SUPPLEMENTAL MATERIALS

Ismail S, Jonsson Funk M, and Flythe JE. Ondansetron and the Risk of Sudden Cardiac Death among Individuals Receiving Maintenance Hemodialysis.

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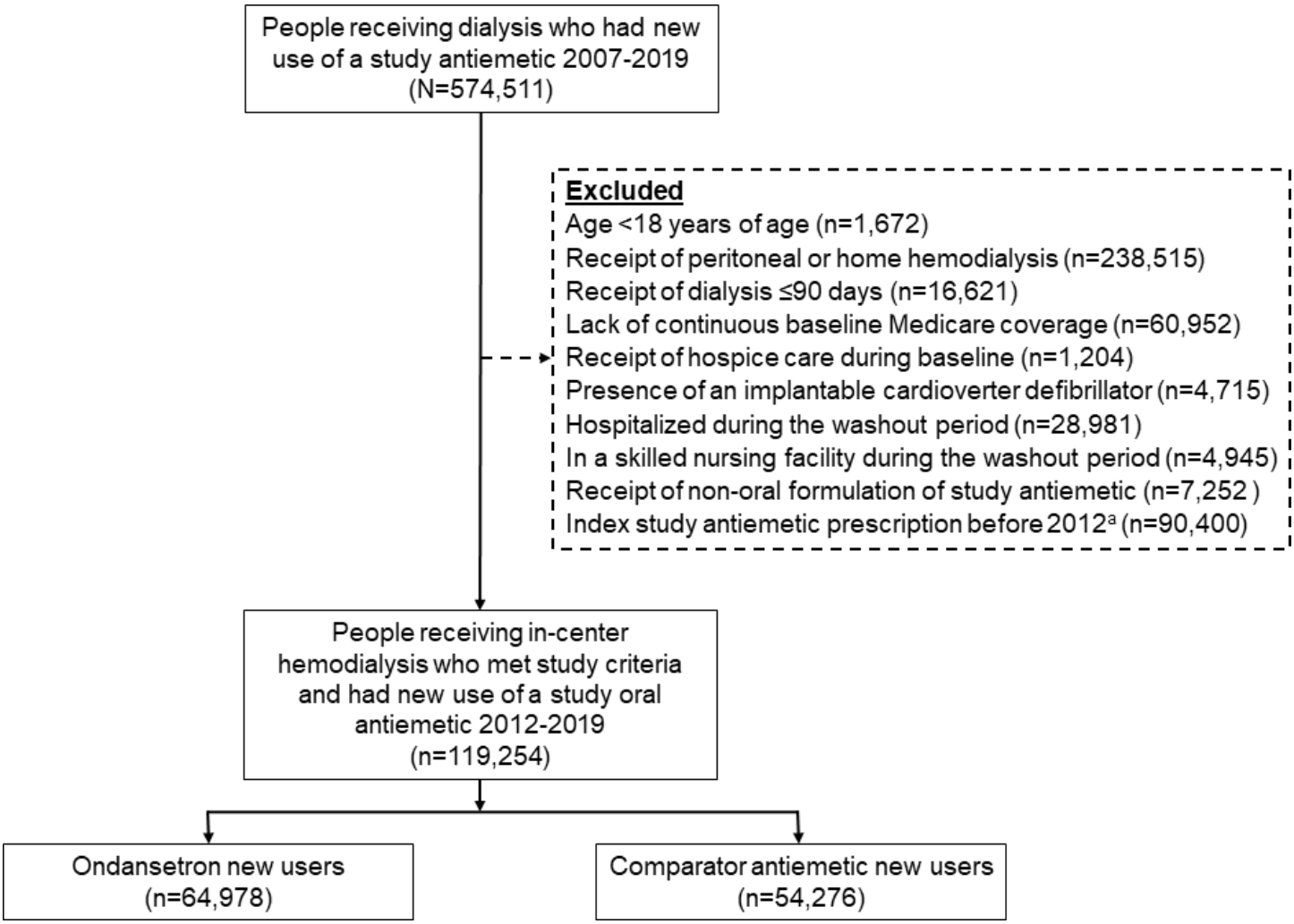
Supplemental Figures

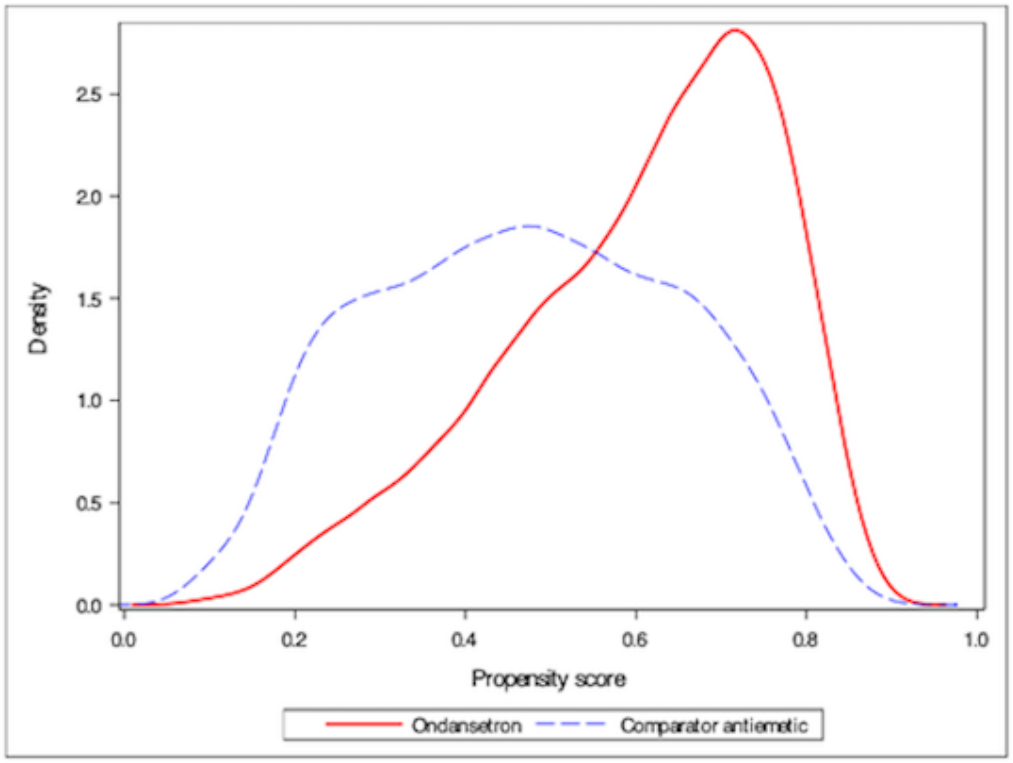
Supplemental Figure 1. Flow diagram depicting study cohort assembly



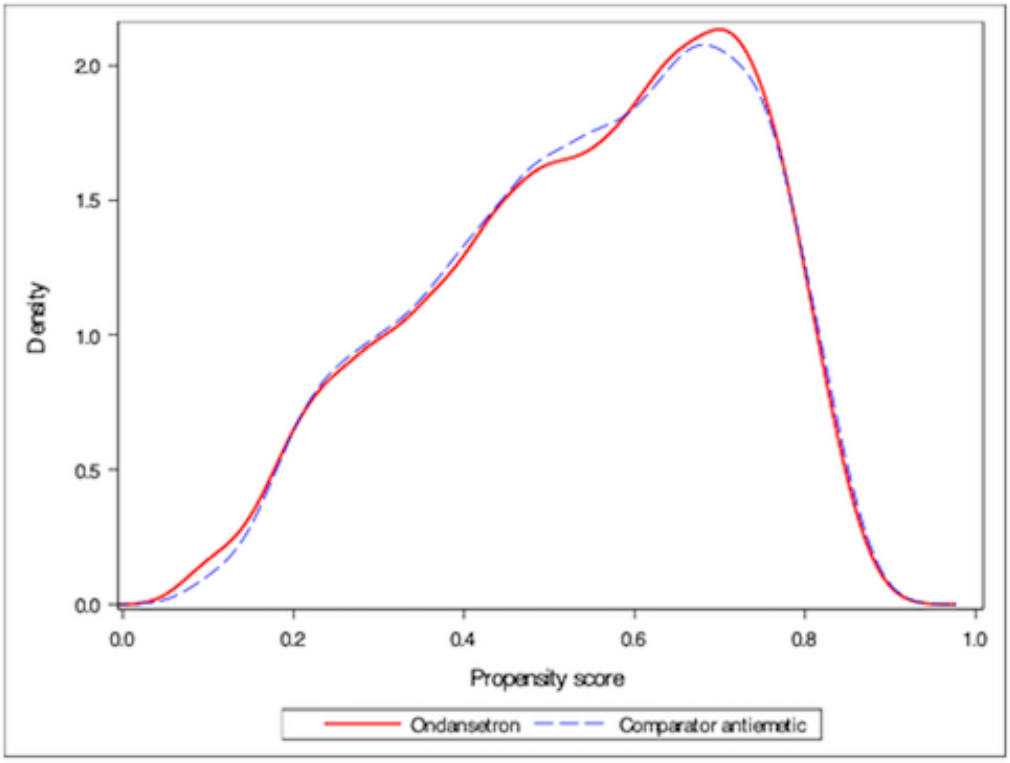
[a] We excluded index study antiemetic prescriptions before 2012 as the Food and Drug Administration (FDA) label warning on ondansetron was updated in 2012.

Supplemental Figure 2. Propensity score distributions

Panel A. Propensity score distributions before inverse probability of treatment weighting



Panel B. Propensity score distributions after inverse probability of treatment weighting



SUPPLEMENTAL TABLES

Supplemental Table 1. Definitions of the Torsades de Pointes risk categories based on the CredibleMeds® website.[1,2]

Classifications	Definitions
Known risk of Torsades de Pointes	"Drugs that prolong the QT interval AND are clearly associated with a known risk of Torsades de Pointes, even when taken as recommended."
Possible risk of Torsades de Pointes	"Drugs that can prolong the QT interval BUT currently lack evidence for a risk of Torsades de Pointes when taken as recommended."
Conditional risk of Torsades de Pointes	"Drugs that are associated with Torsades de Pointes BUT only under certain conditions of their use (e.g., excessive dose, in patients with conditions such as hypokalemia, or when taken with interacting drugs) OR by creating conditions that facilitate or induce Torsades de Pointes (e.g.., by inhibiting metabolism of a QT prolonging drug or by causing an electrolyte disturbance that induces Torsades de Pointes)."

Supplemental Table 2. Outcome definitions.

Study outcome	Definitions
Sudden cardiac death *(primary outcome)*	Death with a cardiac arrhythmia or cardiac arrest death code (28, 29) listed as the *primary* cause of death on the ESRD death notification form.
Composite outcome of sudden cardiac death or hospitalized ventricular arrhythmia *(secondary outcome)*	Death with a cardiac arrhythmia or cardiac arrest death code (28, 29) listed as the *primary* cause of death on the ESRD death notification form. *OR* An inpatient hospitalization for a ventricular arrhythmia based on the *primary* ICD-9/ICD-10 discharge diagnosis code. • ICD-9 codes[a]: 427.1, 427.4 • ICD-10 codes[b]: I47.2, I49.0
Cardiovascular mortality *(secondary outcome)*	Death with a cardiovascular cause of death code (23, 25, 26, 27, 28, 29, 30, 31, 32, 35, 36) listed as the *primary* cause of death on the ESRD notification form.
Hospitalized fracture *(negative control outcome)*	An inpatient hospital admission for fracture defined as: • The presence of an ICD-9 or ICD-10 discharge diagnosis codes for fracture located at any billing position[c]

[a] Specified four-digit ICD-9 diagnosis codes listed included all existing 5th digit codes.

[b] Specified four-digit ICD-10 diagnosis codes listed include all existing 5th, 6th, and 7th digit codes.

[c] Supplemental Table 3 Lists all applicable ICD-9 and ICD-10 codes.

Abbreviations: ESRD, end-stage renal disease, ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases,10th Revision.

Supplemental Table 3. ICD-9/ICD-10 diagnosis codes used to identify hospitalized fracture.

Hospitalized fracture
ICD-9 codes[a]: 800-929
ICD-10 codes[b]: S02.0**A, S02.0**B, S02.1**A, S02.1**B, S02.2**A, S02.2**B, S02.3**A, S02.3**B, S02.4**A, S02.4**B, S02.5**A, S02.5**B, S02.6**A, S02.6**B, S02.8**A, S02.8**B, S02.9**A, S02.9**B, S12.0**A, S12.0**B, S12.1**A, S12.1**B, S12.2**A, S12.2**B, S12.3**A, S12.3**B, S12.4**A, S12.4**B, S12.5**A, S12.5**B, S12.6**A, S12.6**B, S12.8**A, S12.9**A, S22.0**A, S22.0**B, S22.2**A, S22.2**B, S22.3**A, S22.3**B, S22.4**A, S22.4**B, S22.5**A, S22.5**B, S22.9**A, S22.9**B, S32.0**A, S32.0**B, S32.1**A, S32.1**B, S32.2**A, S32.2**B, S32.3**A, S32.3**B, S32.4**A, S32.4**B, S32.5**A, S32.5**B, S32.6**A, S32.6**B, S32.8**A, S32.8**B, S32.9**A, S32.9**B, S42.0**A, S42.0**B, S42.1**A, S42.1**B, S42.2**A, S42.2**B, S42.3**A, S42.3**B, S42.4**A, S42.9**A, S42.9**B, S49.0**A, S49.1**A, S52.0**A, S52.0**B, S52.0**C, S52.1**A, S52.1**B, S52.1**C, S52.2**A, S52.2**B, S52.2**C, S52.3**A, S52.3**B, S52.3**C, S52.5**A, S52.5**B, S52.5**C, S52.6**A, S52.6**B, S52.6**C, S52.9**A, S52.9**B, S52.9**C, S59.0**A, S59.1**A, S59.2**A, S62.0**A, S62.0**B, S62.1**A, S62.1**B, S62.2**A, S62.2**B, S62.3**A, S62.3**B, S62.5**A, S62.5**B, S62.6**A, S62.6**B, S62.9**A, S62.9**B, S72.0**A, S72.0**B, S72.0**C, S72.1**A, S72.1**B, S72.1**C, S72.2**A, S72.2**B, S72.2**C, S72.3**A, S72.3**B, S72.3**C, S72.4**A, S72.4**B, S72.4**C, S72.8**A, S72.8**B, S72.8**C, S72.9**A, S72.9**B, S72.9**C, S79.0**A, S79.1**A, S82.0**A, S82.0**B, S82.0**C, S82.1**A, S82.1**B, S82.1**C, S82.2**A, S82.2**B, S82.2**C, S82.3**A, S82.3**B, S82.3**C, S82.4**A, S82.4**B, S82.4**C, S82.5**A, S82.5**B, S82.5**C, S82.6**A, S82.6**B, S82.6**C, S82.8**A, S82.8**B, S82.8**C, S82.9**A, S82.9**B, S82.9**C, S89.0**A, S89.1**A. S89.2**A, S89.3**A, S92.0**A, S92.0**B, S92.1**A, S92.1**B, S92.2**A, S92.2**B, S92.3**A, S92.3**B, S92.4**A, S92.4**B, S92.5**A, S92.5**B, S92.8**A, S92.8**B, S92.9**A, S92.9**B, S99.0**A, S99.0**B, S99.1**A, S99.1**B, S99.2**A, S99.2**B

[a] Specified three-digit ICD-9 diagnosis codes listed included all existing 4th and 5th digit codes.

[b] Specified four-digit ICD-10 diagnosis codes listed include all existing 5th, 6th, and 7th digit codes. For the specified seven-digit ICD-10 codes, the ** indicates that all existing 5th and 6th digit code combinations were considered.

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases,10th Revision.

Supplemental Table 4. ICD-9/ICD-10 diagnosis and procedure codes used to identify comorbid conditions and other covariates.

Covariates	Diagnosis or procedure codes[a,b,c]
Comorbid conditions	
Diabetes	• ICD-9 diagnosis codes: 250 • ICD-10 diagnosis codes: E10, E11, E13
Arrhythmia	• ICD-9 diagnosis codes: 426 • ICD-10 diagnosis codes: I44–I45
Ischemic heart disease	• ICD-9 Diagnosis codes: 410-414 • ICD-10 diagnosis codes: I20-I25
Heart failure	• ICD-9 Diagnosis codes: 39891, 4021, 4041, 4043, 428 • ICD-10 diagnosis codes: I50, I110, I130, I0981
Liver disease	• ICD-9 Diagnosis codes: 571 • ICD-10 diagnosis codes: K70-K77
Conduction diseases	• ICD-9 Diagnosis codes: 426 • ICD-10 diagnosis codes: I44, I45
Hypertension	• ICD-9 Diagnosis codes: 401- 405 • ICD-10 diagnosis codes: I10 -I16
Dyslipidemia	• ICD-9 Diagnosis codes: 272.0, 272.2, 272.4 • ICD-10 diagnosis codes: E78.0, E78.1, E78.2, E78.4, E78.5
Peripheral arterial disease	• ICD-9 Diagnosis codes: 250.7,440.2-440.9, 443.1, 443.22, 443.81, 443.89, 443.9, 444.22,444.81,445.02 • ICD-10 diagnosis codes: E10.5, E11.5, E13.5, I70.2–I70.9, I73.1, I73.89, I73.9, I74.3-I74.5, I75.02, I77.72, I79.1, I79.8
Stroke	• ICD-9 Diagnosis codes: 430–438 • ICD-10 diagnosis codes: G45, G46, I60-I69
Valvular disease	• ICD-9 Diagnosis codes: 394–397, 424.0-424.3 • ICD-10 diagnosis codes: I05-I08, I09.1, I34-I37
Cardiac pacemaker	• ICD-9 Diagnosis codes: V45.01 • ICD-10 diagnosis codes: Z95.0
Cancer	• ICD-9 Diagnosis codes: 140-208, 209 • ICD-10 diagnosis codes: C00-C97, C7A
Appendicitis	• ICD-9 Diagnosis codes: 540-542 • ICD-10 diagnosis codes: K35 - K37
Cholecystitis	• ICD-9 Diagnosis codes: 574.0, 574.1, 574.3, 574.4, 574.6, 574.7, 574.8 • ICD-10 diagnosis codes: K80.0, K80.1, K80.3, K80.4, K80.8
Cholelithiasis (gallstones)	• ICD-9 Diagnosis codes: 574 • ICD-10 diagnosis codes: K80
Gastric outlet obstruction or small bowel obstruction	• ICD-9 Diagnosis codes: 560, 537.3 • ICD-10 diagnosis codes: K83.1, K56, K91.3, K31.5
Acute gastritis	• ICD-9 Diagnosis codes: 535.0 • ICD-10 diagnosis codes: K29.0, K29.1
Gastroesophageal reflux disease	• ICD-9 Diagnosis codes: 530.81 • ICD-10 diagnosis codes: K21
Gastroparesis	• ICD-9 Diagnosis codes: 536.3, 249.6, 250.6 • ICD-10 diagnosis codes: E08.43, E09.43, E10.43, E11.43, E13.43
Irritable bowel syndrome	• ICD-9 Diagnosis codes: 564.1 • ICD-10 diagnosis codes: K58
Peptic ulcer disease	• ICD-9 Diagnosis codes: 533 • ICD-10 diagnosis codes: K27
Functional dyspepsia	• ICD-9 Diagnosis codes: 564.9, 536.8 • ICD-10 diagnosis codes: K30
Procedures	

Electrocardiogram	• ICD-9 diagnosis codes: 794.31 • ICD-10 diagnosis codes: R94.31 • CPT procedure codes: 93000, 93005, 93010, 93040, 93041, 93042
Cardiac surgery or procedure	• ICD-9 procedure codes[3]: 35, 36, 37 • ICD-10 procedure codes[4]: 02
Other	
History of non-adherence[d]	• ICD-9 diagnosis codes: V15.81, V45.12 • ICD-10 diagnosis codes: Z91.1

[a] Specified four-digit ICD-9 diagnosis codes listed included all existing 5th digit codes.

[b] Specified four-digit ICD-10 diagnosis codes listed include all existing 5th, 6th, and 7th digit codes.

[c] We considered comorbid conditions to be present if an applicable discharge diagnosis code or procedure code (located in any position) was associated with ≥1 institutional or physician supplier claim during the 180-day baseline period

[d] History of non-adherence to medical treatment and regimen including renal dialysis.[5]

Abbreviations: ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases,10th Revision.

Supplemental Table 5. Lists of medications by Torsades de Pointes risk category as per the CredibleMeds® website.[a]

Risk category	Medications
Known risk	Amiodarone, Anagrelide, Arsenic trioxide, Azithromycin, Bepridil*, Cesium chloride, Chloroquine, Chlorpromazine, Cilostazol, Ciprofloxacin, Citalopram, Clarithromycin, Cocaine, Disopyramide, Dofetilide, Donepezil, Dronedarone, Droperidol, Erythromycin, Escitalopram, Metolazone, Metronidazole, Nelfinavir, Olanzapine, Omeprazole, Pantoprazole, Paroxetine, Piperacillin/tazobactam, Posaconazole, Propafenone, Quetiapine, Quinine, Ranolazine, Risperidone, Sertraline, Oxaliplatin, Papaverine, Pentamidine, Pimozide, Procainamide, Propofol, Quinidine, Sevoflurane, Sotalol, Thioridazine, Vandetanib
Possible risk	Alfuzosin, Apalutamide, Apomorphine, Aripiprazole, Artemether/lumefantrine, Asenapine, Atomoxetine, Bedaquiline, Bendamustine, Bicalutamide, Bortezomib, Bosutinib, Buprenorphine, Cabozantinib, Capecitabine, Ceritinib, Clozapine, Cobimetinib, Crizotinib, Dabrafenib, Dasantinib, Degarelix, Desipramine Dextromethorphan/quinidine, Dolasteron, Efavirenz, Eliglustat, Encorafenib, Entrectinib, Epirubicin, Eribulin, Felbamate, Fingolimod, Fluorouracil, Gemifloxacin, Gilteritnib. Glasdegib. Granisertron. Hydrocodone (ER only), Iloperidone, Imatinib, Imipramine. Inotuzumab ozogamicin, Isradipine, Ivosidenib Laoatinib, Lefamulin, Lenvatinib, Leuprolide, Levetiracetam, Levoketoconazole, Lithium, Lofexidine, Lopinavir/ritonavir, Lumateperone, Lurasidone, Maprotiline, Midostaurin, Mifepristone, Mirabegron, Mirtazapine, Necitumumab, Nicardipine, Nilotinib, Nortriptyline, Nusinersen, Ofloxacin, Oliceridine, Osilordrostat, Osimertinib, Oxytocin, Ozanimod, Paliperidone, Palonosetron, Panobinostat, Pasireotide, Pazopanib, Perflutren, Perphenazine, Pimavanserin, Pitolisant, Ponesimod, Pretomanid, Primaquine, Promethazine, Relugolix, Remimazolam, Ribociclib, Rilpivirine, Romidepsin, Rucaparib, Saquinavir, Selpercantib, Siponimod, Sorafenib, Sunitinib, Tacrolimus, Tamoxifen,Tazemetostat,Telavancin,Telithromycin, Tetrabenazine, Tipiracil/trifluridine,Tizanidine, Tolterodine, Tramadol, Trimipramine, Valbenazine, Vardenafil, Vemurafenib, Voclosporin, Varinostat.
Conditional risk	Abiraterone, Amantadine, Amisulpride, Amitriptyline, Amphotericin B, Atazanavir, Bendroflumethiazide (also called bendrofluazide), Chloral hydrate, Cimetidine, Clomipramine, Diltiazem, Diphenhydramine, Doxepin, Esomeprazole, Famotidine, Fluoxetine, Fluvoxamine, Furosemide, Galantamine, Hydrochlorothiazide (also called HCTZ), Hydroxyzine, Indapamide, Itraconazole, Ivabradine, Ketoconazole, Lansoprazole, Loperamide, Metoclopramide, Metolazone, Metronidazole, Nelfinavir, Olanzapine, Omeprazole, Pantoprazole, Paroxetine, Piperacillin/tazobactam, Posaconazole, Propafenone, Quetiapine, Quinine, Ranolazine, Risperidone, Sertraline, Solifenacin, Torsemide, Trazodone, Voriconazole, Ziprasidone.

[a] This list was obtained from the CredibleMeds website on 6/3/2022. According to CredibleMeds, this specific medication list was last revised on 5/26/2022.

Supplemental Table 6. Baseline characteristics of ondansetron and comparator antiemetic new users.[a]

	Unweighted cohort			Weighted cohort[b]		
Characteristic	**Ondansetron (n = 64,978)**	**Comparator antiemetic (n = 54,276)**	**SMD[c]**	**Ondansetron (n= 65,167)**	**Comparator antiemetics (n = 54,264)**	**aSMD[c]**
Age (years)	62 ± 15	58 ±14	0.23	60 ± 15	60 ± 14	<0.01
Female	36,557 (56)	28,888 (53)	0.06	35,761 (55)	29,699 (55)	<0.01
Race			0.11			<0.01
American Indian or Alaska Native	859 (1)	784 (1)		876 (1)	731 (1)	
Asian	1,628 (3)	1,583 (3)		1,776 (3)	1,480 (3)	
Black	21,051 (32)	20,165 (37)		22,530 (35)	18,707 (34)	
Native Hawaiian or Pacific Islander	543 (1)	406 (1)		514 (1)	433 (1)	
Other[d]	111 (<0.01)	78 (<0.01)		100 (<0.01)	86 (<0.01)	
White	40,786 (63)	31,260 (58)		39,372 (60)	32,826 (60)	
Hispanic ethnicity	9,941 (15)	10,255 (19)	0.10	10,866 (17)	9060 (17)	<0.01
Primary cause of kidney failure			0.13			<0.01
Diabetes mellitus	32,004 (49)	30,117 (55)		33,855 (52)	28,053(52)	
Hypertension	17,564 (27)	13,201 (24)		16,774 (26)	13,951 (26)	
Glomerulonephritis	6,205 (10)	4,533 (8)		5,925 (9)	4,974 (9)	
Other causes[e]	9,205 (14)	6,425 (12)		8,608 (13)	7,286 (13)	
Prior kidney transplant	3,728 (6)	3,102 (6)	<0.01	3,793 (6)	3181 (6)	<0.01
Time on maintenance hemodialysis			0.07			<0.01
<1 year	16,924 (26)	15,687 (29)		17,952 (28)	14,936 (28)	
1 to <2 years	12,464 (19)	10,377 (19)		12,482 (19)	10,367 (19)	
2 to <3 years	9,048 (14)	7,274 (13)		8,933 (14)	7,422 (14)	
≥3 years	26,542 (41)	20,938 (39)		25,801 (40)	21,538 (40)	
Medicare Part D low-income subsidy in the last 30 days of baseline	6,008 (9)	4,672 (9)	0.02	5,797 (9)	4,840 (9)	<0.01
History of non-adherence[f]	7,285 (11)	6,215 (11)	0.01	7,556(12)	6,221 (11)	<0.01
Had an ECG during the last 30 days of baseline	18,178 (28)	11,599 (21)	0.15	16,384 (25)	13,757 (25)	<0.01
Had cardiac surgery during baseline	3,755 (6)	2,863 (5)	0.02	3,577 (5)	2,993 (6)	<0.01
Comorbid conditions						
Diabetes mellitus	46,506 (72)	41,736 (77)	0.12	48,172 (74)	40,010 (74)	<0.01
Hypertension	60,494 (93)	49,497 (91)	0.07	60,207 (92)	50,099 (92)	<0.01
Dyslipidemia	42,057 (65)	34,140 (63)	0.04	41,660 (64)	34,693 (64)	<0.01
Ischemic heart disease	29,462 (45)	23,875 (44)	0.03	29,088 (45)	24,229 (45)	<0.01
Heart failure	29,084 (45)	23,344 (43)	0.04	28,672 (44)	23,861 (44)	<0.01
Arrythmia	18,615 (29)	13,823 (25)	0.07	17,798 (27)	14,844 (27)	<0.01
Conduction disorder	7,117 (11)	4,870 (9)	0.07	6,555 (10)	5,485 (10)	<0.01
Valvular disorder	12,390 (19)	9,166 (17)	0.06	11,772 (18)	9,844 (18)	<0.01
Cardiac pacemaker	3,099 (5)	2,093 (4)	0.05	2,825 (4)	2,338 (4)	<0.01
Stroke	14,315 (22)	11,453 (21)	0.02	14,081 (22)	11,692 (22)	<0.01
Peripheral arterial disease	21,344 (33)	17,858 (33)	<0.01	21,362 (33)	17,761 (33)	<0.01
Liver disease	6,826 (11)	4,480 (8)	0.08	6,235 (10)	5,254 (10)	<0.01
Cancer	8,628 (13)	5,694 (10)	0.09	7,924(12)	6,734 (12)	0.01
Appendicitis	53 (<0.01)	66 (<0.01)	0.01	69 (<0.01)	56 (0)	<0.01
Cholecystitis	1,236 (2)	840 (2)	0.03	1,138 (2)	964 (2)	<0.01
Cholelithiasis (gallstones)	3,904 (6)	2,682 (5)	0.05	3,599 (6)	3,007 (6)	<0.01
Gastric outlet obstruction or small bowel obstruction	1,990 (3)	1,678 (3)	<0.01	2,045 (3)	1,693 (3)	<0.01
Acute gastritis	1,494 (2)	1,554 (3)	0.04	1,707 (3)	1,399 (3)	<0.01
Gastroesophageal reflux disease	23,598 (36)	19,226 (35)	0.02	23,579 (36)	19,636 (36)	<0.01
Gastroparesis	3,213 (5)	6,246 (12)	0.24	5,554 (9)	4,368 (8)	0.02
Irritable bowel syndrome	989 (2)	773 (1)	0.01	994 (2)	823 (2)	<0.01
Peptic ulcer disease	923 (1)	846 (2)	0.01	1,005 (2)	821 (2)	<0.01
Functional Dyspepsia	921 (1)	1,356 (3)	0.08	1307 (2)	1,051 (2)	<0.01
Year study medication was filled						
2012	3,618 (6)	10,405 (19)	0.42	7,775 (12)	6,381 (12)	0.01
2013	5,475 (8)	8,759 (16)	0.24	7,832 (12)	6,492 (12)	<0.01
2014	5,468 (8)	6,507 (12)	0.12	6,495 (10)	5,434 (10)	<0.01
2015	7,600 (12)	7,276 (13)	0.05	8,128 (12)	6,773 (12)	<0.01
2016	8,955 (14)	6,706 (12)	0.04	8,550 (13)	7,123 (13)	<0.01
2017	11,073 (17)	5,714 (11)	0.19	9,134 (14)	7,630 (14)	<0.01

2018	11,149 (17)	4,722 (9)	0.25	8,630 (13)	7,202 (13)	<0.01
2019	11640 (18)	4187 (8)	0.31	8,616 (13)	7,235 (13)	<0.01
Use of ≥1 medication with a *known* risk of Torsades de Pointes[g]	13,413 (21)	10,807 (20)	0.02	13,314 (20)	11,127 (21)	<0.01
Use of ≥1 medication with a *possible* risk of Torsades de Pointes[g]	9,500 (15)	6,992 (6)	0.05	9,004 (14)	7,495 (14)	<0.01
Use of ≥1 medication with a *conditional* risk of Torsades de Pointes[g]	37,296 (57)	31,441 (58)	0.01	37,548 (58)	31,295 (58)	<0.01

[a] Values are presented as number (%) for categorical variables and as mean ± standard deviation for continuous variables. All covariates were measured during the 180-day baseline period unless otherwise specified.

[b] The weighted cohort is the pseudo-population generated by the inverse probability of treatment weighting.

[c] A standardized mean difference >0.10 represents meaningful imbalance between groups.

[d] Other race includes American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander, and Multiracial.

[e] Other causes of ESKD include cystic, urologic, other, unknown, and missing (0.12%).

[f] History of non-adherence is defined based on ICD-9-CM and ICD-10-CM as non-compliance to medical treatment and regimen including renal dialysis.

[g] The CredibleMeds® website is a reliable online clinical resource with up-to-date information about medications that can cause QT prolongation and/or Torsades de Pointes. [1,2] Based upon published literature, medication package inserts, data from the US Food and Drug Administration's Adverse Event Reporting System, and other sources CredibleMeds® classifies QT-prolonging medications as having a known, possible, or conditional risk of Torsades de Pointes. [1,2] Definitions for each risk category are provided in **Supplemental Table 1** and lists of medications falling into each category are provided in **Supplemental Table 5**. [1,2]

Abbreviations: aSMD, absolute standardized mean differences; ECG, electrocardiogram.

Supplemental Table 7. Incidence rates (IR) of study outcomes.

Outcomes	Ondansetron		Comparator antiemetic		Incidence rate ratio (95% CI)	
	Events/ person-days	IR/10,000 person-days	Events/ person-days	IR/10,000 person-days	Crude	Adjusted[a]
Sudden cardiac death	133/ 645,653	2.06	65/ 540,752	1.20	1.71 (1.27, 2.31)	1.45 (1.06 2.00)
Sudden cardiac death or ventricular arrythmias	143/ 540,724	2.21	75/ 540,724	1.39	1.60 (1.21, 2.11)	1.38 (1.02, 1.86)
Cardiovascular death	160/ 645,653	2.48	82/ 540,752	1.52	1.63 (1.25, 2.13)	1.39 (1.04, 1.84)

[a] Incidence rate ratio are adjusted for patient demographics, dialysis characteristics, comorbid conditions, and relevant medication use, among other factors (see **Supplemental Table 6** for a comprehensive list of variables similar to the ones used in the propensity score models.

Abbreviations: CI, confidence interval; IR, incidence rate.

Supplemental Table 8. Subgroup analyses.

Population	Ondansetron[a]	Comparator antiemetic[a]	10-day HR[b] (95% CI)
Overall			
Ondansetron *vs.* comparator antiemetic	133/64,978 (0.20%)	65/54,276 (0.12%)	1.44 (1.08, 1.93)
Age (years)			
≥65	84/30,429 (0.28%)	31/18,735 (0.17%)	1.55 (1.03, 2.32)
<65	49/34,549 (0.14%)	34/35,541 (0.10%)	1.47 (0.95, 2.26)
Sex			
Male	62/28,421 (0.22%)	28/25388 (0.11%)	1.64 (1.06, 2.55)
Female	71/36,557 (0.19%)	37/28,888 (0.13%)	1.31 (0.89, 1.93)
Hepatic disease			
Yes	13/6,826 (0.19%)	<11	0.77 (0.35, 1.72)
No	120/58,152 (0.21%)	58/49,796 (0.12%)	1.59 (1.16, 2.17)
Heart failure			
Yes	84/29,084 (0.29%)	37/23,344 (0.16%)	1.58 (1.08, 2.30)
No	49/35,894 (0.14%)	28/30,932 (0.09%)	1.30 (0.82, 2.04)
Arrhythmic condition			
Yes	59/18,615 (0.32%)	26/13,823 (0.19%)	1.40 (0.89, 2.19)
No	74/46,363 (0.19%)	39/40,453 (0.10%)	1.52 (1.03, 2.23)
Use of ≥1 medication with a known risk of Torsades de Pointes			
Yes	31/13,413 (0.23%)	19/10,807 (0.18%)	1.10 (0.62, 1.95)
No	102/51,565 (0.20%)	46/43,469 (0.11%)	1.59 (1.14, 2.23)
Use of ≥1 medication with a possible risk of Torsades de Pointes			
Yes	20/9,500 (0.21%)	<11	1.73 (0.74, 4.00)
No	113/55,478 (0.20%)	56/47,284 (0.12%)	1.41 (1.04, 1.92)
Use of ≥1 medication with a conditional risk of Torsades de Pointes			
Yes	68/37,296 (0.18%)	39/31,441 (0.12%)	1.29 (0.88, 1.89)
No	65/27,682 (0.23%)	26/22,835 (0.11%)	1.70 (1.09, 2.65)

[a] Results are presented as number of events of sudden cardiac death/number of individuals per each subgroup (percentage).

[b] We used Fine and Gray models to account for competing risks and estimated subdistribution hazards ratios (HRs) and 95% CIs. The adjusted (i.e., weighted) subdistribution hazards ratios are adjusted for patient demographics, dialysis characteristics, comorbid conditions, and relevant medication use, among other factors (see **Supplemental Table 6** for a comprehensive list of variables similar to the ones used in the propensity score models).

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval.

Supplemental Table 9. Sensitivity analyses.

Assessment of study outcomes at 30 days of follow up (N= 119,254)						
	Ondansetron	Comparator antiemetic	30-day HR[a] (95% CI)		30-day RD (95% CI)	
Outcome	Events/ Person-days	Events/ Person-days	Crude[b]	Adjusted[c]	Crude[b]	Adjusted[c]
Sudden cardiac death	403/1,908,652	223/1,606,912	1.52 (1.29, 1.79)	1.37 (1.16,1.61)	0.21% (0.13%, 0.30%)	0.16% (0.06%, 0.26%)
Sudden cardiac death or ventricular arrythmias	596/1,904,663	360/1,604,387	1.40 (1.23, 1.59)	1.26 (1.11, 1.44)	0.26% (0.26%, 0.16%)	0.19% (0.07%, 0.30%)
Cardiovascular death	506/1,908,652	287/1,606,912	1.48 (1.28, 1.71)	1.35 (1.17, 1.56)	0.26% (0.16%, 0.35%)	0.19% (0.10%, 0.28%)
Assessment of study outcomes at 10-days using washout periods of varying duration						
	Ondansetron	Comparator antiemetic	10-day HR[a] (95% CI)		10-day RD (95% CI)	
Outcome	Events/ Person-days	Events/ Person-days	Crude[b]	Adjusted[c]	Crude[b]	Adjusted[c]
60-day washout period (N=105,704)						
Sudden cardiac death	123/591,539	55/459,960	1.74 (1.27, 1.39	1.38 (1.02, 1.88)	0.09% (0.04%, 0.14%)	0.05% (0.00%, 0.10%)
Sudden cardiac death or ventricular arrythmias	132/591,496	65/459,932	1.58 (1.17, 2.13)	1.28 (0.96, 1.70)	0.08% (0.03%, 0.13%)	0.05% (-0.01%, 0.11%)
Cardiovascular death	150/591,539	71/459,960	1.64 (1.24, 2.18)	1.30 (0.99, 1.71)	0.10% (0.05%, 0.15%)	0.05% (-0.01%, 0.12%)
90-day washout period (N=98,876)						
Sudden cardiac death	119/558,145	53/425,348	1.71 (1.24, 2.36)	1.40 (1.02, 1.92)	0.09% (0.04%, 0.14%)	0.06% (0.00%, 0.11%)
Sudden cardiac death or ventricular arrythmias	128/558,102	61/425,329	1.60 (1.18, 2.17)	1.33 (1.00, 1.79)	0.09% (0.03%, 0.14%)	0.05% (0.00%, 0.11%)
Cardiovascular death	146/558,145	68/425,348	1.64 (1.23, 2.18)	1.32 (1.00, 1.74)	0.10% (0.05%, 0.16%)	0.06% (-0.01%, 0.13%)
180-day washout period (N= 87,371)						
Sudden cardiac death	109/499,285	48/369,646	1.68 (1.20, 2.36)	1.40 (1.01, 1.95)	0.09% (0.03%, 0.14%)	0.06% (0.01%, 0.11%)
Sudden cardiac death or ventricular arrythmias	117/499,250	55/369,632	1.57 (1.14, 2.17)	1.33 (0.98, 1.82)	0.09% (0.02%, 0.15%)	0.06% (-0.01%, 0.11%)
Cardiovascular death	136/499,285	63/369,646	1.60 (1.19, 2.15)	1.31 (0.98, 1.75)	0.10% (0.04%, 0.17%)	0.06% (-0.01%, 0.13%)
Assessment of negative control outcome at 10-days in a cohort excluding patients with history of cancer or fracture at baseline (N=96,056)						
	Ondansetron	Comparator antiemetic	10-day HR[a] (95% CI)		10-day RD (95% CI)	
Outcome	Events/ Person-days	Events/ Person-days	Crude[b]	Adjusted[c]	Crude[b]	Adjusted[c]
Hospitalized fracture	233/ 511,345	166/446,669	1.23 (1.00,1.50)	1.17 (0.95, 1.43)	0.08% (0.00%, 0.17%)	0.06% (-0.02%, 0.14%)
Assessment of sudden cardiac death during different time intervals						
	Ondansetron	Comparator antiemetic	HR[a] (95% CI)		RD (95% CI)	
Time intervals	Events/ Person-days	Events/ Person-days	Crude[b]	Adjusted[c]	Crude[b]	Adjusted[c]
10-30 days *(N=117,922)*	270/190,389,9	158/160,448,0	1.39 (1.14,1.69)	1.29 (1.06, 1.58)	0.11% (0.04%,0.18%§)	0.09% (0.01%, 0.16%)
30-90 days *(N=114,797)*	710/543,309,2	504/465,356,3	1.21 (1.08, 1.36)	1.08 (0.96, 1.21)	0.19% (0.08%. 0.31%)	0.07% (-0.06%, 0.21%)

90-180 days *(N=106,566)*	994/992,742,6	723/874,711,3	1.18 (1.07, 1.30)	1.05 (0.95, 1.16)	0.25% (0.10%, 0.40%)	0.07% (-0.09%, 0.23%)
180-365 days *(N= 95,308)*	1817/170,986,56	1440/158,367,21	1.10 (1.03, 1.19)	1.00 (0.93, 1.08)	0.32% (0.08%, 0.55%)	0.02% (-0.25%, 0.29%)

[a] We used Fine and Gray models to account for competing risks in the unweighted (crude) and weighted (adjusted) cohorts and estimated subdistribution HRs, RDs and 95% CIs.

[b] Crude estimates reflect the unadjusted (i.e., unweighted) estimates prior to the implementation of inverse probability of treatment weights that were used for confounding control.

[c] Adjusted estimates reflect the weighted estimates after the implementation of inverse probability of treatment weights. The adjusted (i.e., weighted) models are adjusted for patient demographics, dialysis characteristics, comorbid conditions, and relevant medication use, among other factors (see **Supplemental Table 6** for a comprehensive list of variables used in the propensity score models).

Abbreviations: CI, confidence intervals; HR: hazard ratio; RD, risk difference.

Supplemental Material References

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