated. QTc-RS advisory clinical decision support alerted clinicians placing orders for medications with known risk of TdP among high-risk patients who had a QTc risk score ≥ 12; the clinicians then can take action to mitigate the risk. Implementation of a QTc-RS advisory clinical decision support results in a significant reduction in hospital mortality across rural and urban intensive care unit facilities.

The project aligned with the Agency for Healthcare Research and Quality mission and research priorities by improving the quality and safety of health care.

Methods

Aim 1:

Programming of the computer-based QT CDS was performed in the Cerner (Kansas City, Missouri) Millenium® EHR within Banner Health (Phoenix, Arizona). This health system includes now 30 hospitals (28 at the initiation of the study) mostly in the southwestern United States. The QTc risk advisory was programmed as a Cerner Discern® advisory to increase its functionality within the EHR.

Prior to implementation, we conducted end-user evaluation of the advisory with 4 physicians at a tertiary facility. A test patient profile was created and clinicians were asked to simulate placing an order for a medication with a known risk of TdP that triggered the CDS to display to the clinicians. Using a think-aloud protocol, participants were asked to verbalize their thoughts and actions when reading and responding the warning.

The advisory algorithm to evaluate a patient's risk score for excessive QT prolongation is the ordering of a medication on the CredibleMeds® "Known Risk" list of drugs, which includes medications that prolong the QT interval and are clearly associated with a risk of TdP, even when taken as recommended. [1] When a "Known Risk" drug is prescribed, a Tisdale QT risk score is calculated by the computer. Display of the QTc-RS advisory can be pre-empted by pre-existing QT drug-drug interaction alerts that are part of the Multum medication clinical decision support (mCDS) that is built into the Cerner EHR and provided by the vendor. If the mCDS QT drug interaction alert appears and an offending medication is discontinued, the QTc-RS advisory will not display. If the drug mCDS alert is disregarded and the QT-prolonging medication continues to be ordered with the risk threshold achieved, the QTc-RS advisory appears.

Implementation of the QTc-RS risk advisory was approved by the health system's Pharmacy and Therapeutics Committee, Hospital Medicine Clinical Consensus Group, and Critical Care Clinical Consensus Group. Prior to implementation of the advisory, data on the distribution of Tisdale QT risk scores of Banner patients were evaluated to determine the frequency for different threshold scores that would trigger the advisory. Based on this distribution, a Tisdale QT risk score cut-off of >12 was chosen, which represents approximately 5% of inpatients with the highest risk of QT prolongation within the Banner Health population and, based on the prior data with the score, should identify only a high-risk population.

After implementation, clinicians who received the QTc-RS advisory were subsequently asked to complete an anonymous survey requesting their feedback. The survey link was sent via email in April – May, 2020. Conduct of this study was approved by the University of Arizona Institutional Review Board and a waiver of informed consent was granted. The project was also reviewed by the University of Utah IRB as well. This survey included demographic characteristics and multiple-choice questions pertaining to the QTc-RS risk advisory. Descriptive statistics were used to analyze the data.

Aim 2:

We conducted a cross-sectional study that evaluated healthcare professional self-reported knowledge on the QTc interval and the changes in their knowledge after attending a continuing medical education program (CME) on prolonged QTc and TdP. The Institutional Review Boards at the University of Utah and the University of Arizona approved the project. The program was accredited for both physician CME and continuing pharmacy education (CPE). We asked participants who attended a 1-hour CME program we to complete a

program evaluation and knowledge test at the end of the program. The knowledge test contained questions related to interpreting an ECG, multiple choice questions about QT intervals, medications that affect the QT interval, and risk factors for prolonged QTc. Respondents also rated their ability to identify the QT interval. Survey also collected demographic information.

Subjects: Participants included those who attended in-service educational program on QTc prolongation and risks of TdP at medical facilities associated with a multi-hospital organization located in six western states in the United States. Participation in the educational session was voluntary and subjects were not provided any additional incentives beyond obtaining either CME or CPE credit. We delivered the program in-person at 11 acute care institutions in Arizona, Colorado, and Nevada starting in July 2019 through February 2020. Participants could also attend the program virtually for remote facilities located in California and Arizona. The delivery of the program was coordinated through a site-specific individual. Hospitalists, attending physicians, fellows, residents, nursing, and pharmacy personnel were invited to attend. For persons attending remotely, a site coordinator collected completed CME/CPE forms as well as knowledge tests and program evaluation materials. Study-related data was collected anonymously and separately from CME/CPE credit.

Intervention: A physician and/or pharmacist delivered the one-hour CME/CPE program in-person at each medical facility over a 6-month period. The program focused on cardiac electrophysiology, QTc interval measurement, QTc prolongation and its association with TdP, risk factors for TdP, medications associated with known risk of TdP, QTc-RS clinical decision support (CDS), and management options. The content of the program was developed by a group of experts in prolonged QTc and medication induced TdP. These experts included physicians, pharmacists, and nurses, as well as individuals with over 20 years of experience in developing CME/CPE programs. Participants were encouraged to ask questions during and after the presentation. Many presentations occurred in classroom or conference room with a roundtable format that encouraged participation.

Outcomes: At the conclusion of the CME/CPE program, we asked participants to complete a knowledge test based on the content of the program (the complete survey is available as Supplemental Digital Appendix 1) and consisted of two short-answer questions related to identifying the QT interval on an ECG and calculating the rate-corrected QTc interval, seven multiple choice questions related to prolonged QTc and TdP, as well as medications and management strategies for persons at risk for prolonged QTc. Participants also completed a before/after self-assessment of knowledge about identifying prolonged QTc, awareness of risk factors, ability to measure the QT interval, resources related to medications that affect the QT interval, and management of patients with prolonged QTc. Response choices for the self-rated abilities were weak, fair, good, and very good. The self-assessment section included side-by-side ratings for before and after attending the program. Attendees were informed that participation in the knowledge test was voluntary and a written consent document was provided. Subjects were given the opportunity to ask questions about the study prior to completing the knowledge tests. Knowledge tests were scored at a latter point in time.

The primary outcome of interest included the changes in self-reported knowledge and awareness of QTc interval, risk factors and prolonged QTc management before and after the educational program. Participants' performance on the QTc knowledge questionnaire were also outcomes of interest. We also collected participant demographic including type of profession/discipline (i.e, physician attending, physician fellow or resident, nurse practitioner, pharmacist, nursing, other) and specialty (i.e, hospitalist, internal medicine, cardiology, surgeon, emergency medicine, family medicine, other). We used descriptive statistics to describe frequency distribution of participant demographics, self-assessed awareness, knowledge of QTc intervals, and performance on the QTc knowledge test questionnaire.

We also created enduring materials about prolonged QTc and the advisory. Topics covered included how to measure the QT interval, known risk factors for TdP, recognizing the medications that pose a risk of QT prolongation, and clinical decision support for the TdP risk advisory. The content is available at the Credible Meds website (https://www.crediblemeds.org/index.php?cID=639). The materials include a short, narrated video for each topic, PDF of the slides, a post-test for respondents to self-assess their knowledge, and a glossary of terms. Over time we have tracked the number of visits to the materials, including what pages were visited and the region of the world the computer was located. No personally identifiable information was collected from individuals visiting the enduring materials.

Aim 3:

The advanced QTc-RS CDS tool was ultimately implemented across a health system comprising 30 hospitals in 6 western states in the United States. The TdP risk CDS tool was programmed within the Cerner (Kansas City, MO) Millennium® electronic health record (EHR) and designed to appear when clinicians attempt to order a medication with a CredibleMeds.org "Known Risk of TdP" for inpatients who had a modified Tisdale QT risk score ≥12. The advisory could potentially be pre-empted and not displayed if alternative DDI alerts on the EHR platform (Multum medications CDS incorporated in the Cerner EHR and provided by the vendor) led to discontinuing a medication order that would otherwise evoke the QTc-RS advisory. The advisory presented the clinician with the patient's QT risk score, those factors contributing to the score, and relevant single click management options including 1) ordering a routine or STAT ECG, 2) ordering electrolyte replacement protocols conditionally appearing if a patient is deficient (magnesium < 2 mEq/L, potassium < 3.5 mmol/L, calcium < 7.5 mg/dL, or ionized calcium < 4.5 mg/dL), and 3) cancelling incoming or existing medication orders for medications with a known risk of TdP. Incoming medications were those that evoked the TdP CDS and existing medications were those that the patient had already been receiving.

Data were collected retrospectively for advisories provided between April 2020 through December 2020. We evaluated the actions taken by clinicians in response to the advisory, categorized by drug class evoking the advisory. Because ondansetron is frequently ordered in the inpatient setting as an "as needed" medication, it was placed in its own class for analysis. A chi-square statistic was calculated for differences in rates of each action taken between each medication class. Logistic regression was performed to calculate odds ratios for cancelling the incoming medication order comparing each medication class to the class with the highest frequency of evoking the CDS. The α-value was set at 0.05 for all analyses.

We also conducted an analysis of pre-post implementation of the QTc-RS by collecting data from electronic health records (EHR) from January 1, 2020 through March 30, 2020 (pre-implementation period), and from April 1, 2020 through December 31, 2020 (post-implementation period). To control for patient acuity, we restricted data to ICU patients with QTc-RS ≥ 12 were selected from the identical facilities and units for both pre-implementation and post-implementation cohorts. Descriptive statistics were used to evaluate risk factors, the number of known TdP medications, and inpatient mortality. Comparisons were performed using Chi-square test for categorical variables (death, risk factors: medications with known risk of TdP, HF, sepsis, AMI, serum K+, loop diuretics, female, age > 67 years, QTcF > 500 ms) and a generalized linear model with gamma distribution and log-linked to handle skewness of length of stay. Logistic regression was also conducted to assess the impact of implementation of QTc-RS advisory on inpatient mortality as well as the impact of each attribute the QTc-RS on mortality. Statistical tests were performed using SAS 9.4 version (Cary, North Carolina).

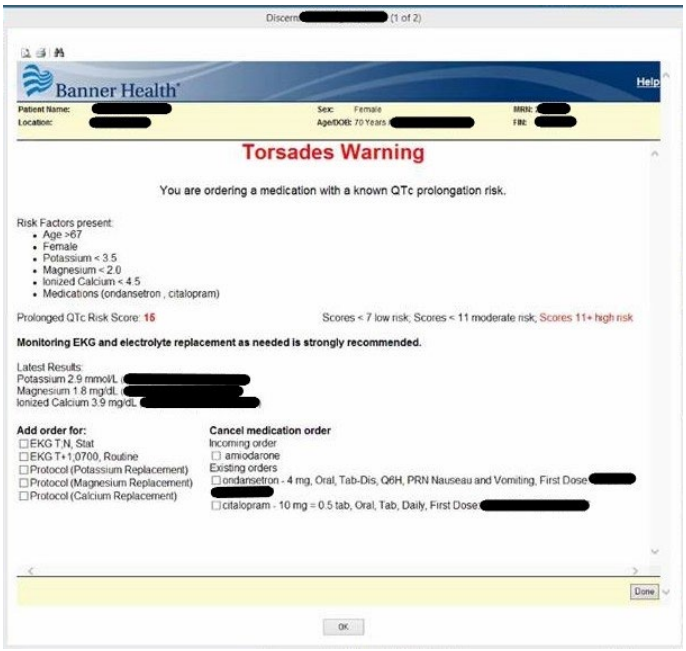
We also evaluated clinician satisfaction with the advisory. Clinicians who received the QTc-RS advisory were subsequently asked to complete an anonymous survey requesting their feedback. The survey link was sent via email during the period April through May 2020. Clinicians were only sent one email to provide feedback, even though they may have received many advisories. Participants were asked to evaluate the advisory with respect to: 1) providing better care; 2) information in the advisory being accurate; 3) appearing at a good place in the work flow; 4) frequency of the advisory; and 5) statement that the advisory did not apply to their patient. Reponses were collected using Likert-type responses from strongly disagree to strongly agree. This survey included demographic characteristics. Descriptive statistics were used to analyze the data.

Results

Aim 1:

The QTc-RS advisory was implemented on April 1, 2020 across all institutions within the Banner system. While our plan was for a staged roll-out of the advisory, the Covid-19 pandemic derailed those plans because of broad interest in hydroxychloroquine being used to treat the virus. Hydroxychloroquine is a medication with a known risk for TdP, hence the leadership of Banner was keen on having the advisory available to all institution as soon as possible. Figure 1 below displays QTc-RS and includes the Tisdale score, the patient's risk factors that contribute to the risk score, most recent relevant laboratory results, and gives providers options such as 1)

ordering electrocardiograms, 2) ordering electrolyte replacement by protocols if the patient is deficient, or 3) cancelling the current order or existing “Known Risk” QT interval-prolonging medications.



Over a period of 9 months, there were 7,794 QTc-RS risk advisories displayed to clinicians, and these advisories serve as the basis for our analyses in Aim 1 and Aim 3. That said, the QTc-RS continues to operate within the Banner Healthcare System as of the date of this report (June 2022).

Basic demographics of patients for whom the advisory appeared are shown in Table 1. The mean age was 70 years (SD ± 15) and 927 (12%) patients expired in the hospital.

Table 1. Characteristics of patients with QTc Risk Score 12 or greater

Characteristic	Value
Total number of patients (n)	7794
Mean age in years (SD)	70 (15)
Number of females (n, %)	4647 (59.6%)
Median modified Tisdale QT risk score (range)*	12 (12-21)
COVID-19 (+)	963 (12.4%)
Long QT syndrome diagnosis code (ICD-10)	252 (3.2%)
Expired in hospital	927 (11.9%)

The distribution of medications triggering the CDS are shown in Table 2. Antibiotics were the most frequent medications evoking the TdP risk advisory (n = 2578, 33.1%), followed by ondansetron (n = 2530, 32.5%).

Table 2. Classes of medications that evoked a QTc risk score advisory

Medication class	Frequency (% of all TdP risk advisories)	Known risk of TdP medications in class (in descending order of frequency within class)
Antibiotic	2578 (33.1)	Azithromycin, levofloxacin, ciprofloxacin, erythromycin, moxifloxacin, clarithromycin
Antiemetic	2530 (32.5)	Ondansetron
Antiarrhythmic	980 (12.6)	Amiodarone, sotalol, flecainide, dofetilide, dronedarone, ibutilide, quinidine, procainamide
Other	917 (11.8)	Propofol, escitalopram, citalopram, donepezil, methadone, hydroxychloroquine, cilostazol, oxaliplatin
Antipsychotic	443 (5.7)	Haloperidol, chlorpromazine
Antifungal	346 (4.4)	Fluconazole, voriconazole, posaconazole, pentamidine, itraconazole

Table 3 provides a distribution of the responses by clinicians to the advisory by medication class that triggered the warning. At least one immediate action was taken within the advisory window for 2700 (34.6%). In general, the most common action taken was ordering a routine electrocardiogram (ECG), N=1584 (20.3% of all warnings). There were 1385 medication orders cancelled through the advisory with 793 (10.2%) cancellations of incoming medications and 592 of existing medications (1, 2 or 3 existing medications were cancelled 570, 17, and 5 times, respectively). Incoming orders for ondansetron were the most likely to be cancelled (n = 458, 18.1%) as compared to all other medication classes ($p<0.05$), with orders for other drug classes being cancelled between 4.7% and 7.4% of the time (Table 3). Ordering electrolyte replacement protocols was the least frequent action taken. Among the electrolyte replacement protocol ordering, calcium replacement in patients with the incoming medication an antibiotic was the least frequent (n = 5, 0.2%) and potassium replacement with the incoming medication ondansetron was the most frequent (n = 107, 4.2%).

Table 3. Actions taken in response to QTc risk score advisories categorized by drug class

Action Taken	Antibiotic (n, %)	Antipsychotic (n, %)	Antifungal (n, %)	Antiarrhythmic (n, %)	Ondansetron (n, %)	Other (n, %)
Incoming drug order cancelled	173 (6.7)	22 (5.0)	25 (7.2)	72 (7.4)	458 (18.1)	43 (4.7)
Existing drug order cancelled	230 (8.9)	48 (11.2)	24 (6.9)	106 (10.8)	118 (4.7)	66 (7.2)
STAT ECG ordered	37 (1.4)	18 (4.1)	11 (3.2)	29 (3.0)	19 (0.8)	25 (2.7)
Routine ECG ordered	470 (18.2)	93 (21.0)	79 (22.8)	230 (23.5)	351 (13.9)	222 (24.2)
Potassium replacement protocol ordered	48 (1.9)	3 (0.7)	3 (0.9)	17 (1.7)	107 (4.2)	23 (2.5)
Magnesium replacement protocol ordered	38 (1.5)	3 (0.7)	4 (1.2)	22 (2.2)	60 (2.4)	20 (2.2)
Calcium replacement protocol ordered	5 (0.2)	1 (0.2)	1 (0.3)	4 (0.4)	5 (0.2)	13 (1.4)

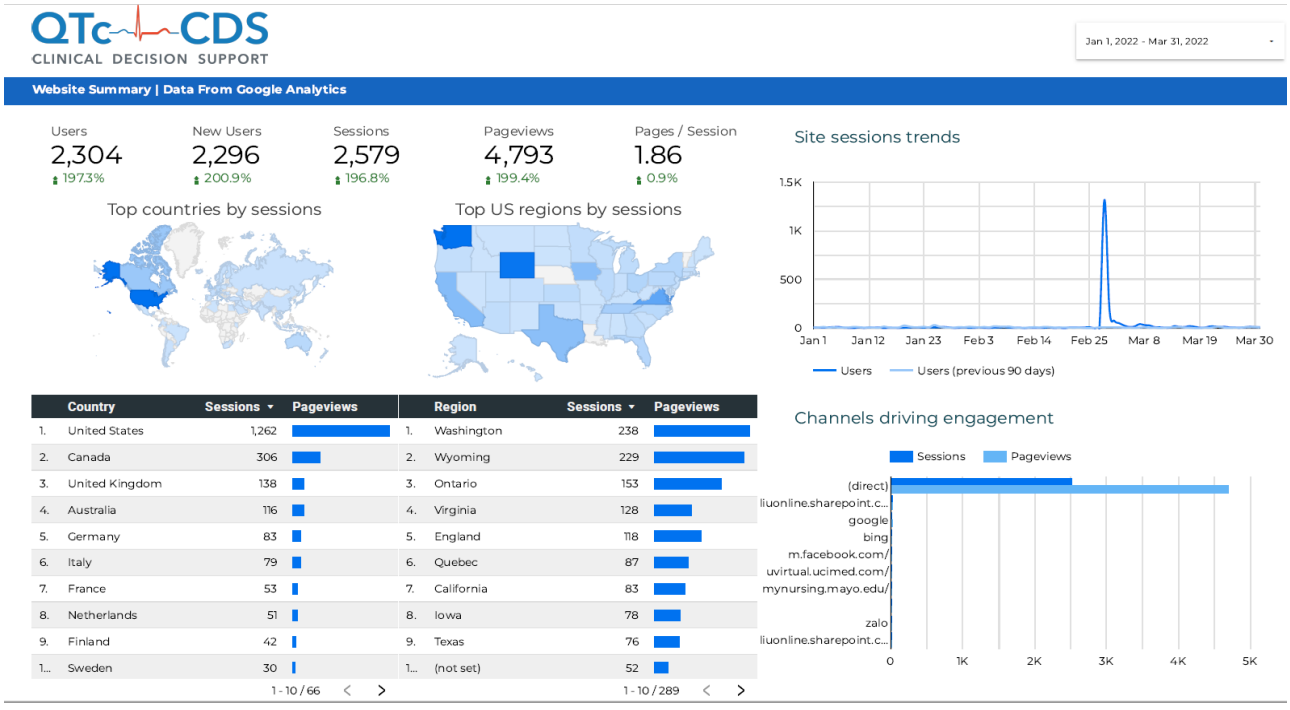
*For each action taken, there was a statistically significant difference in the action taken by medication class ($p<0.05$ for magnesium replacement protocol ordered, $p<0.0001$ for all other actions). ECG = electrocardiogram.

Aim 2

Presentations to various healthcare facilities were conducted starting in July 2019 and continued until March 2020, when the Covid-19 outbreak effectively shut down access to facilities. In-person delivery of the educational modules were provided to the following Banner facilities (listed by location): Page, Payson, Fallon NV (broadcast to facility in California), Greeley CO (broadcast to other Northern Colorado facilities), Estrella, Casa Grande, Phoenix, and Mesa, Arizona.

Across these facilities, 49 participants completed all questions on the knowledge test. Among the 48 participants reporting professions/disciplines, 21 (44%) were pharmacists, 11 (23%) were attending physicians, 5 (10%) were nurses and 4 (8%) were physician fellows or residents. The most common reported specialty was other 19 (44%), followed by family medicine 8 (18.6%), and emergency medicine 5 (11.6%). Approximately 70% and 65% of participants reported weak or fair on the ability to identify QTc interval and measure QTc interval, respectively, prior to the CME/CPE activity. After participating in the CME/CPE program, the majority of participants reported good or very good on awareness of QTc risk factors (93%), ability to identify prolonged QTc interval (85%), and ability to manage patients with prolonged QTc interval (81%). These corresponded to a 61%, 57% and 49% improvement, respectively, from prior to participating in the CME/CPE program.

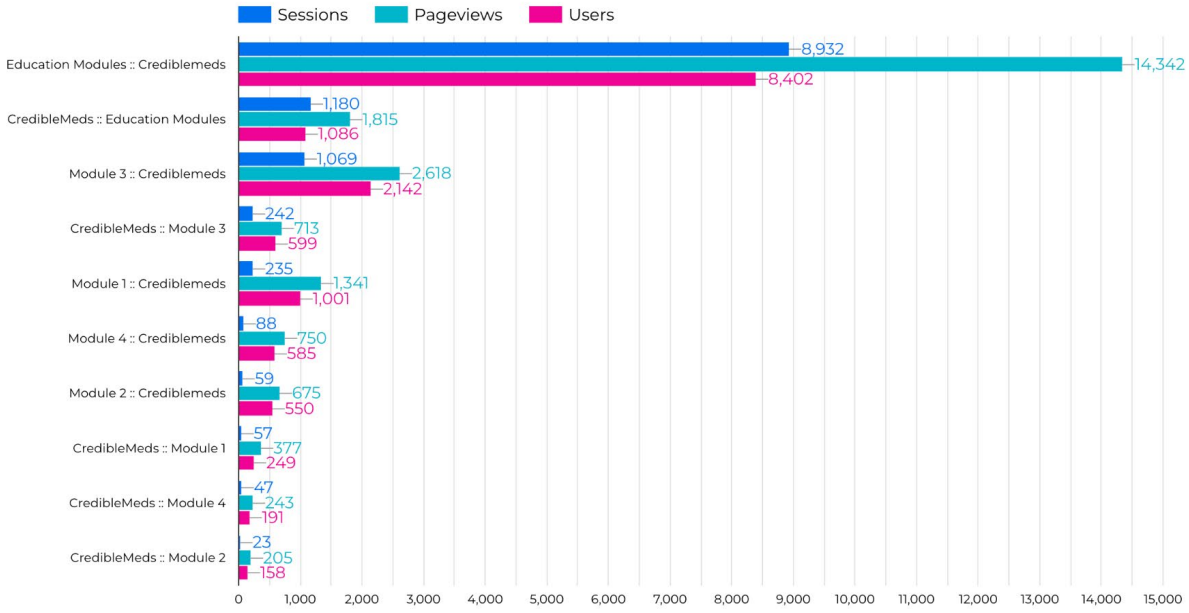
For the two short answer questions, nearly 60% and 80% of participants correctly identified the Q wave on the electrocardiogram and the duration of the uncorrected QT interval. For the seven multiple choice test questions, the overall correct mean (SD) score was 4.4 (1.3). Of the 49 participants, nearly all (98%) of them correctly selected the appropriate action not to take when patients were identified with a prolonged QTc interval. The vast majority knew that there are over 50 medications that have a known risk of TdP (86%) and were able to distinguish medications that are not likely to affect the QTc interval (88%). However, only half of the participants correctly answered a question related to risk factors for TdP (51%) and correctly identified a medication that was likely to affect the QTc interval (53%). For the enduring materials that were made available on the CredibleMeds.org website, over the course of project we had many page views. The figures below display the results for a combination of the last 3 months of the project and over the entire project duration.



QTc CDS
CLINICAL DECISION SUPPORT

Oct 1, 2020 - Jun 26, 2022

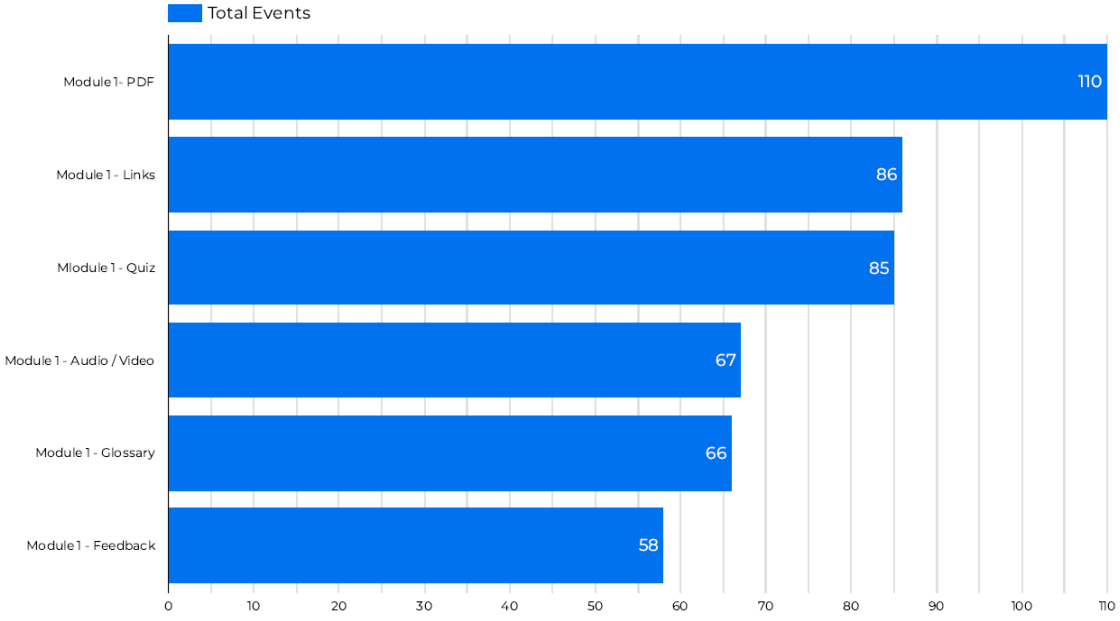
Website Pages Performance Summary | Data From Google Analytics



QTc CDS
CLINICAL DECISION SUPPORT

Jan 1, 2022 - Mar 31, 2022

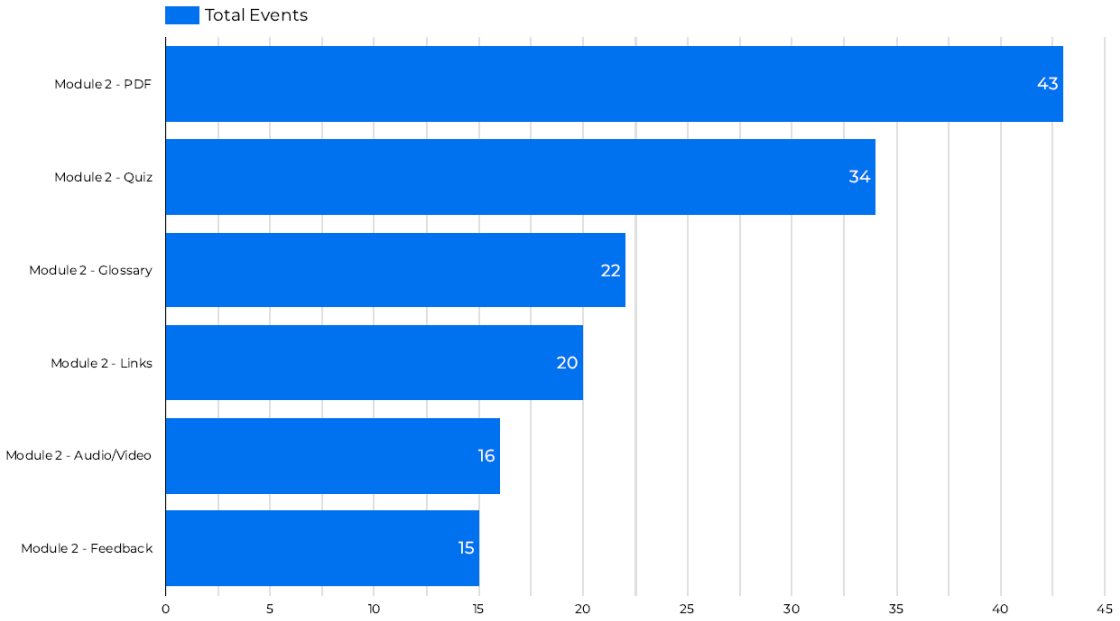
Module 1 Content Engagement | Data From Google Tag Manager



QTc CDS
CLINICAL DECISION SUPPORT

Jan 1, 2022 - Mar 31, 2022

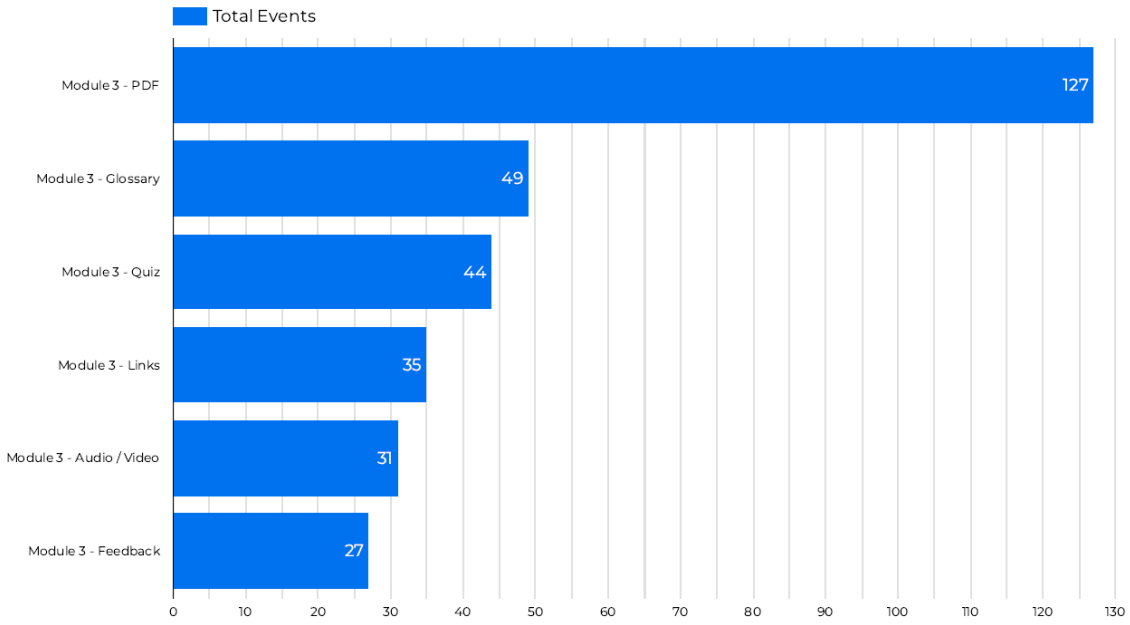
Module 2 Content Engagement | Data From Google Tag Manager



QTc CDS
CLINICAL DECISION SUPPORT

Jan 1, 2022 - Mar 31, 2022

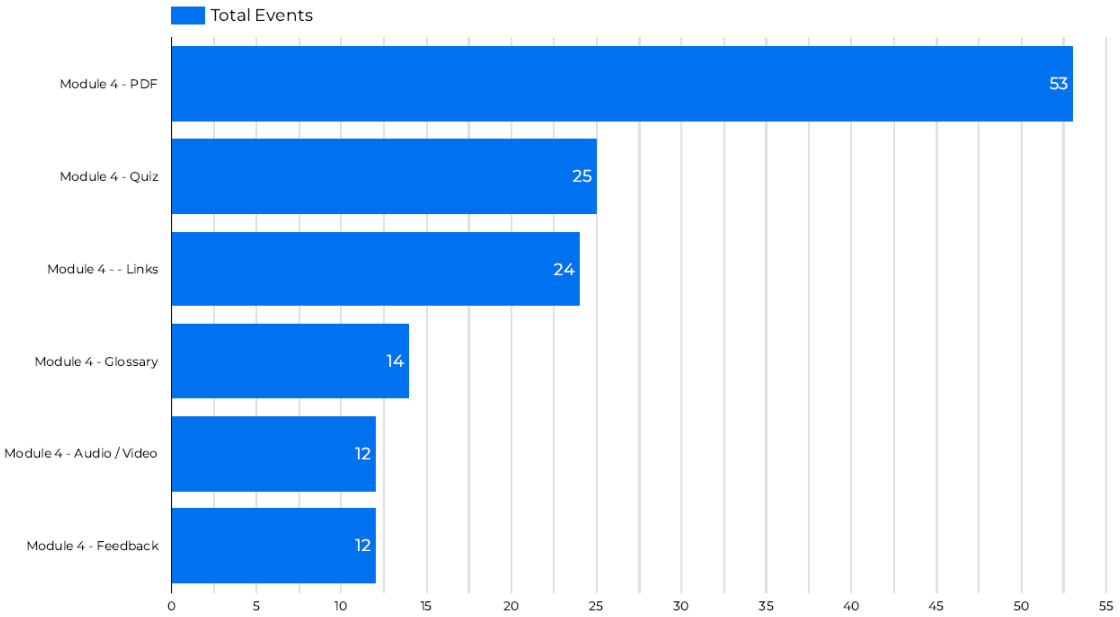
Module 3 Content Engagement | Data From Google Tag Manager



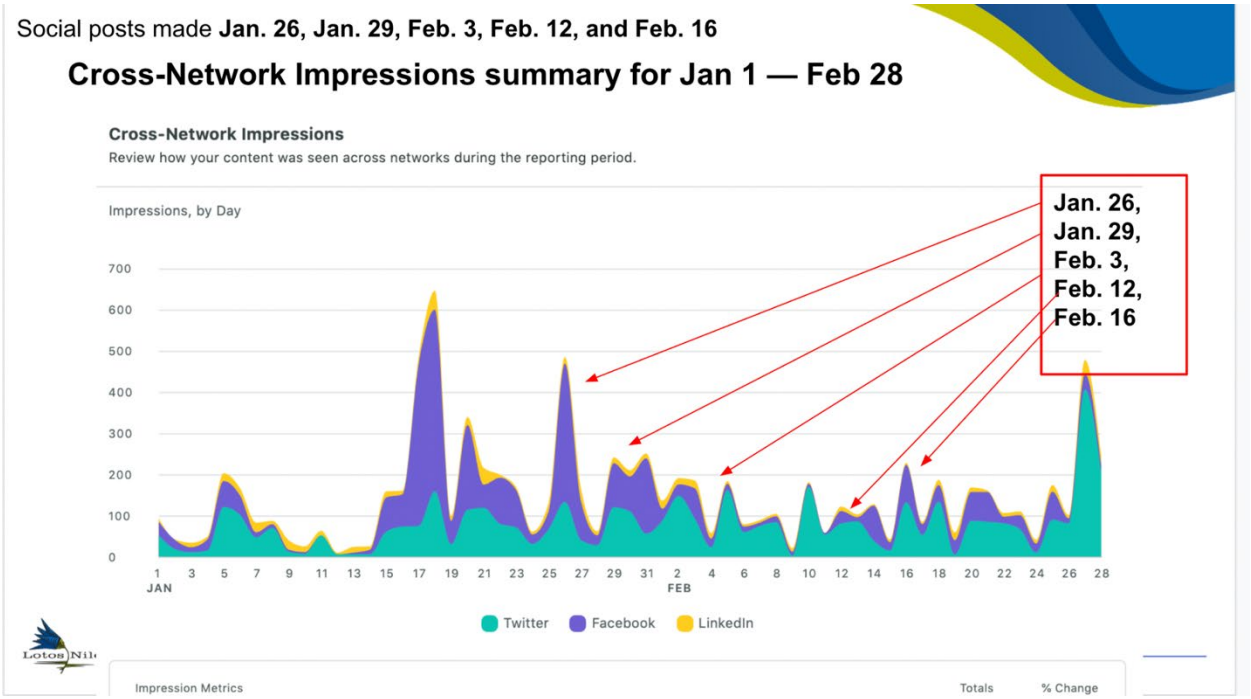
QTc CDS
CLINICAL DECISION SUPPORT

Jan 1, 2022 - Mar 31, 2022

Module 4 Content Engagement | Data From Google Tag Manager



Social media posts advertising the education modules also drove a 28% increase in total impressions overall for CredibleMeds's Twitter, Facebook, and Linkedin accounts with a high level of engagement during the first two months of availability for the modules.



Aim 3

The effectiveness of the QTc-RS was evaluated by examining a 3-month period prior to implementation of the advisory and then an 8-month period after implementation. To reduce potential bias, we matched pre- and post-data by facilities contributing to both periods and also limited the analysis to patients receiving care in the ICU. The QTc-RS was calculated for 620 unique ICU patients during the pre-implementation period and 3,112 ICU patients during the post-implementation timeframe. The proportion of patients receiving 2 or more medications with a known risk of TdP was 82.4% as compared to 9.9% after implementation of the QT-RS advisory ($p<0.0001$) (see Table 1). However, the pre-implementation cohort had a higher frequency of sepsis, acute myocardial infarction, and QTcF > 500 ms compared to the post-implementation cohort ($p<0.0001$) (Table 1). The two cohorts were similar with respect to the prevalence of heart failure, serum $K^+ \leq 3.5$ mEq/L, exposure to diuretics, proportion of females, and age > 67 years (Table 4).

Table 4: Patient Characteristics

Characteristic	Pre- implementation of QTc-RS advisory n=620	Post-implementation of QTc-RS advisory n=3112	P-value
Expired during stay	137 (22.1)	433 (13.9)	<0.0001
Length of stay (mean ± SD)	11.8 ± 10.2	7.9 ± 9.1	<0.0001
Length of stay (median, interquartile range)	8.9 (4.6,16.2)	5.3 (2.7,9.7)	
Risk factors			
Medications with known risk of TdP			
0 medication	1 (0.2)	1260 (40.5)	<0.0001
1 medication	108 (17.4)	1544 (49.6)	
≥ 2 medications	511 (82.4)	308 (9.9)	
HF	212 (34.2)	992 (31.9)	0.26
Sepsis	551 (88.9)	2162 (69.5)	<0.0001
AMI	532 (85.8)	69 (2.2)	<0.0001
Serum $K^+ \leq 3.5$ mEq/L	147 (23.7)	729 (23.4)	0.88
Loop diuretics	140 (22.6)	670 (21.5)	0.56
Female	348 (56.1)	1750 (56.2)	0.96
Age > 67 years	401 (64.7)	2065 (66.4)	0.42
QTcF > 500 ms	147 (23.7)	422 (13.6)	<0.0001

AMI = Acute myocardial infarction; QTcF = Fridericia-corrected QT interval; HF = Heart failure; QTc-RS = Corrected QT interval risk score; TdP = Torsades de pointes.

Multiple logistic regression was conducted to predict inpatient mortality. The results of the analysis found that the post-implementation cohort had a lower inpatient mortality compared to the pre-implementation cohort (Odds ratio (OR) = 0.61; 95% CI: 0.49-0.76) (Table 2). To further evaluate which components of the QTc-RS might influence mortality, we conducted a separate multivariate analysis. After adjusting for all individual risk factors in the same multivariate logistic regression model, post-implementation of QTc-RS advisory was not associated with lower mortality (OR =0.69, 95% CI, 0.41-1.14). In addition, among all risk factors, only sepsis and age > 67 years were significantly associated with increased mortality (OR = 1.53, 95% CI, 1.67-2.01), and (OR = 1.25, 95% CI, 1.02-1.53), respectively (Table 5).

Table 5: Multivariate logistic regression model predicting mortality by QTc-RS risk factors

Variable	Odds Ratio (95% CI)
Implementation of QTc-RS advisory	0.69 (0.41-1.14)
1 medication with known risk of TdP	0.99 (0.80-1.22)
≥ 2 medications with known risk of TdP	0.87 (0.62-1.22)
HF	0.94 (0.75-1.19)
Sepsis	1.53 (1.17-2.01)
AMI	1.26 (0.82-1.94)
Serum K^+ ≤ 3.5 mEq/L	0.81 (0.64-1.03)
Diuretics	0.88 (0.70-1.11)
Female	0.96 (0.80-1.16)
Age > 67 years	1.25 (1.02-1.53)
QTcF > 500 ms	1.24 (0.95-1.61)

AMI = Acute myocardial infarction; HF = Heart failure; QTcF = Fridericia-corrected QT interval; QTc-RS = Corrected QT interval risk score; OR_{adj} = Adjusted odds ratio; TdP = Torsades de pointes

Based on these results, we conducted several subgroup analyses to understand whether implementation of QTc-RS could potentially be more helpful in the sepsis cohort and age > 67 years cohort. A subgroup analysis of patients who had sepsis also showed that implementation of QTc-RS advisory was not statistically associated with lower mortality, and among all the risk factors, only year of age > 67 was associated with increased mortality (OR = 1.27, 95% CI, 1.01-1.58). Another subgroup analysis of patients > 67 years of age found that implementation of QTc-RS advisory was associated with lower mortality (OR = 0.52, 95% CI, 0.28-0.99), and among all the independent risk factors, sepsis was associated with higher mortality (OR = 1.57, 95% CI, 1.14-2.15).

We also evaluated clinician satisfaction with the advisory. As described above, an email link to the survey was sent to 442 clinicians who received the QTc-RS advisory and 38 responded for a response rate of 8.6%. Among the clinicians who completed the survey, 24 responded that they were an attending physician, 7 were physician residents or fellows, 3 were pharmacists, 1 was a physician assistant, 1 was a nurse practitioner, and 1 was a nurse anesthetist. The most common specialties were hospitalist service (n=18, 47%), internal medicine (n=5, 13%), and pulmonology (n=3, 8%). More survey respondents were associated with community medical centers (n=24, 63%) than with academic affiliated institutions.

Table 6 shows the survey responses related the QTc-RS advisory. Most clinicians agreed that the patient information in the advisory was correct, actions needed to be considered were clearly specified in the advisory, and the advisory appeared at a good place in the workflow. However, almost half of the respondents indicated that the advisory appears too frequently, and more than 1/3 responded that the advisory did not apply to their patient.

Table 6. Clinician survey responses related to the Torsades de Pointes risk advisory

Statement	Strongly disagree, (%)	Disagree, (%)	Agree (%)	Strongly Agree, (%)
This advisory helps me provide better care for my patients.	3 (8)	5 (13)	23 (61)	7 (18)
The patient information included in this advisory was correct.	1 (3)	3 (8)	25 (68)	8 (22)
The actions I need to consider are clearly specified in the advisory.	1 (3)	4 (11)	24 (63)	9 (24)
The advisory appeared at a good place in the workflow.	3 (8)	4 (11)	22 (58)	9 (24)
This advisory appears too frequently.	4 (11)	16 (43)	9 (24)	8 (22)
The advisory did not apply to my patient(s).	7 (18)	17 (45)	10 (26)	4 (11)

List of Publications

Publications

Gallo T, Heise CW, Woosley RL, Tisdale JE, Antonescu CA, Gepheart SM, Malone DC. *Clinician Satisfaction With Advanced Clinical Decision Support to Reduce the Risk of Torsades de Pointes* J Patient Safety. 2022 Mar 2. PMID: 35238815 DOI: 10.1097/PTS.0000000000000996

Gallo T, Heise CW, Woosley RL, Tisdale JE, Tan MS, Gephart SM, Antonescu CC, Malone DC. *Clinician Responses to a Clinical Decision Support Advisory for High Risk of Torsades de Pointes*. J Am Heart Assoc. 2022 Jun 7;11(11):e024338. doi: 10.1161/JAHA.122.024338. Epub 2022 Jun 3. PMID: 35656987 DOI: 10.1161/JAHA.122.024338

Pending papers

Tan MS, Heise WC, Gallo T, Woosley RL, Tisdale JE, Antonescu CC, Gephart SM, Malone DC. *Relationship between prolonged QTc risk score and in-hospital mortality across rural and urban inpatient facilities*.

Tan MS, Heise WC, Gallo T, Woosley RL, Tisdale JE, Antonescu CC, Gephart SM, Malone DC. *Evaluation of Educational Program for Prolonged QT Interval and Torsades de Pointes*

Heise CW, Tan MS, Gallo T, Tisdale JE, Woosley RL, Antonescu CC, Gephart SM, Malone DC. *Impact of a QTc risk score advisory on hospital mortality across rural and urban intensive care unit facilities*

Presentations

Tisdale J, Tan MS, Heise CW, Gallo T, Woosley RL, Antonescu CC, Gephart SM, Malone DC. *Relationship Between Increased QTc Risk Score and In-Hospital Mortality*. American Heart Association (AHA) annual meeting, Boston MA, November 2021

Gallo T, Heise CW, Tan MS, Tisdale JE, Woosley RW, Antonescu CC, Gephart SM, Malone DC. *Medications Evoking Torsades de Pointes Clinical Decision Support and Clinician's Responses to an Advisory.* American College of Clinical Pharmacy annual meeting, Phoenix AZ, October 20, 2021

Gallo T, Heise CW, Wooley RL, Tisdale JE, Antonescu CC, Gephart SM, Malone DC. *Clinician Satisfaction with Clinical Decision Support to Reduce the Risk of Torsades de Pointes*. AMIA Clinical Informatics Meeting (virtual), May 23, 2021