

# **SUPPLEMENTAL MATERIAL**

**Table S1. Overview of criteria used to define ECG abnormalities.**

<b>ECG Abnormalities</b>	<b>Criteria</b>
LVH <sup>32</sup>	Sokolow-Lyon criteria: S wave in lead V1 and R wave in leads V5–V6 (largest) $\geq 35$ mm Cornell voltage criteria: S wave in lead V3 and R wave in lead aVL $> 28$ mm (male) or $> 20$ mm (female) Requiring absence of: RBBB, LBBB, and IVCD
Atrial fibrillation/flutter <sup>19</sup>	Fibrillation or flutter waves with irregular or regular RR intervals, respectively
First-degree AV block <sup>19</sup>	PR interval $> 200$ ms
RBBB <sup>19</sup>	QRS duration $> 120$ ms rSR' pattern in leads V1–V2 S-wave duration $> R$ -wave duration or $> 40$ ms in leads I and V6 Normal R peak in leads V5–V6 but $> 50$ ms in lead V1
Incomplete RBBB <sup>19</sup>	QRS duration $< 120$ ms RBBB pattern
LBBB <sup>19</sup>	QRS duration $> 120$ ms Absent Q waves in leads I and V5–V6 R-wave peak time $> 60$ ms in leads V5–V6 Notched R wave in leads I, aVL, and V5–V6
Incomplete LBBB <sup>19</sup>	QRS duration $< 120$ ms LBBB pattern
LAFB <sup>19</sup>	QRS duration $< 120$ ms Frontal plane axis between $-45$ and $-90$ degrees qR pattern in lead aVL R-wave peak time in lead aVL $> 45$ ms
LPFB <sup>19</sup>	QRS duration $< 120$ ms Frontal plane axis between $90$ and $180$ degrees rS pattern in leads I and aVL qR pattern in leads III and aVF
IVCD	QRS duration $> 120$ ms Requiring absence of: RBBB and LBBB
QTc prolongation <sup>33</sup>	Fridericia-corrected QT interval $> 450$ ms (male) or $> 470$ ms (female)
Q waves <sup>34</sup>	Any Q wave in leads V2–V3 $> 20$ ms or QS complex in leads V2–V3 Q wave $\geq 30$ ms and $\geq 1$ mm or QS complex in leads I, II, aVL, aVF, or V4–V6 in any two leads of a contiguous lead grouping (I, aVL; V1–V6; II, III, aVF) R wave $> 40$ ms in leads V1–V2 and R/S $> 1$ with a concordant positive T wave Requiring absence of: LVH, RBBB, LBBB, and IVCD
ST depression or inverted T waves <sup>34,35</sup>	New horizontal or downsloping ST depression $\geq 0.5$ mm in any two leads of a contiguous lead grouping (I, aVL; V1–V6; II, III, aVF) T-wave inversion $> 1$ mm in any two leads of a contiguous lead grouping (I, aVL; V1–V6; II, III, aVF) with prominent R wave or R/S ratio $> 1$ Requiring absence of (in leads V1–V3): RBBB, LBBB, and IVCD
ST elevation <sup>34,35,36</sup>	New ST elevation at the J point* in any two leads of a contiguous lead grouping (I, aVL; V1–V6; II, III, aVF) with the cut-off levels:

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≥1 mm in all leads other than leads V2–V3, where the following cut-off levels apply:  
≥2 mm in male ≥40 years  
≥2.5 mm in male <40 years  
≥1.5 mm in female regardless of age  
Requiring absence of (in leads V1–V3):  
RBBB, LBBB, IVCD

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\*Criteria for ST elevation were slightly modified as measurement of the ST segment was performed at QRS offset + 1/16 of the average RR interval, known as the STM point in the 12SL algorithm and equivalent to ~80 ms after QRS offset. STM was chosen instead of the J point as a notched or slurred appearance of the terminal QRS complex (i.e. early repolarization) can make it difficult to define the J point.

Abbreviations: AV, atrioventricular; ECG, electrocardiogram; IVCD, intraventricular conduction disturbance; LVH, left ventricular hypertrophy; QTc, corrected QT; RBBB, right bundle branch block; LAFB, left anterior fascicular block; LBBB, left bundle branch block; LPFB, left posterior fascicular block.

**Table S2. Overview of ICD-8, ICD-10, NCSP, and ATC codes used to identify medical comorbidities, procedures, and cardiovascular medications.**

<b>Covariates</b>	<b>ICD-8/-10 Codes</b>	<b>NCSP Codes</b>	<b>ATC Codes</b>
Pacemaker/implantable cardioverter-defibrillator	Z95.0	BFCA–B	
Heart failure	425, 427.0–.1; I11.0, I13.0, I13.2, I42, I50, J81		
Coronary artery disease including myocardial infarction	410–414; I20–25	KFNG0, KFNA–E	
Atrial fibrillation/flutter	427.93–.94; I48	BFFB03–04	
Valvular heart disease	394–396, 424.0–.1; I05–06, I34–35	KFK, KFM	
Hypertension	400–404; I10–15		C02–03, C07–09
Hyperlipidemia	279.00; E78.0–.5		C10
Diabetes	250; E10–14		A10
Chronic obstructive pulmonary disease	490–492; J40–44		R03AC, R03AL, R03AK, R03BB
Chronic kidney disease	250.02, 400.39, 403–404, 581–584, 590.09, 593.20, 753.10–.11, 753.19; I12.0, N02–08, N11–14, N15.8–.9, N16, N18–19, N26, N39.1, M32.1B, Q61, Z99.2	BJFD2	
Diuretics			C03A, C03C, C03EB
ACEIs/ARBs			C09A–D
Beta-blockers			C07

**Table S3. Overview of QT-prolonging medications. From <https://www.crediblemeds.org/>. Up to date as of September 01, 2020.**

<b>Overall Classes</b>	<b>Individual Medications</b>	<b>ATC Codes</b>
Alimentary tract and metabolism	Cisapride	A03FA02
	Domperidone	A03FA03
	Ondansetron	A04AA01
	Granisetron	A04AA02
	Tropisetron	A04AA03
	Dolasetron	A04AA04
	Palonosetron	A04AA05
	Eliglustat	A16AX10
Blood and blood-forming organs	Cilostazol	B01AC23
Cardiovascular system	Quinidine	C01BA01
	Procainamide	C01BA02
	Disopyramide	C01BA03
	Hydroquinidine	C01BA13
	Flecainide	C01BC04
	Amiodarone	C01BD01
	Dofetilide	C01BD04
	Ibutilide	C01BD05
	Dronedarone	C01BD07
	Ketanserin	C02KD01
	Sotalol	C07AA07
	Isradipine	C08CA03
	Nicardipine	C08CA04
	Lacidipine	C08CA09
	Bepidil	C08EA02
	Moexipril	C09AA13
	Probucol	C10AX02
	Genitourinary system and sex hormones	Mifepristone
Terodiline		G04BD05
Tolterodine		G04BD07
Mirabegron		G04BD12
Vardenafil		G04BE09
Alfuzosin		G04CA01
Systemic hormonal preparations	Terlipressin	H01BA04
	Oxytocin	H01BB02
	Carbetocin	H01BB03
	Pasireotide	H01CB05
	Osilodrostat	H02CA02
Antiinfectives	Erythromycin	J01FA01

	Roxithromycin	J01FA06
	Clarithromycin	J01FA09
	Azithromycin	J01FA10
	Telithromycin	J01FA15
	Ofloxacin	J01MA01
	Ciprofloxacin	J01MA02
	Norfloxacin	J01MA06
	Sparfloxacin	J01MA09
	Grepafloxacin	J01MA11
	Levofloxacin	J01MA12
	Moxifloxacin	J01MA14
	Gemifloxacin	J01MA15
	Gatifloxacin	J01MA16
	Telavancin	J01XA03
	Lefamulin	J01XX12
	Fluconazole	J02AC01
	Bedaquiline	J04AK05
	Delamanid	J04AK06
	Clofazimine	J04BA01
	Saquinavir	J05AE01
	Efavirenz	J05AG03
	Rilpivirine	J05AG05
	Lopinavir and ritonavir	J05AR10
	Fluorouracil	L01BC02
	Capecitabine	L01BC06
	Epirubicin	L01DB03
	Aclarubicin	L01DB04
	Oxaliplatin	L01XA03
	Necitumumab	L01XC22
	Inotuzumab ozogamicin	L01XC26
	Sunitinib	L01XE04
	Sorafenib	L01XE05
	Dasatinib	L01XE06
	Lapatinib	L01XE07
Antineoplastic and immunomodulating agents	Nilotinib	L01XE08
	Pazopanib	L01XE11
	Vandetanib	L01XE12
	Bosutinib	L01XE14
	Vemurafenib	L01XE15
	Crizotinib	L01XE16
	Dabrafenib	L01XE23
	Cabozantinib	L01XE26
	Ceritinib	L01XE28
	Lenvatinib	L01XE29
	Osimertinib	L01XE35
	Cobimetinib	L01XE38

	Midostaurin	L01XE39
	Ribociclib	L01XE42
	Encorafenib	L01XE46
	Entrectinib	L01XE56
	Arsenic trioxide	L01XX27
	Bortezomib	L01XX32
	Anagrelide	L01XX35
	Vorinostat	L01XX38
	Romidepsin	L01XX39
	Eribulin	L01XX41
	Panobinostat	L01XX42
	Rucaparib	L01XX55
	Bendamustine	L01AA09
	Leuprorelin	L02AE02
	Tamoxifen	L02BA01
	Toremifene	L02BA02
	Apalutamide	L02BB05
	Abarelix	L02BX01
	Degarelix	L02BX02
	Tacrolimus	L04AD02
	Fingolimod	L04AA27
	Siponimod	L04AA42
Musculoskeletal system	Tizanidine	M03BX02
	Nusinersen	M09AX07
	Sevoflurane	N01AB08
	Propofol	N01AX10
	Cocaine	N01BC01
	Buprenorphine	N02AE01
	Tramadol	N02AX02
	Felbamate	N03AX10
	Retigabine	N03AX21
	Apomorphine	N04BC07
	Perphenazine	N05AB03
	Thioridazine	N05AC02
	Mesoridazine	N05AC03
Nervous system	Haloperidol	N05AD01
	Melperone	N05AD03
	Pipamperone	N05AD05
	Benperidol	N05AD07
	Droperidol	N05AD08
	Sertindole	N05AE03
	Lurasidone	N05AE05
	Flupentixol	N05AF01
	Chlorprothixene	N05AF03
	Zuclopenthixol	N05AF05
	Pimozide	N05AG02

	Clozapine	N05AH02
	Asenapine	N05AH05
	Clotiapine	N05AH06
	Sulpiride	N05AL01
	Sultopride	N05AL02
	Tiapride	N05AL03
	Levosulpiride	N05AL07
	Lithium	N05AN01
	Prothipendyl	N05AX07
	Zotepine	N05AX11
	Aripiprazole	N05AX12
	Paliperidone	N05AX13
	Iloperidone	N05AX14
	Pimavanserin	N05AX17
	Dexmedetomidine	N05CM18
	Chlorpromazine	N05AA01
	Levomepromazine	N05AA02
	Cyamemazine	N05AA06
	Citalopram	N06AB04
	Escitalopram	N06AB10
	Mianserin	N06AX03
	Mirtazapine	N06AX11
	Venlafaxine	N06AX16
	Atomoxetine	N06BA09
	Donepezil	N06DA02
	Memantine	N06DX01
	Desipramine	N06AA01
	Imipramine	N06AA02
	Trimipramine	N06AA06
	Nortriptyline	N06AA10
	Maprotiline	N06AA21
	Methadone	N07BC02
	Levacetylmethadol	N07BC03
	Lofexidine	N07BC04
	Levomethadone	N07BC05
	Tetrabenazine	N07XX06
	Pitolisant	N07XX11
	Valbenazine	N07XX13
	Dextromethorphan	N07XX59
	Chloroquine	P01BA01
	Hydroxychloroquine	P01BA02
	Primaquine phosphate	P01BA03
	Arthemether	P01BF01
	Artemimol and piperaquine	P01BF05
	Halofantrine	P01BX01
	Pentamidine	P01CX01
Antiparasitics, insecticides, and repellents		



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Respiratory system	Hydrocodone	R05DA03
	Alimemazine	R06AD01
	Promethazine	R06AD02
	Astemizole	R06AX11
	Terfenadine	R06AX12

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**Table S4. Patient characteristics stratified by subtype of SMI diagnosis.**

	<b>Controls (n=336 524)</b>	<b>Schizophrenia (n=4477)</b>	<b>Bipolar disorder (n=2571)</b>	<b>Severe depression (n=2980)</b>	<b><i>P</i></b>
Age at ECG recording, years	56 [41–69]	50 [39–61]	58 [44–70]	58 [45–72]	<0.001
Males	161 282 (47.9)	2443 (54.6)	987 (38.4)	1034 (34.7)	<0.001
SMI duration, years	NA	10 [5–16]	7 [3–12]	5 [2–9]	NA
Heart failure	10 433 (3.1)	158 (3.5)	117 (4.6)	146 (4.9)	<0.001
Coronary artery disease	29 232 (8.7)	304 (6.8)	250 (9.7)	334 (11.2)	<0.001
Atrial fibrillation/flutter	14 903 (4.4)	120 (2.7)	135 (5.3)	169 (5.7)	<0.001
Valvular heart disease	3690 (1.1)	36 (0.8)	36 (1.4)	51 (1.7)	0.001
Hypertension	50 432 (15.0)	490 (10.9)	420 (16.3)	569 (19.1)	<0.001
Hyperlipidemia	49 201 (14.6)	689 (15.4)	462 (18.0)	535 (18.0)	<0.001
Diabetes	26 732 (7.9)	644 (14.4)	288 (11.2)	290 (9.7)	<0.001
Chronic obstructive pulmonary disease	29 093 (8.6)	655 (14.6)	337 (13.1)	359 (12.0)	<0.001
Chronic kidney disease	6328 (1.9)	108 (2.4)	119 (4.6)	84 (2.8)	<0.001
ACEIs/ARBs	64 743 (19.2)	515 (11.5)	378 (14.7)	508 (17.0)	<0.001
Beta-blockers	32 384 (9.6)	290 (6.5)	200 (7.8)	275 (9.2)	<0.001
Diuretics	45 533 (13.5)	565 (12.6)	430 (16.7)	472 (15.8)	<0.001
QT-prolonging medications	44 377 (13.2)	2885 (64.4)	1878 (73.0)	2056 (69.0)	<0.001

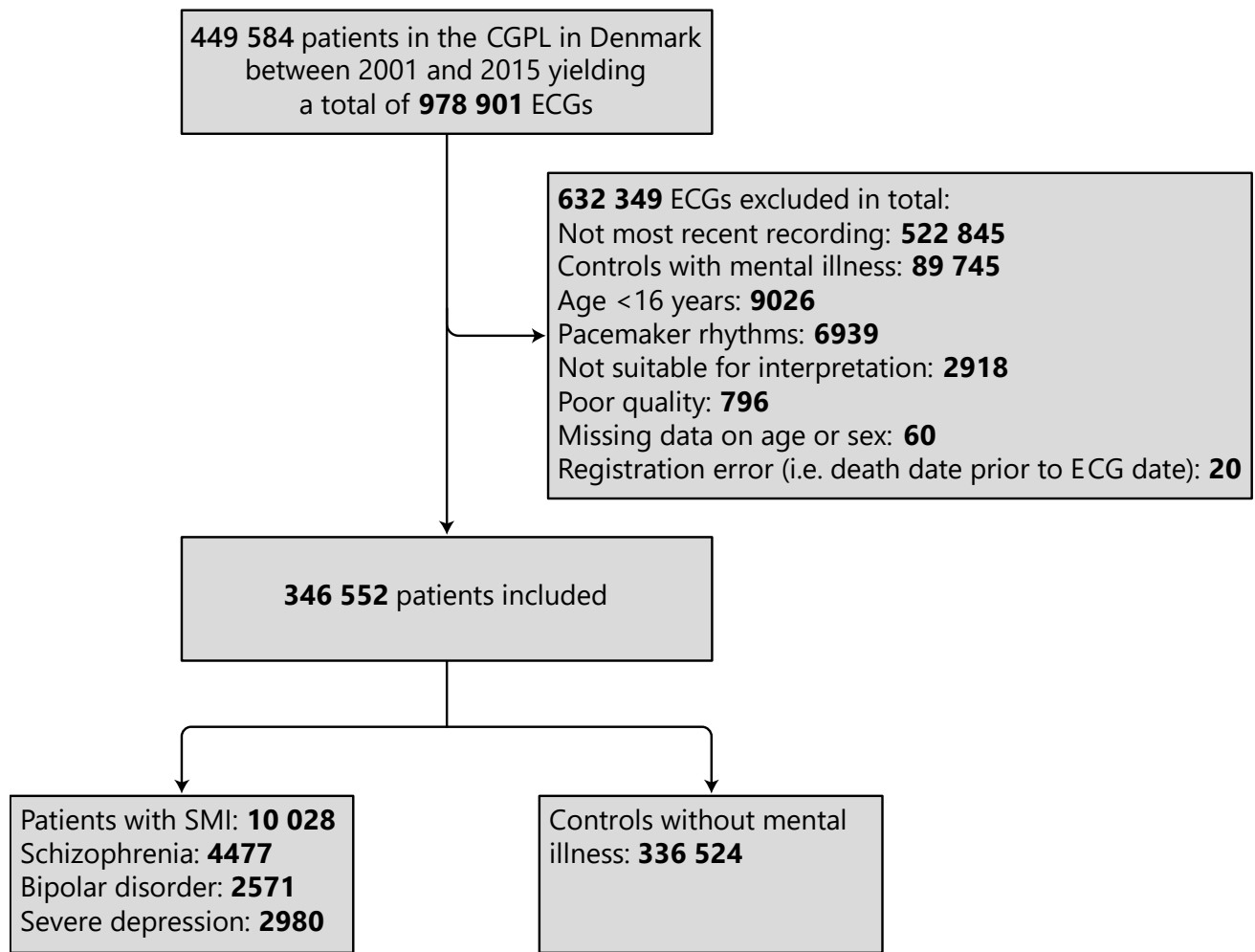
**Table S5. ECG characteristics stratified by subtype of SMI diagnosis.**

	<b>Controls (n=336 524)</b>	<b>Schizophrenia (n=4477)</b>	<b>Bipolar disorder (n=2571)</b>	<b>Severe depression (n=2980)</b>	<b>P</b>
Heart rate, bpm	69 [61–78]	78 [68–89]	72 [64–82]	75 [66–85]	<0.001
Missing	30 361	219	228	239	
P-wave duration, ms	108 [100–116]	106 [98–114]	110 [102–118]	108 [100–116]	<0.001
Missing	30 361	219	228	239	
PR interval, ms	156 [144–174]	154 [140–168]	162 [146–178]	156 [142–172]	0.782
Missing	30 361	219	228	239	
QRS duration, ms	92 [84–100]	90 [84–98]	92 [84–100]	90 [84–98]	<0.001
Missing	30 361	219	228	239	
QT interval, ms	396 [376–416]	384 [362–404]	394 [374–416]	390 [370–410]	<0.001
Missing	30 361	219	228	239	
QTcF interval, ms	414 [402–427]	416 [402–430]	418 [404–431]	417 [405–431]	<0.001
Missing	30 361	219	228	239	
No ECG abnormality	237 397 (70.5)	3380 (75.5)	1789 (69.6)	2126 (71.3)	<0.001
Minor ECG abnormality	18 541 (5.5)	292 (6.5)	189 (7.4)	179 (6.0)	<0.001
First-degree atrioventricular block	13 477 (4.0)	107 (2.4)	144 (5.6)	133 (4.5)	<0.001
Incomplete bundle branch block	8504 (2.5)	97 (2.2)	58 (2.3)	55 (1.8)	0.036
Incomplete right bundle branch block	7680 (2.3)	92 (2.1)	49 (1.9)	51 (1.7)	0.076
Incomplete left bundle branch block	824 (0.2)	5 (0.1)	9 (0.4)	4 (0.1)	0.116
Left fascicular block	4504 (1.3)	85 (1.9)	42 (1.6)	50 (1.7)	0.002
Left anterior fascicular block	2743 (0.8)	40 (0.9)	30 (1.2)	32 (1.1)	0.088
Left posterior fascicular block	1761 (0.5)	45 (1.0)	12 (0.5)	18 (0.6)	<0.001
QTcF prolongation	5831 (1.7)	159 (3.6)	90 (3.5)	75 (2.5)	<0.001
Major ECG abnormality	80 586 (23.9)	805 (18.0)	593 (23.1)	675 (22.7)	<0.001
Left ventricular hypertrophy	35 832 (10.6)	322 (7.2)	242 (9.4)	286 (9.6)	<0.001
Atrial fibrillation/flutter	12 561 (3.7)	52 (1.2)	84 (3.3)	98 (3.3)	<0.001
Bundle branch block	11 550 (3.4)	104 (2.3)	97 (3.8)	101 (3.4)	<0.001
Right bundle branch block	7803 (2.3)	77 (1.7)	69 (2.7)	71 (2.4)	0.035
Left bundle branch block	3747 (1.1)	27 (0.6)	28 (1.1)	30 (1.0)	0.013
Intraventricular conduction disturbance	2786 (0.8)	29 (0.6)	23 (0.9)	24 (0.8)	0.590
Q waves	17 064 (5.1)	244 (5.5)	127 (4.9)	170 (5.7)	0.278
ST-T deviations	15 283 (4.5)	149 (3.3)	114 (4.4)	118 (4.0)	<0.001

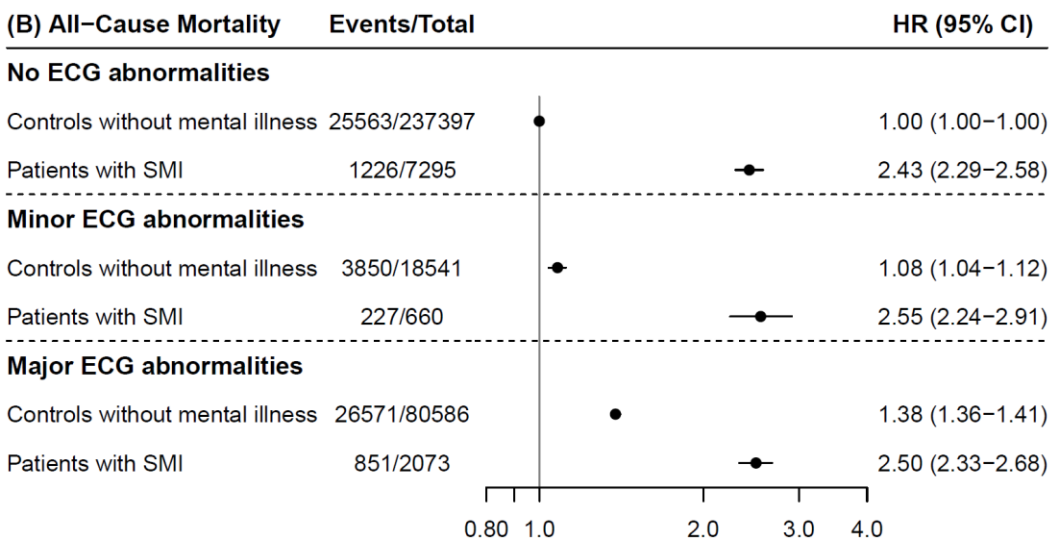
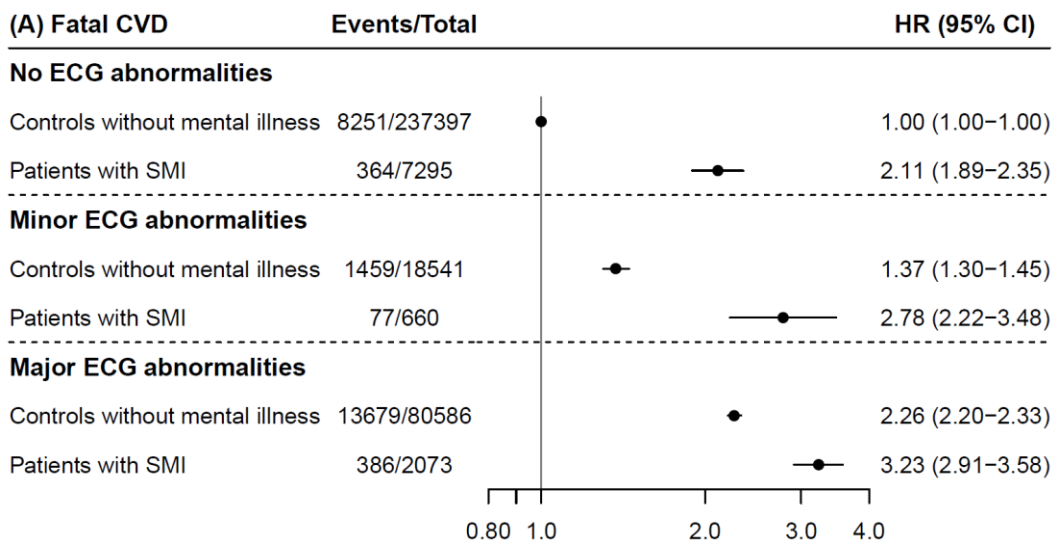
**Table S6. Brier scores.**

<b>Population</b>	<b>Brier Score (95% CI) For Conventional Model</b>	<b>Brier Score (95% CI) For ECG Abnormality Model</b>
Controls		
Cardiovascular disease	0.186 (0.182–0.190)	0.182 (0.178–0.187)
No cardiovascular disease	0.053 (0.052–0.054)	0.052 (0.051–0.053)
SMI		
Cardiovascular disease	0.223 (0.198–0.251)	0.222 (0.194–0.253)
No cardiovascular disease	0.082 (0.072–0.093)	0.081 (0.071–0.092)

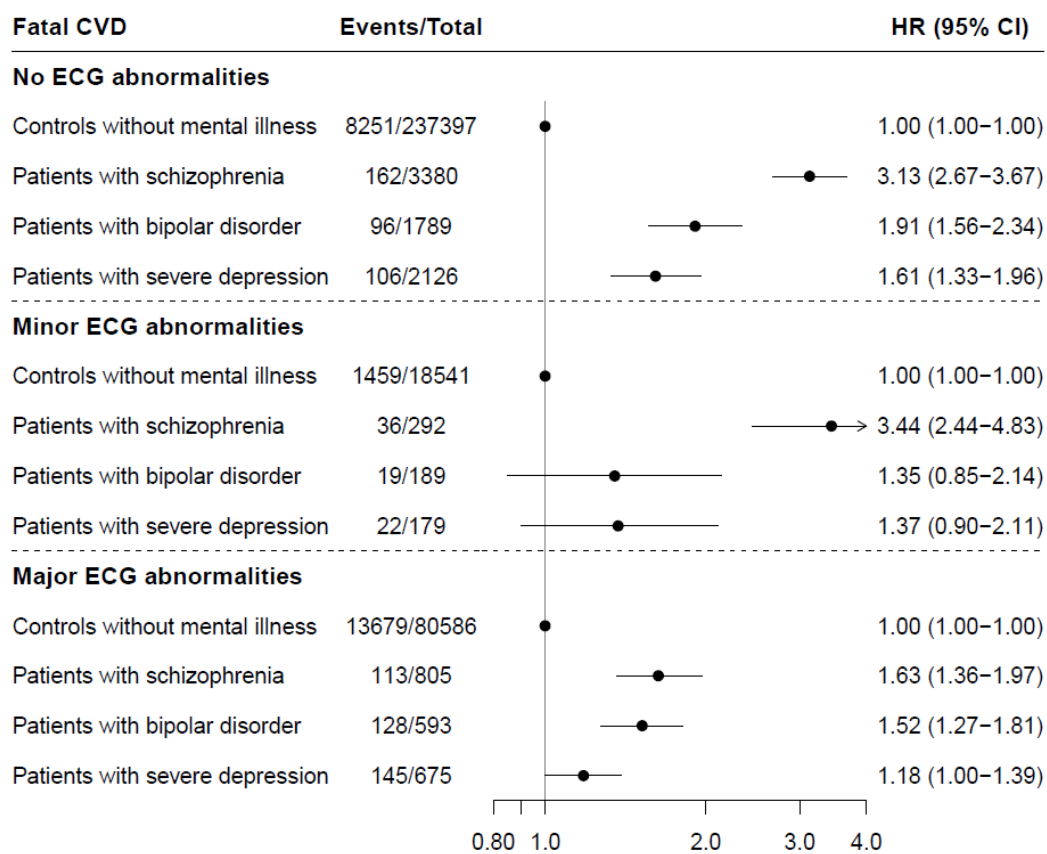
**Figure S1. Flowchart.**



**Figure S2. Association between SMI status and ECG abnormalities combined and long-term outcomes.**



**Figure S3. ECG abnormalities and fatal CVD risk stratified by subtype of SMI diagnosis.**



**Figure S4. AUC values.**

