

Ventricular repolarization in hospitalized patients with inflammatory bowel disease: a weighted real-world ECG study

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Abstract

Whether inflammatory bowel disease (IBD) is accompanied by a longer QT interval is unsettled: prior clinical studies were small, predominantly involved outpatient or selected populations, and varied in comparators, ECG metrics and findings. We studied hospitalized patients using MIMIC-IV linked to MIMIC-IV-ECG (2008–2019). Adults whose first electrocardiogram of an admission was analysable were included once; patients with an IBD diagnosis code ($n = 1,618$) were compared with inpatients never coded with IBD ($n = 86,913$). Overlap propensity-score weights balanced demographics, heart rate, calendar period, clinical setting and timing of the recording, prior cardiac and kidney disease, and ECG device bandwidth class (all standardized differences < 0.02). Mean Fridericia-corrected QT (QTcF) was 415.5 ms with IBD and 416.7 ms without; the adjusted difference, the single confirmatory outcome, was -1.22 ms (95% CI -2.74 to 0.29 ; $P = 0.11$), and the confidence interval excluded an adjusted mean difference of 5 ms or greater. Fifteen pre-specified supporting analyses gave estimates between -2.3 and $+0.2$ ms. One device bandwidth class was associated with QTcF about 7–9 ms longer. In hospitalized patients selected for electrocardiography, IBD was not associated with a longer mean QTcF after balancing clinical context and accounting for device configuration.

Introduction

Hospitalized patients with inflammatory bowel disease (IBD) may encounter electrolyte depletion, infection and exposure to QT-active treatment, each of which can influence ventricular repolarization[1, 2]. IBD is associated with an increased risk of cardiovascular events[3], a population cohort reported a higher long-term risk of arrhythmia[4], and systemic inflammation has been linked to QT prolongation[5]. Whether the diagnosis itself is accompanied by a longer QT interval in hospital has not been established; an analysis of a national inpatient database found fewer, not more, arrhythmia-related hospitalizations in IBD[6].

Prior clinical studies of the QT interval in IBD differ in population, comparator, ECG metric and result. A longer QTc was reported in 20 patients compared with 18 healthy controls[7], more frequent prolongation of QTc dispersion in 104 patients compared with 47 controls[8], and QTc prolongation in more than 40% of 142 patients in an uncontrolled chart review[9]. Controlled comparisons that included 38 to 175 patients found QTc similar to controls[10–12], as did a study of QRS duration and fragmentation in 217 patients[13], whereas dispersion measures were prolonged in children in remission[14]. Where the correction was stated, these studies used Bazett's formula; the controlled studies compared patients with healthy or symptom-free controls, and several excluded patients with electrolyte disturbance, cardiac disease or QT-active treatment[10, 11, 14].

Three features of the inpatient setting remain insufficiently addressed together: a comparator drawn from other hospitalized patients; control of heart rate, because Bazett's formula overestimates QTc at higher heart rates[15]; and control of the recording device, because automated QT measurements differ systematically between electrocardiograph algorithms[16]. We used a hospital-wide ECG archive linked

to clinical records[17, 18] to estimate, under a protocol frozen before the outcome was examined, the difference in Fridericia-corrected QT between inpatients with and without IBD.

Results

Study population

Of 10,094 admissions with an IBD code and 486,424 admissions of patients never coded with IBD, 2,819 and 159,171 had an analysable first ECG, yielding 1,618 patients with IBD and 86,913 comparators (Fig. 1). Patients with IBD were younger (55.9 vs 59.2 years), more often women (55.7% vs 51.4%), had a higher heart rate (85.7 vs 80.4 bpm), were more often under a medical service, and more often had a previous admission (41.6% vs 19.0%) (Table 1). Crohn's disease accounted for 888 and ulcerative colitis for 728; IBD was the principal diagnosis in 443.

Table 1
Characteristics at the index ECG before and after overlap weighting.

Characteristic	Unweighted			Overlap-weighted		
	IBD (n = 1,618)	Non-IBD (n = 86,913)	SMD	IBD	Non-IBD	SMD
Age, years, mean (s.d.)	55.9 (18.0)	59.2 (18.1)	-0.183	56.1 (18.0)	56.1 (18.0)	0.000
Female, n (%)	901 (55.7)	44,665 (51.4)	0.086	55.5%	55.5%	0.000
Heart rate, bpm, mean (s.d.)	85.7 (21.7)	80.4 (19.7)	0.258	85.6 (21.6)	85.6 (21.6)	0.000
Hours from presentation to ECG, median (IQR)	2.2 (0.3–20.7)	1.1 (0.2–8.1)	0.282 ^a	—	—	0.000 ^a
<i>Calendar period, n (%)</i>						
2008–2010	739 (45.7)	34,255 (39.4)	0.127	45.4%	45.4%	0.000
2011–2013	404 (25.0)	21,951 (25.3)	-0.007	25.0%	25.0%	0.000
2014–2016	308 (19.0)	19,651 (22.6)	-0.088	19.2%	19.2%	0.000
2017–2019	167 (10.3)	11,056 (12.7)	-0.075	10.4%	10.4%	0.000
<i>Location of the ECG, n (%)</i>						
Emergency department	898 (55.5)	55,841 (64.2)	-0.179	55.9%	55.9%	0.000
Ward	621 (38.4)	24,044 (27.7)	0.229	37.9%	37.9%	0.000
Intensive care unit	99 (6.1)	7,028 (8.1)	-0.077	6.2%	6.2%	0.000
<i>Admission type, n (%)</i>						
Emergency or urgent	1,093 (67.6)	49,281 (56.7)	0.225	67.3%	67.3%	0.000
Values are n (%) unless stated otherwise; overlap-weighted columns show weighted means (s.d.) or percentages. SMD, standardized mean difference (IBD minus non-IBD); IQR, interquartile range. Effective sample size after weighting: IBD 1,616.8; non-IBD 48,768.5. Prior diagnoses come from admissions discharged before the index presentation. IBD subtype: Crohn's disease 888, ulcerative colitis 728, both codes 2; IBD was the principal diagnosis in 443. ^a Standardized difference computed on log(1 + hours).						

Characteristic	Unweighted		Overlap-weighted			
	IBD (n = 1,618)	Non-IBD (n = 86,913)	SMD	IBD	Non-IBD	SMD
Observation	395 (24.4)	31,710 (36.5)	-0.265	24.7%	24.7%	0.000
Elective	130 (8.0)	5,922 (6.8)	0.047	8.0%	8.0%	0.000
<i>Admission source, n (%)</i>						
Emergency room	1,086 (67.1)	59,736 (68.7)	-0.035	67.1%	67.1%	0.000
Referral or self-referral	321 (19.8)	14,348 (16.5)	0.086	19.8%	19.8%	0.000
Transfer from another facility	189 (11.7)	10,952 (12.6)	-0.028	11.8%	11.8%	0.000
Procedure site or other	22 (1.4)	1,877 (2.2)	-0.061	1.4%	1.4%	0.000
Emergency-department registration, n (%)	1,283 (79.3)	69,455 (79.9)	-0.015	79.3%	79.3%	0.000
<i>First clinical service before the ECG, n (%)</i>						
None assigned	895 (55.3)	54,518 (62.7)	-0.151	55.7%	55.7%	0.000
Medicine	429 (26.5)	13,141 (15.1)	0.283	26.0%	26.0%	0.000
Cardiac	69 (4.3)	7,273 (8.4)	-0.169	4.4%	4.4%	0.000
Neurological	31 (1.9)	3,024 (3.5)	-0.097	2.0%	2.0%	0.000
Surgical	194 (12.0)	8,957 (10.3)	0.054	12.0%	12.0%	0.000
ICU admission before ECG, n (%)	119 (7.4)	7,960 (9.2)	-0.066	7.4%	7.4%	0.000
Any prior admission in database, n (%)	673 (41.6)	16,547 (19.0)	0.506	40.8%	40.8%	0.000
<i>Diagnoses on prior admissions, n (%)</i>						
Values are n (%) unless stated otherwise; overlap-weighted columns show weighted means (s.d.) or percentages. SMD, standardized mean difference (IBD minus non-IBD); IQR, interquartile range. Effective sample size after weighting: IBD 1,616.8; non-IBD 48,768.5. Prior diagnoses come from admissions discharged before the index presentation. IBD subtype: Crohn's disease 888, ulcerative colitis 728, both codes 2; IBD was the principal diagnosis in 443. ^a Standardized difference computed on log(1 + hours).						

Characteristic	Unweighted		SMD	Overlap-weighted		
	IBD (n = 1,618)	Non-IBD (n = 86,913)		IBD	Non-IBD	SMD
Chronic kidney disease	81 (5.0)	1,753 (2.0)	0.163	4.9%	4.9%	0.000
Heart failure	49 (3.0)	1,188 (1.4)	0.113	3.0%	3.0%	0.000
Coronary disease or prior myocardial infarction	72 (4.4)	2,105 (2.4)	0.111	4.4%	4.4%	0.000
Atrial fibrillation	57 (3.5)	1,657 (1.9)	0.100	3.5%	3.5%	0.000
<i>ECG bandwidth class, n (%)</i>						
0.0005–150 Hz	300 (18.5)	16,705 (19.2)	−0.017	18.7%	18.7%	0.000
0.005–150 Hz	1,196 (73.9)	64,770 (74.5)	−0.014	73.8%	73.8%	0.000
0.05–150 Hz	122 (7.5)	5,438 (6.3)	0.051	7.5%	7.5%	0.000
Values are n (%) unless stated otherwise; overlap-weighted columns show weighted means (s.d.) or percentages. SMD, standardized mean difference (IBD minus non-IBD); IQR, interquartile range. Effective sample size after weighting: IBD 1,616.8; non-IBD 48,768.5. Prior diagnoses come from admissions discharged before the index presentation. IBD subtype: Crohn's disease 888, ulcerative colitis 728, both codes 2; IBD was the principal diagnosis in 443. ^a Standardized difference computed on log(1 + hours).						

Overlap weighting removed these differences: the largest absolute standardized difference after weighting was 0.012, and the effective sample sizes were 1,616.8 and 48,768.5 (Table 1 and Supplementary Fig. S1 online). Device bandwidth class was similarly distributed in the two groups before weighting.

QTcF at the index ECG

Weighted mean QTcF was 415.5 ms (s.d. 30.9) with IBD and 416.7 ms (s.d. 29.0) without (Table 2 and Supplementary Fig. S2 online). In the confirmatory analysis the difference was −1.22 ms (95% CI −2.74 to 0.29; P = 0.11, weighted linear model). The 95% confidence interval excluded an adjusted mean difference of 5 ms or greater in this ECG-selected inpatient population. Re-estimating the weights in each bootstrap resample gave an interval of −2.52 to 0.10 ms.

Table 2
ECG measurements at the index ECG.

Measure	IBD (n = 1,618)	Non-IBD (n = 86,913)	IBD, overlap-weighted	Non-IBD, overlap-weighted
QT, ms, mean (s.d.)	374.9 (49.7)	386.3 (46.3)	375.2 (49.7)	376.2 (47.9)
RR, ms, mean (s.d.)	744.9 (188.7)	789.8 (187.9)	746.0 (188.6)	746.1 (188.8)
QRS, ms, mean (s.d.)	88.8 (10.1)	90.5 (10.5)	88.8 (10.1)	89.6 (10.6)
QTcF, ms, mean (s.d.)	415.3 (30.8)	419.7 (28.5)	415.5 (30.9)	416.7 (29.0)
QTcB, ms, mean (s.d.)	438.3 (29.6)	438.5 (28.8)	438.3 (29.6)	439.7 (28.6)
QTcF > 450 ms (men) / > 470 ms (women), n (%)	112 (6.92)	7,327 (8.43)	6.98%	7.13%
QTcF > 480 ms, n (%)	43 (2.66)	2,332 (2.68)	2.67%	2.25%
QTcF > 500 ms, n (%)	13 (0.80)	603 (0.69)	0.81%	0.58%
Values are mean (s.d.) or n (%); overlap-weighted columns show weighted means (s.d.) or percentages. Intervals are machine measurements. QTcF, Fridericia-corrected QT; QTcB, Bazett-corrected QT.				

Sex-specific QTc prolongation was present in 6.98% and 7.13% of the weighted groups (risk difference – 0.2 percentage points, 95% CI – 1.4 to 1.1; risk ratio 0.98, 0.82 to 1.17). QTcF exceeded 500 ms in 13 patients with IBD (0.80%) and 603 comparators (0.69%).

Consistency across estimators, recording conditions and cohort definitions

The estimate was consistent across the pre-specified supporting analyses (Table 3, Fig. 2). The doubly robust model gave – 1.22 ms (– 2.53 to 0.09) and matching – 1.46 ms (– 3.12 to 0.20). Bazett correction gave – 1.37 ms (– 2.82 to 0.08). Weighting for selection into the ECG cohort gave – 1.16 ms (– 3.07 to 0.75) (Supplementary Table S4 online). The three device analyses gave – 1.21, – 1.77 and – 1.56 ms, and the four alternative cohort definitions – 1.64, – 1.76, – 0.62 and – 1.07 ms. Across the 15 supporting analyses the point estimates lay between – 2.3 and + 0.2 ms; the widest interval, from the 475 patients with IBD in 2014–2019, was – 3.02 to 3.43 ms (estimates by calendar period are in Supplementary Table S5 online).

Table 3
Difference in QTcF at the index ECG between patients with and without IBD.

Analysis	IBD / non-IBD, n	Difference in QTcF, ms (95% CI)
<i>Primary estimate</i>		
Model M1: overlap-weighted, bandwidth-adjusted, Fridericia correction (confirmatory analysis)	1,618 / 86,913	-1.22 (- 2.74 to 0.29)
Model M1 with bootstrap percentile interval (500 resamples, propensity model re-estimated)	1,618 / 86,913	-1.22 (- 2.52 to 0.10)
Crude, unweighted (context only; not an estimate of the association)	1,618 / 86,913	-4.39 (- 5.90 to - 2.87)
<i>Alternative estimators and outcome definition</i>		
Doubly robust (outcome model with all M1 covariates)	1,618 / 86,913	-1.22 (- 2.53 to 0.09)
Bazett correction	1,618 / 86,913	-1.37 (- 2.82 to 0.08)
Explanatory model M2: M1 plus pre-ECG potassium, magnesium, creatinine and infection work-up markers (multiple imputation)	1,618 / 86,913	-0.82 (- 2.35 to 0.72)
M2 sensitivity: laboratory values restricted to records carrying the index admission identifier	1,618 / 86,913	-0.72 (- 2.24 to 0.80)
ECG-selection inverse-probability weights multiplied by overlap weights	1,618 / 86,913	-1.16 (- 3.07 to 0.75)
Matching: exact on period, sex and age band, then 1:4 on propensity score	1,613 / 6,430	-1.46 (- 3.12 to 0.20)
<i>Measurement and calendar checks</i>		
Device: filter setting added to the outcome model	1,618 / 86,913	-1.21 (- 2.73 to 0.30)
Device: 0.005–150 Hz carts only	1,196 / 64,770	-1.77 (- 3.39 to - 0.15)
Device: cart random intercept (unweighted, covariate-adjusted)	1,618 / 86,913	-1.56 (- 2.82 to - 0.29)
Excluding ECGs with ectopy or irregular-rhythm statements	1,499 / 80,556	-1.39 (- 2.94 to 0.16)
Calendar period 2014–2019 only	475 / 30,707	0.20 (- 3.02 to 3.43)
Differences are IBD minus non-IBD with 95% confidence intervals (CI). Only the primary analysis is confirmatory (two-sided $\alpha = 0.05$; $P = 0.11$); no equivalence margin was pre-specified. Secondary outcome, sex-specific QTc prolongation: risk difference - 0.2 (- 1.4 to 1.1) percentage points; risk ratio 0.98 (0.82 to 1.17).		

Analysis	IBD / non-IBD, n	Difference in QTcF, ms (95% CI)
<i>Cohort-definition checks</i>		
Index ECG defined as the first analysable ECG of the admission	1,662 / 90,329	-1.64 (- 3.14 to - 0.14)
All eligible admissions (patient-clustered errors)	2,819 / 159,171	-1.76 (- 3.27 to - 0.26)
Both groups restricted to the first admission in the database	945 / 70,366	-0.62 (- 2.61 to 1.37)
History defined by prior codes plus chronic codes of the index admission	1,618 / 86,913	-1.07 (- 2.59 to 0.44)
Patients with a prior admission only	673 / 16,547	-2.32 (- 4.65 to 0.02)
Differences are IBD minus non-IBD with 95% confidence intervals (CI). Only the primary analysis is confirmatory (two-sided $\alpha = 0.05$; $P = 0.11$); no equivalence margin was pre-specified. Secondary outcome, sex-specific QTc prolongation: risk difference - 0.2 (- 1.4 to 1.1) percentage points; risk ratio 0.98 (0.82 to 1.17).		

Before the ECG, patients with IBD more often had hypokalaemia (12.5% vs 9.1% of those measured), hypomagnesaemia (13.7% vs 10.9%), a blood culture (9.6% vs 4.3%) and intravenous antibacterial treatment (18.2% vs 10.3%). Adding these variables (model M2) left the difference at - 0.82 ms (- 2.35 to 0.72) (Supplementary Table S6 online).

In one illustrative bias scenario, shifting the estimate to a + 5-ms difference required a factor that was 30 percentage points more prevalent in IBD and associated with a 21-ms shorter QTcF. As a benchmark from measured covariates, removing heart rate from the propensity model moved the estimate by 1.9 ms (Supplementary Table S8 online).

Description of heterogeneity

Estimates were - 0.48 ms (- 2.52 to 1.57) for Crohn's disease and - 2.22 ms (- 4.44 to 0.01) for ulcerative colitis, with no evidence of a difference between them (Supplementary Table S9 online). The estimate was - 5.12 ms (- 7.97 to - 2.28) when IBD was the principal diagnosis and 0.23 ms (- 1.53 to 2.00) when it was a secondary diagnosis (difference - 5.36 ms, - 8.68 to - 2.04). These contrasts use the overall weights and were not balanced within subgroup. These descriptive estimates did not identify a subgroup with a longer mean QTcF, but were not designed to estimate disease-activity effects. A descriptive analysis of 1,641 repeat-ECG pairs within IBD admissions is reported in Supplementary Table S7 online.

Discussion

In 1,618 hospitalized patients with IBD compared with 86,913 other inpatients, QTcF at the index ECG was not longer in IBD. The estimate was precise: the 95% confidence interval spanned about 3 ms and excluded an adjusted mean difference of 5 ms or greater in this ECG-selected inpatient population. It was consistent across estimators, heart-rate corrections, recording conditions and cohort definitions.

Three design features distinguish this estimate. First, recording conditions were measured and controlled. One device bandwidth class was associated with QTcF values about 7–9 ms longer than the others after adjustment – a difference larger than the association under study, of the same order as the differences reported between automated algorithms of digital electrocardiographs[16], and one that comparisons with a single or unreported device configuration cannot detect. Studies of QT that draw on clinical ECG archives should record device configuration and account for it. Second, the comparators were hospitalized patients balanced on the setting and timing of the ECG, on heart rate and on prior cardiac and kidney disease, rather than healthy volunteers. Third, Fridericia correction was the primary measure[15]. In the unweighted data, patients with IBD had a heart rate 5 bpm higher, and Bazett correction placed their QTc about 4 ms higher relative to comparators than Fridericia did, the direction expected from Bazett overcorrection; neither formula showed a prolongation after weighting.

The result agrees with the controlled studies that found similar QTc in patients and controls[10–12] and extends that observation to the inpatient setting with a substantially larger sample; a study of QRS duration and fragmentation likewise recorded no longer QTc in IBD[13]. Reports of longer QTc came from a 20-patient comparison[7] and from an uncontrolled series using Bazett correction[9]. Our data do not address QT dispersion, QRS fragmentation or the Tp-e interval, for which differences have been reported[8, 12, 13], and we did not measure disease activity, so the longer QTc observed during active disease in nine outpatients[11] is neither supported nor contradicted here. The finding is also compatible with the lower rate of arrhythmia-related hospitalization reported for IBD in a national inpatient sample[6]; it does not bear on the long-term arrhythmia risk seen in a population cohort[4], which reflects outcomes this study did not measure.

Patients with IBD had more hypokalaemia, hypomagnesaemia and infection work-up before the ECG than other inpatients, yet their mean QTcF was not longer, and including those factors did not reveal a prolongation. These findings do not support treating an IBD diagnosis alone as a marker of longer average QTcF among hospitalized patients selected for electrocardiography. Individual clinical risk factors remain relevant to decisions about QT assessment[1]. As a point of scale only, ICH E14 identifies an effect of approximately 5 ms as a regulatory threshold of concern in drug evaluation, while defining a negative thorough-QT study by an upper one-sided 95% confidence bound below 10 ms[19]; this observational comparison was not designed as an equivalence study and no margin was pre-specified.

The findings apply to inpatients who underwent electrocardiography and whose first ECG was analysable; patients with IBD were less likely than others to have an ECG, and weighting for measured determinants of that selection did not change the estimate. IBD was identified from diagnosis codes without endoscopic or biochemical activity. QT was measured by machine algorithms, and the database

does not state whether RR and QT were taken from the same representative beat (excluding ECGs with ectopy did not change the result). The data come from one centre.

In hospitalized patients selected for electrocardiography, IBD was not associated with a longer mean QTcF after balancing clinical context and accounting for device configuration. The confidence interval excluded an adjusted mean difference of 5 ms or greater, and the estimate was consistent across alternative estimators, recording conditions and cohort definitions.

Methods

Design, data source and reporting

This was a retrospective cohort comparison using MIMIC-IV [17] and the MIMIC-IV-ECG Diagnostic Electrocardiogram Matched Subset v1.0[18], which contains diagnostic 12-lead ECGs recorded at one academic medical centre between 2008 and 2019 together with machine-generated measurements and report statements. The cohort definition and statistical analysis plan were frozen on 3 October 2026, before any QTc value was compared between groups. Two amendments were documented in the protocol and audit trail on 4 October 2026 (Supplementary Table S1 online), after a blinded device check and before any group-wise QTc was computed: ECG device bandwidth class was added to the propensity model and the outcome model, and one additional sensitivity cohort was specified. Reporting follows STROBE[20]. MIMIC-IV and MIMIC-IV-ECG contain de-identified data. Their collection and sharing were approved by the Institutional Review Board of Beth Israel Deaconess Medical Center, which granted a waiver of informed consent. The authors completed the required training and accessed the data under the PhysioNet credentialed data use agreement. All methods were performed in accordance with relevant guidelines and regulations.

ECG eligibility and measurements

ECGs were assigned to an admission when recorded between emergency-department registration (or admission, if earlier registration was absent) and discharge; the plausibility of ECG time stamps was checked against contemporaneous clinical heart-rate measurements (Supplementary Table S3 online). QT was calculated as T-wave end minus QRS onset and QRS duration as QRS end minus QRS onset, using the machine measurements. An ECG was analysable when QT was 200–800 ms, RR 300–2000 ms and QRS < 120 ms, and when the machine statements contained no pacing, atrial fibrillation or flutter, bundle-branch block or intraventricular conduction block[21]. QTcF was $QT/(RR \text{ in seconds})^{1/3}$; Bazett-corrected QT (QTcB) was $QT/\sqrt{RR}$.

Study population

Adults (≥ 18 years) admitted in the 2008–2019 calendar groups were eligible when the first ECG of the admission was itself analysable; this ECG was the index ECG. Admissions whose first ECG was not analysable were excluded rather than represented by a later ECG, so that the index time did not depend on when a patient returned to an analysable rhythm. Each patient contributed the first eligible admission. IBD was defined by ICD-9 codes 555/556 or ICD-10 codes K50/K51 on the index admission. Comparators had no IBD code on any admission in the database.

Covariates

Covariates were restricted to information available before the index ECG: age, sex, calendar period, heart rate on the index ECG, location of the ECG (emergency department, ward or intensive care unit), time from presentation to the ECG, admission type, admission source, emergency-department registration, first clinical service assigned before the ECG, intensive-care admission before the ECG, and chronic kidney disease, heart failure, coronary disease or prior myocardial infarction and atrial fibrillation coded on admissions completed before the index presentation, with an indicator for any prior admission. Diagnoses coded on the index admission were not used as baseline covariates because their timing relative to the ECG is unknown. ECG bandwidth class (0.0005–150, 0.005–150 or 0.05–150 Hz) was included as a measurement covariate after a check blinded to IBD status showed that bandwidth class was associated with adjusted differences in QTcF of about 7–9 ms that calendar period did not explain (Supplementary Table S2 online).

Statistical analysis

A logistic propensity model for IBD included all covariates, with B-splines for age, heart rate and log time to ECG and an interaction between calendar period and ECG location. Overlap weights were used, so the estimand is the mean difference in the population with clinical equipoise between groups[22]. Balance was pre-specified as an absolute standardized mean difference below 0.10 for every covariate[23], with an effective sample size of at least 50% of the IBD group and at least 500 in each group; these criteria were checked, with QT data withheld, before the outcome analysis.

The single confirmatory analysis (model M1) was a weighted linear model of QTcF on IBD and bandwidth class with heteroskedasticity-robust standard errors (two-sided $\alpha = 0.05$). No equivalence margin was pre-specified, and no formal sample-size calculation was made; all eligible patients in the database were included. The secondary outcome was sex-specific QTc prolongation (QTcF > 450 ms in men, > 470 ms in women)[24], expressed as weighted risk difference and risk ratio. QTcF > 480 and > 500 ms are reported descriptively.

Pre-specified supporting analyses were: a doubly robust model; Bazett correction; inverse-probability weighting for selection into the ECG cohort; exact matching on period, sex and age band followed by 1:4 propensity matching; exclusion of ECGs with ectopy or irregular-rhythm statements; restriction to 2014–

2019; restriction to patients with a prior admission; three device analyses (filter setting in the outcome model, restriction to 0.005–150 Hz carts, cart random intercept); and four alternative cohort definitions (index ECG defined as the first analysable ECG of the admission; all eligible admissions with patient-clustered errors; both groups restricted to the first admission in the database; history defined by prior codes plus chronic codes of the index admission). A percentile bootstrap (500 resamples) re-estimated the propensity model in each resample.

An explanatory model (M2) added potassium, magnesium and creatinine measured during the index encounter within 24 hours before the ECG, and markers of infection work-up and treatment before the ECG (blood culture, intravenous antibacterial, Sepsis-3 criteria in intensive care). Laboratory values were taken from the index encounter, defined as records carrying the index admission identifier or, for emergency-department records without an admission identifier, records drawn after presentation; restriction to records carrying the admission identifier was a sensitivity analysis. Because these variables may lie on the pathway between IBD and repolarization, M2 is interpreted as the association remaining after their inclusion, not as a direct effect. Missing laboratory values were multiply imputed by chained equations (20 data sets, Rubin's rules)[25]. Crohn's disease versus ulcerative colitis, and IBD as principal versus secondary diagnosis, were pre-specified as descriptions of heterogeneity. An illustrative bias scenario expressed the unmeasured confounding that would be needed to shift the estimate to a 5-ms prolongation[26]. A descriptive analysis of repeat ECGs within IBD admissions is given in the Supplementary Methods online.

A prespecified analysis of QT-prolonging medications was not conducted because the required versioned reference list was unavailable; no post hoc drug list was constructed (Supplementary Table S1 online).

Analyses used Python 3.11 with statsmodels 0.14.6 and scikit-learn 1.6.1.

Declarations

Ethics. Use of MIMIC-IV was approved under the database's data use agreement; the requirement for individual informed consent was waived because the data are de-identified. All methods were performed in accordance with relevant guidelines and regulations.

Competing interests.

The authors declare no competing interests.

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Author Contribution

YYT and LYL collected and analysed the data. JRH and JG drafted and revised the manuscript. All authors reviewed and approved the final manuscript.

Data Availability

The data analysed in this study are available from PhysioNet: MIMIC-IV v3.1 (<https://doi.org/10.13026/kpb9-mt58>) and MIMIC-IV-ECG v1.0 (<https://doi.org/10.13026/4nqg-sb35>). Access to MIMIC-IV requires user credentialing, completion of the required training, and acceptance of the PhysioNet data use agreement. Access to and use of these data are governed by that agreement. MIMIC-IV-ECG is openly available under the Open Data Commons Open Database License v1.0.

Code availability

The analysis code and a list of software versions are archived at Zenodo (<https://doi.org/10.5281/zenodo.23137131>).

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Figures

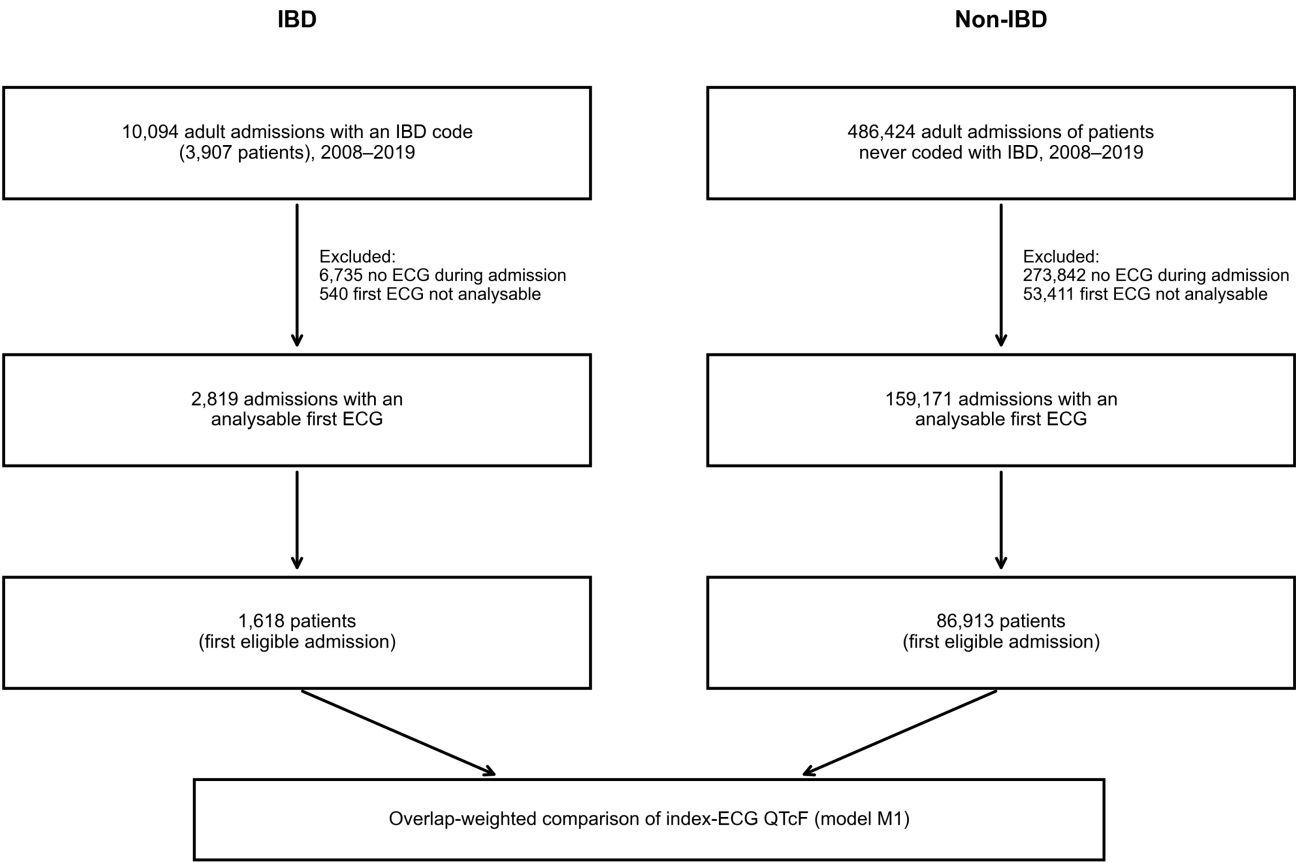


Figure 1

Study flow. Reasons for a non-analysable first ECG (invalid QT or RR, paced rhythm, atrial fibrillation or flutter, QRS ≥120 ms or bundle-branch/intraventricular conduction block) can overlap; the combined number is shown.

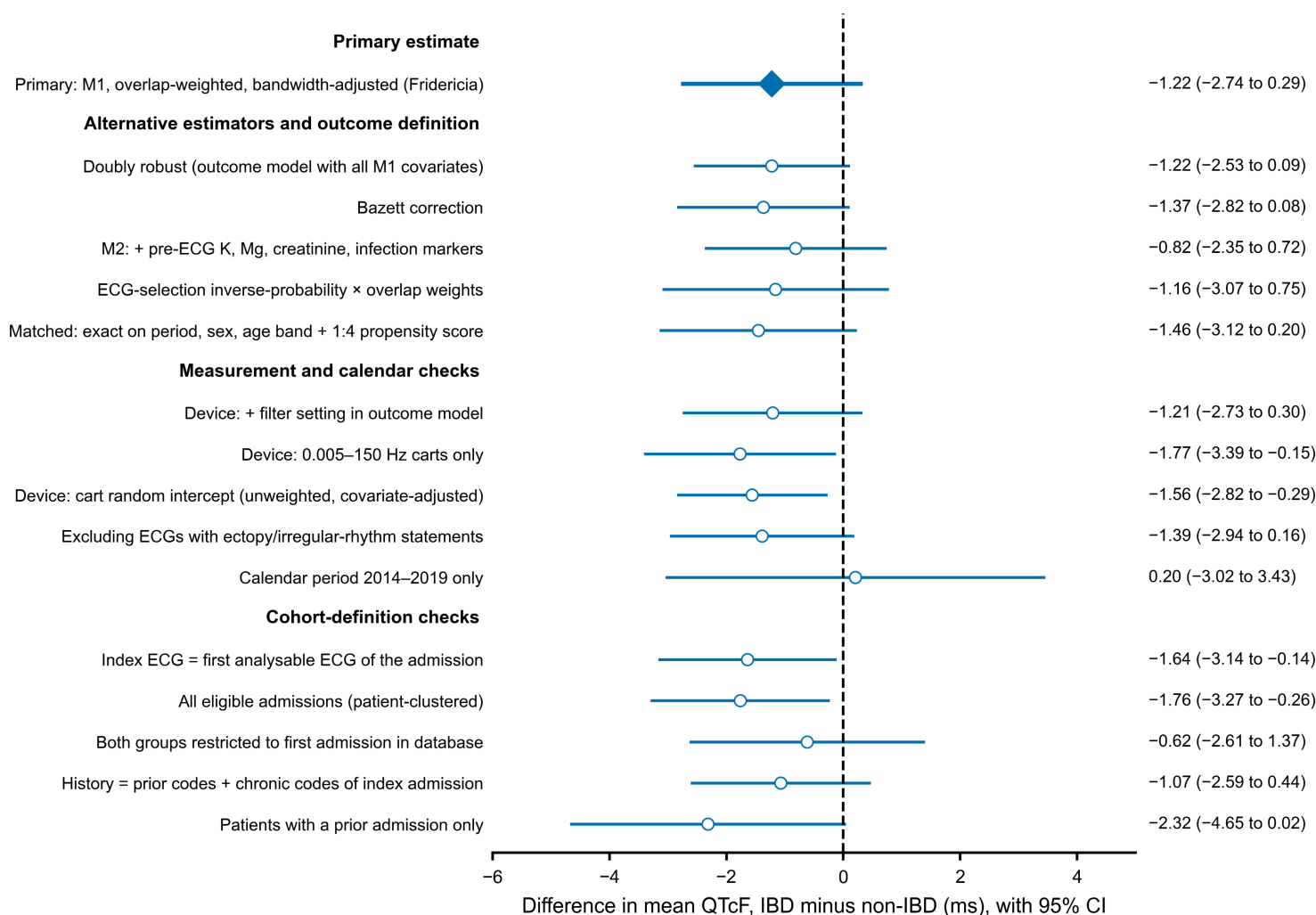


Figure 2

Difference in mean QTcF between IBD and non-IBD inpatients across pre-specified analyses. Points are differences (IBD minus non-IBD) with 95% confidence intervals. The filled diamond is the single confirmatory analysis; open circles are pre-specified supporting analyses grouped by purpose. The dashed line marks no difference. The crude unweighted difference is reported in Table 3 only.

Supplementary Files

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- [IBDQTcFSciRepsupplementaryinformationv0.7.docx](#)