

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Generic Names Used to Capture Medications of Interest**

	<b>Generic Name</b>
<b>Fluoroquinolones<sup>a</sup></b>	Ciprofloxacin, Gemifloxacin, Levofloxacin, Moxifloxacin, Norfloxacin, Ofloxacin
<b>Active comparators<sup>a</sup></b>	Amoxicillin/Clavulanate, Azithromycin, Cephalexin, Clindamycin, Sulfamethoxazole/Trimethoprim
<b>Antihypertensives</b>	
Beta-blockers	Atenolol, Carvedilol, Esmolol, Metoprolol, Nebivolol, Sotalol
ACE inhibitors	Benazepril, Captopril, Enalapril, Lisinopril, Ramipril
ARBS	Losartan, Olmesartan, Valsartan
Calcium channel blockers	Amlodipine, Diltiazem, Nicardipine, Nifedipine, Nimodipine, Verapamil
Alpha blockers	Doxazosin, Prazosin, Terazosin
Central agonists	Clonidine
Vasodilators	Minoxidil
Loop diuretics	Bumetanide, Furosemide, Torsemide, Ethacrynic acid
Other diuretic	Chlorothiazide, Chlorthalidone, Hydrochlorothiazide, Metolazone
<b>Oral diabetic medication</b>	Acarbose, Albiglutide, Alogliptin, Canagliflozin, Dapagliflozin, Dulaglutide, Empagliflozin, Exenatide, Glimepiride, Glipizide, Glyburide, Linagliptin, Liraglutide, Metformin, Nateglinide, Pioglitazone, Repaglinide, Rosiglitazone, Sitagliptin, Saxagliptin, Tolbutamide
<b>Insulin</b>	Insulin aspart, Insulin detemir, Insulin glargine, Insulin glulisine, Insulin lispro, Insulin human isophane (NPH), Insulin human regular, Insulin human zinc
<b>Lipid-lowering medications</b>	Atorvastatin, Cerivastatin, Fenofibrate, Fluvastatin, Gemfibrozil, Lovastatin, Niacin, Pravastatin, Simvastatin
<b>Anticoagulants</b>	Apixaban, Dabigatran, Enoxaparin, Fondaparinux, Heparin, Rivaroxaban, Warfarin
<b>Antiplatelets</b>	Clopidogrel, Dipyridamole, Eptifibatide, Prasugrel, Ticagrelor, Ticlodipine
<b>Beta agonist inhalants</b>	Albuterol, Budesonide/formoterol fumarate, Formoterol, Fluticasone propionate/salmeterol Xinafoate, Levalbuterol, Metaproterenol, Pirbuterol, Salmeterol
<b>Corticosteroids (inhaled)</b>	Beclomethasone, Budesonide, Ciclesonide, Flunisolide, Fluticasone, Momatasone
<b>Anticholinergics (inhaled)</b>	Ipratropium bromide, Tiotropium bromide
<sup>a</sup> Medication form was restricted to capsules (including extended and delayed release), tablets, powders for suspension/solution, syrups, and tablets (including delayed and extended release)	

**eTable 2. ICD-9-CM and ICD-10-CM Codes Used to Capture Baseline Covariates and Indications for Antibiotic Use**

	ICD-9-CM	ICD-10-CM <sup>a</sup>
<b>CCI components</b>		
Prior myocardial infarction	410.00 – 410.92, 412	I21.01-I21.A9, I22.0-122.9, 125.2
Congestive heart failure	428.0-428.9	I50.01-I50.9
Peripheral vascular disease	443.9, 785.4, V43.4	E08.52, E09.52, E10.52, E11.52, E13.52, H49.20-H49.23, I70.361-I70.769, I71.00-I71.9, I73.01, I73.9, I96, Z95.820, Z95.828
Cerebrovascular disease	430-438.9	G45.0-G46.8, I60.00-I63.9, I65.01-I66.9, I67.1, I67.2, I67.4-I67.7, I67.81, I67.82, I67.41, I67.48, I67.89, I67.9, 168.0-169.998
Dementia	290.0-290.9	F01.50, F01.51, F03.90, F05
COPD	490-496, 500-505, 506.4	J40-J47.9, J60-J67.9, J68.4
Connective tissue disease	710.0, 710.1, 710.4, 714.0, 714.1, 714.81, 725	M05.00-M06.09, M06.20-M06.39, M06.80-M06.9, M32.0-M32.9, M33.20-M33.29, M34.0-M34.9, M35.3
Peptic ulcer disease	531.00-534.91	K25.0-K28.9, K56.699
Diabetes	<i>Uncomplicated:</i> 250.0-250.3, 250.7  <i>Complicated:</i> 250.4-250.6, 250.8, 250.9	<i>Uncomplicated:</i> E10.10, E10.11, E10.51-E10.59, E10.641, E10.9, E11.00, E11.01, E11.10, E11.11, E11.51-E11.59, E11.641, E11.69, E11.9, E13.00, E13.01, E13.10, E13.11, E12.51-E13.59, E13.641, E13.9  <i>Complicated:</i> E10.21-E10.29, E10.311-E10.39, E10.40-E10.49, E10.610, E10.65, E10.69, E11.21-E11.29, E11.311-E11.39, E111.40-E11.49, E11.610, E11.65, E13.21-E13.29, E13.311-E13.39, E13.40-E13.49, E13.610
Hemiplegia/paraplegia	342.00-342.92, 344.1	G37.70, G37.5, G81.00-G81.94
Renal disease	582.0-582.9, 583.0-583.7, 585.1-586, 588.0-588.9	N03.0-N03.9, N05.2-N05.9, N06.2-N06.5, N07.2-N07.5, N08, N17.1, N17.2, N18.1-N18.9, N19, N25.0-N25.9
Liver disease, mild	571.2, 571.4, 571.5, 571.6	K70.2, K70.30, K70.31, K73.0-K73.9, K74.0, K74.3-K74.69, K75.4
Liver disease, severe	572.2-572.8, 456.0-456.2	I85.00-I85.11, K70.41, K71.11, K72.01, K72.10, K72.11, K72.90, K72.91, K76.6, K76.7
Cancer	140.0-172.9, 174.0-195.8, 200.00-208.92	C00.0-C41.9, C43.0-C43.9, C45.0-C45.7, C46.0-C76.8, C81.00-C86.6, C88.2-C88.9, C90.00-C96.Z, D03.0-D03.9, D45
Metastatic cancer	196.0-199.1	C45.9, C77.0-C79.9, C80.0, C80.1
HIV/AIDS	042, 079.53	B20, B97.35
<b>Other comorbidities</b>		
Secondary diabetes	249.00-249.91	E08.00-E09.9
Hyperlipidemia	272.0, 272.2-272.4, 277.7	E78.00, E78.01, E78.2-E78.5, E88.81
Vasculopathy	290.40-290.43, 357.1	I77.1-I77.3, I77.89, I77.9, I87.8, I87.9, I99.8, I99.9, K55.1, K55.8, K55.9, M30.0, M30.2, M30.8, M31.1, M31.5-M31.7
Aneurysmal disease	362.14, 414.10, 414.11, 414.19, 417.1, 437.3	H35.041-H35.043, H35.049, I25.3, I25.41, I28.1, I67.1

Acute rheumatic disease	390-392	I00, I01.0-I01.9, I02.0, I02.9
Chronic rheumatic disease	393, 394.0, 394.1, 395.0-395.9, 396.0, 397.0-398.99	I05.0-I09.9
Hypertension	401.0-405.99	I10-I13.2, I15.0-I15.9, I16.0-I16.9, N26.2
Coronary artery disease	411.0-411.89, 414.12, 414.2-414.9	I20.0, I24.0-I24.9, I25.110, I25.42, I25.5, I25.6, I25.700, I25.710, I25.720, I25.730, I25.750, I25.760, I25.790, I25.82-I25.84, I25.89, I25.9
Angina	413.0-413.9	I20.1, I20.8, I20.9, I25.111, I25.118, I25.119, I25.701, I25.708, I25.709, I25.711, I25.718, I25.719, I25.721, I25.728, I25.729, I25.731, I25.738, I25.739, I25.751, I25.758, I25.759, I25.761, I25.768, I25.769, I25.791, I25.798, I25.799
Atherosclerosis	414.00-414.07, 440.00-440.9	I25.10, I25.110-I25.119, I25.700-I25.799, I25.810-I25.812, I70.0-I70.92
Pulmonary disease	415.0-416.9, 417.0, 417.8, 417.9	I26.01-I27.9, I28.0, I28.8, I28.9, T80.0XXA, T81.718A, T17.72XA, T82.817A, T82.818A
Pericarditis	420.0-420.99, 423.0-423.9	I30.0-I32, M32.12
Endocarditis	421.0-421.9, 424.90-424.99	I33.0, I33.9, I38, I39, M2.11
Myocarditis	422.0-422.99	I40.0, I40.1, I40.8, I40.9, I41
Other valve disease	424.2, 424.3	I34.0-I37.9
Cardiomyopathy	425.0-425.9	I42.0-I42.9, I43
Arrhythmia	426.2, 427.0-427.9	I44.4, I44.5, I44.60, I44.69, I46.2-I47.9, I48.0-I49.9, R00.1
History of brain bleed	430-432.9	I60.00-I62.9
VTE	444.01-445.89, 453.2-453.9	I74.01-I75.89, I82.210-I82.291, I82.3, I82.401-I82.C29,
<b>Indications</b>		
Gastrointestinal	001, 003-009, 022.2, 032.9, 039.2, 040.2, 058.1-9, 080, 084, 140, 148, 178, 530.1 – 530.8, 531 – 534, 537.4, 539.01, 550 – 551, 555, 556, 558.1-558.9, 560.0-569.9, 572.0, 577.0, 579.1, 619.1, 685.0, 777.5, 862, 863, 868.1, 946, 999.3	A00, A02 – A09, A18, A22, K20, K22, K25 – K28, K31.6, K40.1 – K40.4, K41.1-K41.4, K42 – K44, K50.000-K50.1XX, K50.8-K51.01X, K51.012-K51.014, K51.112-K51.114, K51.2 – K51.3, K51.4, K51.5, K51.8 – K51.9XX, K52.0-K52.9, K55.20, K55.21, K56.0-K56.7, K57.00-K57.93, K58.0-58.9, K59.00-K59.9, K60.0-K63.9, K65.0-K66.9, K67, K68.12, K68.19, K68.9, K75.0, K85.92, K90.1, K90.81, K91.1, K91.7, K91.850, K91.858, K91.89, K92.89, K92.9, K94.00-K94.32, N82.3, N99.4, R11.13, R18.8, T28.1-T28.2, T81.539A, Z20, Z22
Streptococcal/staphylococcus	034.0, 034.1, 035, 038.0-038.2, 320.2, 320.3, 381.0-381.9, 041.00-041.9	A38.0-A38.9, A40, A41, A46, A49.01-A49.9, B95.0-B69.89, G00.2, G00.3, J02.0, J03.00, J03.01, L00, M00.00-M00.89, O99.82, Z22.3,
Bacterial pneumonia	003.22, 011, 481-482.9, 483.0, 484, 485, 486,	A01.03, A15.0, A37, A48.1, A54.84, B77.81, J09X1, J10.00-J11.08, J13-J15.9, J16.0, J17, J18.2, J85.1, J86, J95.851,

	487.8, 488.01, 488.11, 488.81, 997.3	
Upper respiratory infection <sup>b</sup>	006.4, 020, 021, 031-033, 039.1, 040.1, 047.5, 048.8, 049.4, 098.6, 100.0 – 101.4, 108 – 123, 128, 130.4, 136.3, 137.0, 172.0, 174, 188.3, 277.02, 380.1 – 380.2, 382 – 386, 415.12, 461.0-466.19, 472 – 474, 478, 483, 487.1, 491 – 492, 494, 510-511, 513.0, 527, 528, 647.32, 872 – 874, 995.1	A06.5, A15.4-9, A18.6, A20.2, A24.1, A31.0, A36, A37, A42 – 43, A54.5, A56.4, A70, A78, B59=59, B90.9, E84.0, E84.9, H60.1 – H60.9, H62.4, H66.0 – H66.93, H67, H70, H72 – 75, H83.0, H95.32, J00, J01.00-J01.91, J02, J03.80, J03.81, J03.90, J03.91, J04.0-J04.31, J05.0-J05.11, J06.0, J06.9, J09 – J11.83, J16.8, J18, J20.0-J20.9, J21.0-J21.9, J22, J31, J32, J35, J39, J41 – J44, J47, J85, J86.9, J90, J91.8, J95.72, K11.2 – K11.3, O74.0, S11.2, T27.3
Urethritis/UTI	078.88, 079.8 – 079.9, 098, 099.4 – 099.9, 131, 137.2, 160.0, 161 – 165, 167, 169.0 – 169.3, 199.49, 595.0-595.9, 597.80, 597.81, 597.89, 599.0, 604.0-604.99, 607.1, 607.2, 608.0, 614 – 616.9, 634 – 637.51, 638.0, 639, 646.5 – 646.6, 647, 658.1 – 658.43, 659.3, 665.3, 670, 672.0, 867, 995.83, 996.64, 996.65	A06, A18.1, A36.85, A51.31, A54, A56, A59, A63.8, A64, A74.8 – A74.9, N28.8, N30.00-N30.91, N34.1, N34.2, N39.0, N43.1, N45.1-N45.5, N48.1, N49, N70 – N77, N82, N98.0, N99.7, O03 – O04.88, O07, O08, O23.0 – O23.93, O41.1, O42, O71.3, O86.1 – O86.29, O98.2 - O98.3, R82.7, R84.5, R86.5, R87.5, T28.3 – T28.8, T74.2, T76.2, T83.5, Z11.3, Z20.2, Z22.3 – Z22.4, Z87.4400
Cholecystitis/BTI	130.5, 574.00-576.9, 864.1, 868.12	A06.5, B58.1, K80.00-K80.81, K81.0-K83.9, K87, K91.5
Appendicitis	540.0-542, 863.95	K35.2-K35.89, K36, K37
Pyelonephritis	016.02, 016.06, 590.0-601.9	A02.25, A18.14, A56.01, N10-N13.9, N15.1, N15.9, N16, N20.0-N22, N28.0-N37, N39.0, N39.8, N39.9, N40.0-N41.9, N42.83, N51, N99.110-N99.115, N99.12, N99.510-N99.518, R31.0-R31.9, R80.2, T86.13
Skin/soft tissue/bone/lymph	020.1 – 022.0, 026.9, 027.1, 030 – 032, 037, 039, 040.0, 044.9, 045.2, 066, 068, 076.0, 078.3, 081 – 083, 085.1 – 085.5, 099.3, 102 – 103, 132, 137.3, 150 – 152, 155.0 – 159.6, 170.0 – 172.5, 174.0 – 177.5, 245, 254, 289, 323, 324.1, 349.31, 370, 373, 374.86, 375 – 377.32, 379.60, 380, 383, 384, 404.2, 408.1, 440.24, 451, 457.2, 478.21, 513.1, 519, 526.5, 536, 539.81, 572.1, 603.1, 611.0, 664 – 665, 670 –	A01, A02, A18, A20.1, A21.0, A26.0, A26.9, A28.1, A30.9, A31.1, A36.3, A39.84, A40.9, A42.2, A43.1, A44.1, A48, A52.1, A54.4, A57, A58, A66, A69, A71, A77, A79, B55, B85.0 – B85.3, D73.3, E06, E08, E09, E10, E11, E13, E32.1, E36.12, E87, E90.6, E92.05, E92.83, G04 – G06.1, G08, G98, H00.0 – H02.8, H05, H16, H60.0 – H61.039, H70.11, H73.01, H83.01, I26.90, I70.26, I73.01, I76, I80, I88 – I89.1, I96, I97.5, J18.9, J34.0, J36, J85.3, J95.02, J98.51, K04 – K05.2, K12.2, K68.11, K76.1, K95, L01.00 – L05.92, L08.0 – L08.9, L30.3, L60.0, L70.0 – L71.9, L76.12, L88.0 – L89.95, L97.1 – L98.499, M01X, M02.1 – M02.9, M46.20 – M46.58, M54 – M54.09, M60 – M60.9, M65.01 – M65.19, M70, M71.00 – M72.6,

	675, 680 – 682, 685 – 686, 695, 703 – 704.8, 706 – 707.9, 711, 723.6, 728 – 729.4, 730, 785.4, 800.5 - 802, 805 – 816.13, 817.1, 818.1, 819.1, 820 - 830.1, 831.1 – 839.9, 851.0 – 854.19, 860.0 – 862.9, 864 – 869.1, 870.0, 872.0 – 887.7, 890 – 897.7, 910 – 917.9, 919, 940 – 949.5, 985, 991, 996.6 – 999.33	M75, M79.0 – M79.5, M86.0 – M86.9, N47.6, N48.2, N48.5, N49.2, N49.3, N61, N76, N77, O22, O70.0 – O70.9, O71.4, O86.8 – O88.33, O91, O98.813, S00.0 – S02.9, S05, S08.0X – S12.200B, S162XXA, S20.1 – S22.42XB, S29.021A, S30.8, S31.0 - S32.9, Sd8.232D, S38.3XXA, S39, S39.02, S40.2, S40.8, S41.0 – S42.4, S46.0 – S46.9, S48.0 – S48.9, S50.3, S50.8, S51.0 – S51.8, S52.0 – S52.9, S56.0 – S56.9, S58.0 – S58.9, S60.3 – S60.5, S60.8, S61.0 – S61.5, S62.0 – S62.9, S65.2 – S65.3, S66.0 – S66.929, S68.0 – S68.7, S70.2 – S70.372, S71.0 – S71.15, S72.0 – S72.9, S76.0 – S76.9, S78.0 – S78.9, S80.2, S80.8, S81.0 – S82.92, S86, S88, S90.4 – S90.9, S91.0 – S92.9, S96.0 – S96.9, S98.0 – S98.9, T20.0 – T26.4, T28.0 – T28.5, T30.0 – T34.5, T80.2, T81.5, T84.5 – T84.7, T85.7, T86.8, T87.4, T87.8, W45.0 – W46.1, W53.0 – W59.81, W61, Z18.1 – Z18.9, Z20.8
Ocular	017.3, 021.3, 076.1 – 076.9, 077.98, 98.4 – 98.81, 130.1 – 130.2, 132.3, 139.1, 173, 360.0 – 360.19, 363.0 – 364.3, 368.1, 370.01 – 370.55, 373.01 – 373.9, 375.31 – 375.41, 376.0 – 376.3, 377.30, 377.31, 379.61 – 379.63, 802.7, 870.1 – 871.9, 940.2 – 940.9	A18.5, A36.86, A54.3, A71, A74.0, B58.0, B60.1, B85.4, E91.4, H01.0 – H02.8, H04.0 – H04.433, H05.011 – H05.53, H16.0 – H16.9, H20.0 – H20.9, H30.0 – H30.23, H44.0 – H44.792, H46.0 – H46.9, H59.2 – H59.4, S00.29A, S01.10, S05.2 – S05.72XS, T26.00 – T26.9
Dental	522 – 523, 526, 873.72, V9032	A69.1, K04.0- K04.9, K05.0 – K05.32, M27.3, S02.5XXB, Z18.32
Syphilis	096.0, 090.3 – 092.9, 093.0 – 093.9, 094.2 – 094.9, 095.0 – 095.9, 097.0 – 097.9, 104.0, 647.00 – 647.04	A50.02 – A50.9, A51.0 – A51.9, A52.02 – A52.9, A53.0, A53.9, A65, O98.11 – O98.13
Other	002.0 – 008.0, 020.0 – 023.9, 026.0 – 027.9, 030.1 – 032.6, 036.0 – 036.9, 038.2 – 039.9, 040.3, 078.2, 081.0 – 083.8, 085.9, 087.0 – 088.9, 094.1, 098.8, 100.0 – 100.9, 101.3, 102.0, 102, 103.1, 104.8, 104.9, 108.0, 130.0 – 139.8, 150.2, 170.6, 179.0 – 180.5, 188.0 – 189.6, 282.4 - 282.69, 288.0, 320.0 – 324.9, 364.0 – 364.2, 368.9,	A01.0 – A01.4, A02.1, A02.8, A06.8 – A06.9, A17.0 – A25.9, A27.0 – A28.9, A31, A32.9, A34 – A36.9, A39.0 – A42.9, A44.0 – A44.9, A48.2 – A48.8, A52.17, A59.8, A66 – A69.9, A75, A77.1 – A77.9, A79.9, B55.9, B58.2, B58.89, B58.9, B60.0 – B60.8, B64, B89, B90.0, B90.8, B94.8,B 94.9, B99.8, B99.9, D57.0 – D57.819, D70.3 – D70.9, E87.2, E87.5, E91.5, G00.0 – G07.0, G97.49, I00.0 – I02.9, I26.01, I30, I32 – I33.9, I38 – I40.9, I70, I73, M02.3, O03, O75.2, O75.3, O85, O86.4, O98.01 – O98.92, R57, R65, R89.5, T28.4, T80.29, T81.1- T81.59, T82, T86.23, T86.43, T86.812, T86.842,

	384, 391.0 – 392.9, 408.2, 408.9, 420.0 – 422.9, 424.9, 517.3, 647.3 – 647.9, 659.3, 669.1, 670.2, 771.8, 785.5, 790.7, 795.3, 824.0 – 824.1, 995.5, 995.9, 996.6, 998.0 – 998.59, 999.3	T86.93, W45.8, Y64.0, Y64.9, Z20, Z22.2 – Z22.9
Abbreviations: ICD-9-CM, International Classification of Diseases, 9 <sup>th</sup> edition, Clinical Modification; ICD-10-CM, International Classification of Diseases, 10 <sup>th</sup> edition; CCI, Charlson comorbidity index; UTI, urinary tract infection; BTI, biliary tract infection <sup>a</sup> ICD-10-CM codes were identified using forward and backward mapping to the Generalized Equivalence Mappings (GEMs) provided by CMS <sup>b</sup> Includes pharyngitis, sinusitis, laryngitis, and bronchitis		

**eTable 3. ICD-9-CM, ICD-10-CM, and CPT Codes Used to Capture Outcomes of Interest**

	<b>ICD-9-CM</b>	<b>ICD-10-CM<sup>a</sup></b>	<b>CPT</b>
<b>Aortic aneurysm</b>			
Thoracic	441.1, 441.2	I71.1, I71.2	
Abdominal	441.3, 441.4	I71.3, I71.4	
Thoracoabdominal	441.6, 441.7	I71.5, I71.6	0001T, 0002T, 0033T, 0035T, 0036T, 0038T, 0039T, 0040T, 0078T, 0079T, 0080T, 0081T,
Unspecified	441.5, 441.9, 447.70-447.73	I71.8, I71.9	33877, 33880, 33881, 34800, 34802, 34803, 34804, 34805, 34830, 34831, 34832, 75952, 75953
<b>Aortic dissection</b>	441.00-441.03	I71.00-I71.03	
<b>Iliac artery aneurysm</b>	442.2	I72.3	
<b>Other abdominal aneurysm</b>	442.1, 442.83, 442.84	I72.2, I77.810-I77.812, I79.0	
<b>Other aneurysm</b>	442.0, 442.3, 442.81, 442.82, 442.89, 442.9	I72.0, I72.1, I72.4-I72.9	
Abbreviations: ICD-9-CM, International Classification of Diseases, 9 <sup>th</sup> edition, Clinical Modification; ICD-10-CM, International Classification of Diseases, 10 <sup>th</sup> edition, Clinical Modification; CPT, current procedural terminology <sup>a</sup> ICD-10-CM codes were identified using forward and backward mapping to the Generalized Equivalence Mappings (GEMs) provided by CMS			



**eTable 4. Outcomes of Entire Cohort on 90-Day Incidence of Aneurysm After Fluoroquinolone or Active Comparator, Stratified for Subanalysis**

	Antibiotic Group	n	Aneurysm										
			Aneurysm	Aortic Aneurysm	Thoracic Aortic Aneurysm	Abdominal Aortic Aneurysm	Thoracoabdominal Aortic Aneurysm	Unspecified Aortic Aneurysm	Aortic Dissection	Iliac Artery Aneurysm	Other abdominal aneurysm	Other/unknown aneurysm	Aneurysm Repair
<b>Overall (n=47,596,545)</b>	F	9,053,961	6,752 (0.07)	5,110 (0.06)	1,127 (0.01)	3,067 (0.03)	70 (0.00)	1,392 (0.02)	366 (0.00)	230 (0.00)	478 (0.01)	959 (0.01)	66 (0.00)
	C	38,542,584	17,627 (0.05)	13,188 (0.03)	3,719 (0.01)	6,807 (0.02)	237 (0.00)	3,919 (0.01)	1,088 (0.00)	397 (0.00)	880 (0.00)	2,988 (0.01)	172 (0.00)
<b>Sex</b>													
Female (n=28,484,133)	F	550,141	2,631 (0.05)	1,733 (0.03)	358 (0.01)	996 (0.02)	33 (0.00)	511 (0.01)	149 (0.00)	40 (0.00)	301 (0.01)	532 (0.01)	20 (0.00)
	C	22,933,922	6,776 (0.03)	4,387 (0.02)	1,170 (0.01)	2,231 (0.01)	89 (0.00)	1,325 (0.01)	417 (0.00)	88 (0.00)	524 (0.00)	1,663 (0.01)	46 (0.00)
Male (n=19,112,412)	F	3,503,820	4,121 (0.12)	3,377 (0.10)	769 (0.02)	2,071 (0.06)	37 (0.00)	881 (0.03)	217 (0.01)	190 (0.01)	177 (0.01)	427 (0.01)	46 (0.00)
	C	15,608,592	10,851 (0.07)	8,801 (0.06)	2,549 (0.02)	4,576 (0.03)	148 (0.00)	2,594 (0.02)	671 (0.00)	309 (0.00)	356 (0.00)	1,325 (0.01)	126 (0.00)
<b>Age</b>													
18-34 (n=14,097,210)	F	2,103,974	197 (0.01)	127 (0.01)	28 (0.00)	49 (0.00)	1 (0.00)	62 (0.00)	23 (0.00)	1 (0.00)	7 (0.00)	48 (0.00)	1 (0.00)
	C	11,993,236	980 (0.01)	622 (0.01)	187 (0.00)	187 (0.00)	15 (0.00)	297 (0.00)	79 (0.00)	12 (0.00)	38 (0.00)	265 (0.00)	10 (0.00)
35-49 (n=15,493,370)	F	2,897,767	897 (0.03)	583 (0.02)	159 (0.01)	300 (0.01)	12 (0.00)	187 (0.01)	75 (0.00)	25 (0.00)	86 (0.00)	187 (0.01)	10 (0.00)
	C	12,595,603	2,949 (0.02)	1,926 (0.02)	699 (0.01)	725 (0.01)	41 (0.00)	722 (0.01)	253 (0.00)	44 (0.00)	137 (0.00)	744 (0.01)	12 (0.00)
50-64 (n=18,005,965)	F	4,052,220	5,658 (0.14)	4,400 (0.11)	940 (0.02)	2,718 (0.07)	57 (0.00)	1,143 (0.03)	268 (0.01)	204 (0.01)	385 (0.01)	724 (0.02)	92 (0.00)
	C	13,953,745	13,698 (0.10)	10,640 (0.08)	2,833 (0.02)	5,895 (0.04)	181 (0.00)	2,900 (0.02)	756 (0.01)	341 (0.00)	705 (0.01)	1,979 (0.01)	150 (0.00)
<b>Diabetes</b>													
No Diabetes Mellitus (n=43,573,891)	F	8,147,012	5,540 (0.07)	4,206 (0.05)	980 (0.01)	2,478 (0.03)	58 (0.00)	1,169 (0.01)	301 (0.00)	190 (0.00)	395 (0.00)	770 (0.01)	86 (0.00)
	C	35,426,879	14,888 (0.04)	11,159 (0.03)	3,294 (0.01)	5,565 (0.02)	200 (0.00)	3,424 (0.01)	922 (0.00)	333 (0.00)	752 (0.00)	2,511 (0.01)	141 (0.00)
Diagnosis Only (n=806,545)	F	187,647	320 (0.17)	238 (0.13)	41 (0.02)	144 (0.08)	4 (0.00)	64 (0.03)	21 (0.01)	8 (0.00)	22 (0.01)	51 (0.03)	3 (0.00)
	C	618,898	673 (0.11)	508 (0.08)	110 (0.02)	310 (0.05)	11 (0.00)	124 (0.02)	42 (0.01)	11 (0.00)	23 (0.00)	113 (0.02)	5 (0.00)
Oral Medications (n=2,365,839)	F	524,049	680 (0.13)	523 (0.10)	81 (0.02)	144 (0.08)	8 (0.00)	132 (0.03)	33 (0.01)	28 (0.01)	40 (0.01)	94 (0.02)	10 (0.00)
	C	1,841,790	1,525 (0.08)	1,144 (0.06)	234 (0.01)	713 (0.04)	19 (0.00)	272 (0.01)	87 (0.00)	48 (0.00)	71 (0.00)	255 (0.01)	20 (0.00)
Insulin-Requiring (n=850,270)	F	195,253	212 (0.11)	143 (0.07)	25 (0.01)	93 (0.05)	0 (0.00)	27 (0.01)	11 (0.01)	4 (0.00)	21 (0.01)	44 (0.02)	4 (0.00)
	C	655,017	541 (0.08)	377 (0.06)	81 (0.01)	219 (0.03)	7 (0.00)	99 (0.02)	37 (0.01)	5 (0.00)	34 (0.01)	109 (0.02)	6 (0.00)
<b>Hypertension</b>													
No Hypertension (n=35,670,172)	F	6,438,596	2,712 (0.04)	2,022 (0.03)	439 (0.01)	1,186 (0.02)	25 (0.00)	606 (0.01)	150 (0.00)	98 (0.00)	197 (0.00)	402 (0.01)	36 (0.00)
	C	29,231,576	7,210 (0.02)	5,176 (0.02)	1,404 (0.00)	2,595 (0.01)	83 (0.00)	1,689 (0.01)	426 (0.00)	149 (0.00)	371 (0.00)	1,425 (0.00)	60 (0.00)
Diagnosis Only (n=1,244,636)	F	281,924	374 (0.13)	278 (0.10)	55 (0.02)	179 (0.06)	1 (0.00)	70 (0.02)	23 (0.01)	11 (0.00)	29 (0.01)	61 (0.02)	5 (0.00)
	C	962,712	850 (0.09)	608 (0.06)	149 (0.02)	328 (0.03)	10 (0.00)	191 (0.02)	47 (0.00)	23 (0.00)	34 (0.00)	180 (0.02)	9 (0.00)
Oral Medications (n=10,681,737)	F	2,333,441	3,666 (0.16)	2,810 (0.12)	633 (0.03)	1,702 (0.07)	44 (0.00)	716 (0.03)	193 (0.01)	121 (0.01)	252 (0.01)	496 (0.02)	62 (0.00)
	C	8,348,296	9,567 (0.11)	7,404 (0.09)	2,166 (0.03)	3,884 (0.05)	144 (0.00)	2,039 (0.02)	615 (0.01)	225 (0.00)	475 (0.01)	1,383 (0.02)	103 (0.00)
<b>Hyperlipidemia</b>													
No Hyperlipidemia (n=38,118,246)	F	6,936,480	3,491 (0.05)	2,547 (0.04)	650 (0.01)	1,414 (0.02)	36 (0.00)	740 (0.01)	224 (0.00)	118 (0.00)	259 (0.00)	562 (0.01)	54 (0.00)
	C	31,181,766	9,528 (0.03)	6,845 (0.02)	2,110 (0.01)	3,183 (0.01)	139 (0.00)	2,277 (0.01)	639 (0.00)	194 (0.00)	519 (0.00)	1,837 (0.01)	85 (0.00)
Diagnosis Only (n=3,223,729)	F	723,648	886 (0.12)	695 (0.10)	125 (0.02)	436 (0.06)	10 (0.00)	193 (0.03)	34 (0.00)	25 (0.00)	63 (0.01)	117 (0.02)	14 (0.00)
	C	2,500,081	2,155 (0.09)	1,623 (0.06)	411 (0.02)	871 (0.03)	17 (0.00)	465 (0.02)	113 (0.00)	55 (0.00)	118 (0.00)	344 (0.01)	19 (0.00)
Oral Medications (n=6,254,570)	F	1,393,833	2,375 (0.17)	1,868 (0.13)	352 (0.03)	1,217 (0.09)	24 (0.00)	459 (0.03)	108 (0.01)	87 (0.01)	156 (0.01)	280 (0.02)	35 (0.00)
	C	4,860,737	5,944 (0.12)	4,720 (0.10)	1,198 (0.02)	2,753 (0.06)	81 (0.00)	1,177 (0.02)	337 (0.01)	148 (0.00)	243 (0.00)	1,837 (0.01)	68 (0.00)
<b>Antibiotic Type</b>													
Comparator (38,542,584)	-		17,627 (0.05)	13,188 (0.03)	3,719 (0.01)	6,807 (0.02)	237 (0.00)	3,919 (0.01)	1,088 (0.00)	397 (0.00)	880 (0.00)	2,988 (0.01)	172 (0.00)
Ciprofloxacin (5,190,117)	-		3,656 (0.07)	2,717 (0.05)	539 (0.01)	1,683 (0.03)	40 (0.00)	719 (0.01)	186 (0.00)	147 (0.00)	320 (0.01)	501 (0.01)	67 (0.00)
Levofloxacin (2,465,316)	-		2,267 (0.09)	1,762 (0.07)	450 (0.02)	995 (0.04)	25 (0.00)	506 (0.02)	129 (0.01)	68 (0.00)	123 (0.00)	317 (0.01)	30 (0.00)
Moxifloxacin (1,073,082)	-		670 (0.06)	514 (0.05)	108 (0.01)	323 (0.03)	5 (0.00)	137 (0.01)	44 (0.00)	11 (0.00)	32 (0.00)	108 (0.01)	6 (0.00)
Other FQ (326,446)	-		159 (0.05)	117 (0.04)	30 (0.01)	66 (0.02)	0 (0.00)	30 (0.01)	7 (0.00)	4 (0.00)	3 (0.00)	33 (0.01)	0 (0.00)

**eTable 5. Association between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations After Restricting to Individuals with Indications Identified**

	<b>HR (95% CI)<sup>a</sup></b>	<b>p-value</b>
<b>Aneurysm<sup>b</sup></b>	1.22 (1.16, 1.29)	<0.0001
Aortic aneurysm <sup>b</sup>	1.25 (1.17, 1.33)	<0.0001
Thoracic	1.24 (1.09, 1.40)	0.001
Abdominal	1.26 (1.16, 1.37)	<0.0001
Thoracoabdominal	0.66 (0.40, 1.07)	0.09
Unspecified	1.28 (1.14, 1.44)	<0.0001
Aortic dissection	1.10 (0.87, 1.38)	0.43
Iliac artery aneurysm	1.23 (0.89, 1.70)	0.20
Other abdominal aneurysm	1.22 (0.99, 1.51)	0.06
Other/unknown aneurysm	1.19 (1.04, 1.36)	0.01
<b>Aneurysm surgery</b>	2.47 (1.56, 3.91)	<0.0001

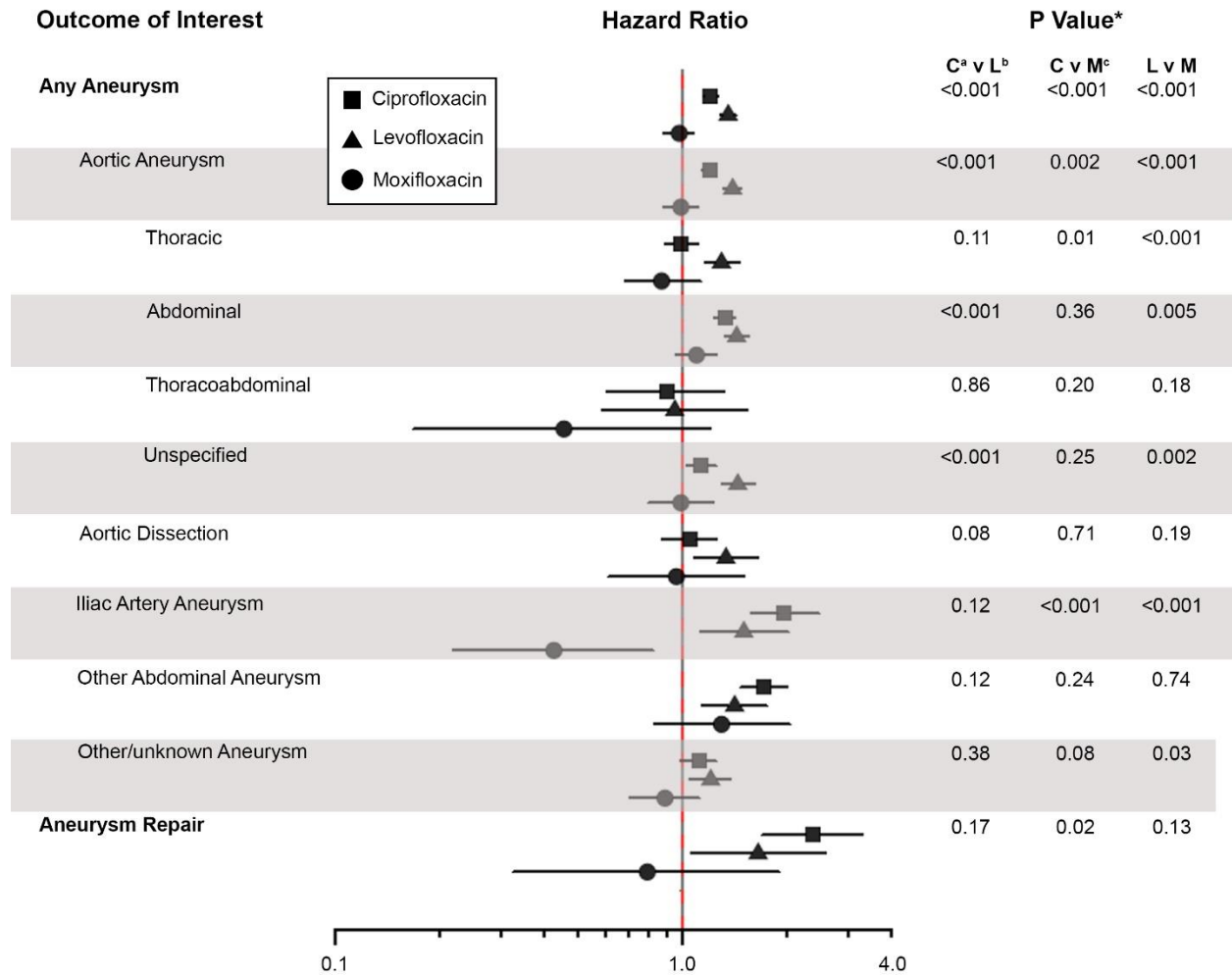
Abbreviations: FQ, fluoroquinolone; HR, hazard ratio; CI, confidence interval

<sup>a</sup> Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators

<sup>b</sup> Adults were able to have multiple aneurysm diagnoses during follow-up; total may be less than the sum of its parts

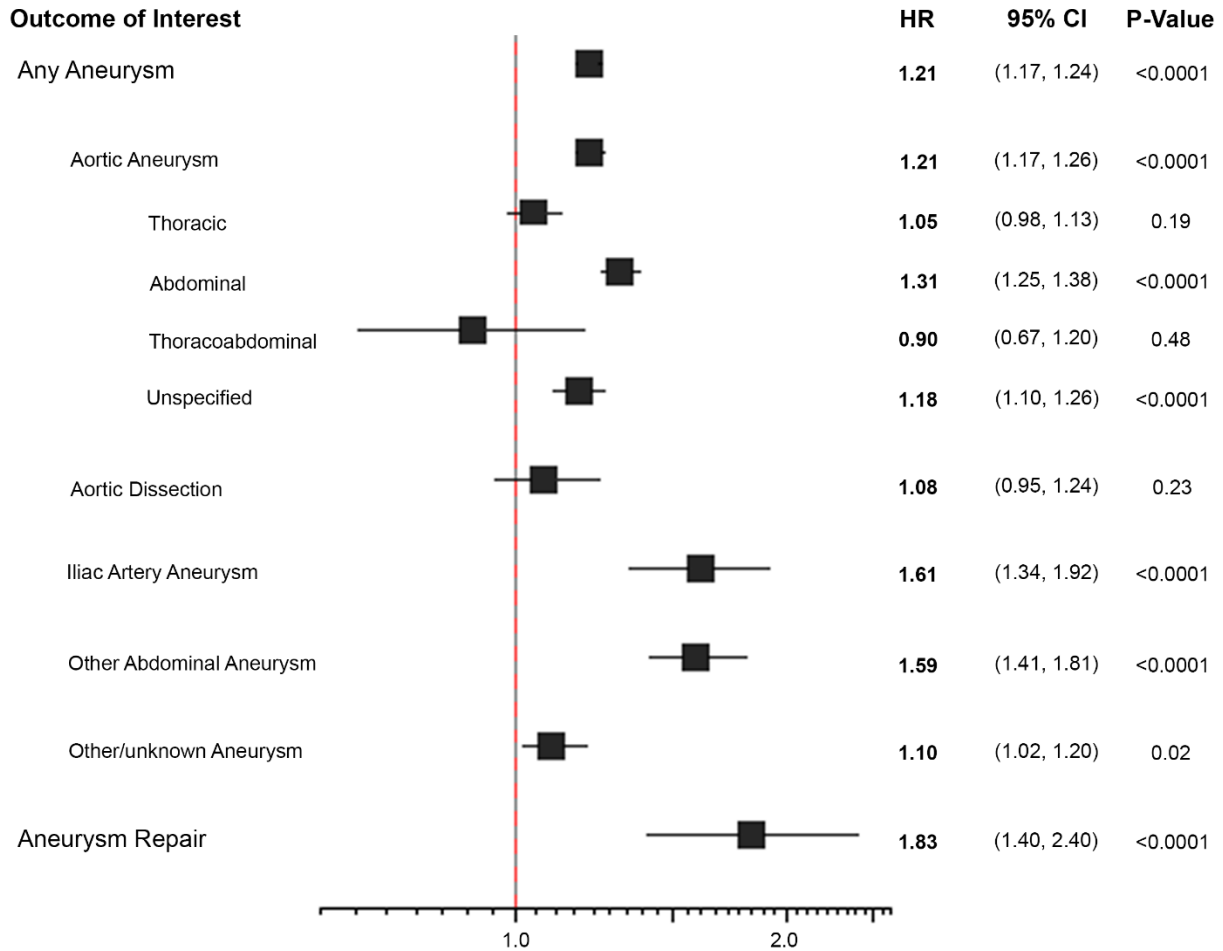
### eFigure 1. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Fluoroquinolone Type

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm (including aortic dissection) stratified by specific fluoroquinolone. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by fluoroquinolone status. Abbreviations used: <sup>a</sup>Ciprofloxacin, <sup>b</sup>Levofloxacin, <sup>c</sup>Moxifloxacin. \*P-value comparing at each sub-category level between fluoroquinolone type.



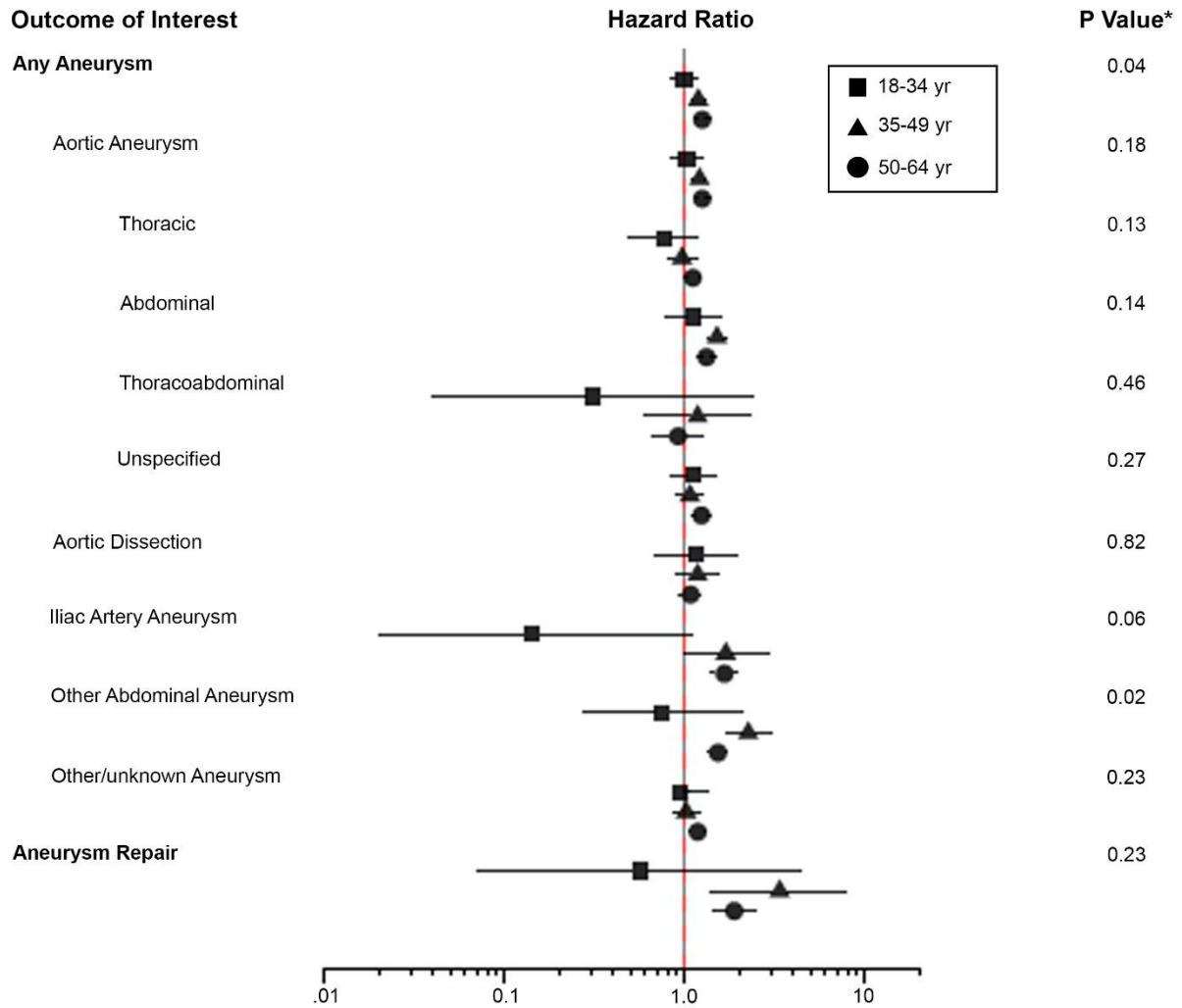
## eFigure 2. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Removing Repeated Observations

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm; antibiotic fills (fluoroquinolone or antibiotic comparator) after an episode with an aneurysm event were excluded (13,732 fills, 238 additional aneurysm events were removed).



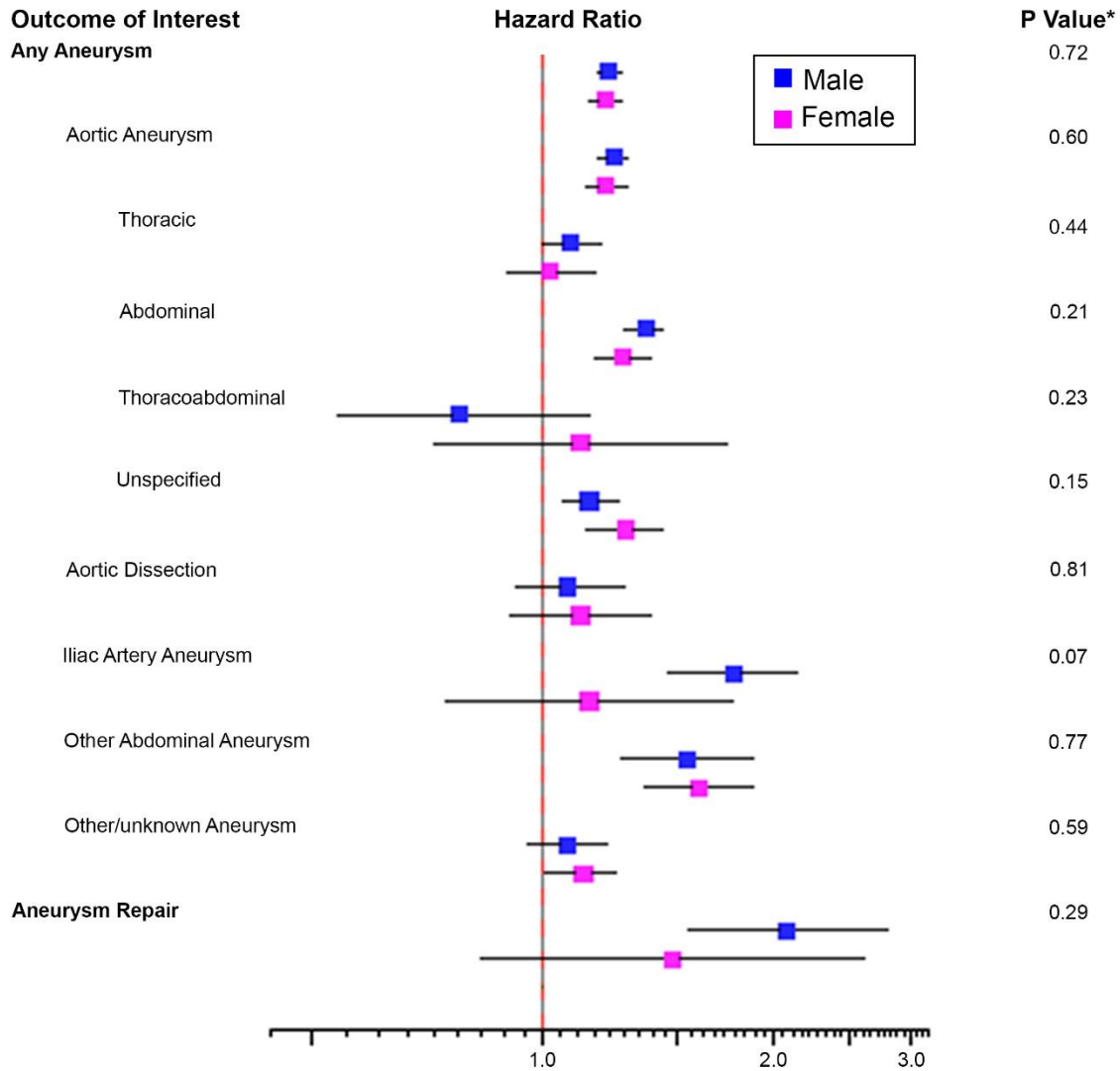
### eFigure 3. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Age

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm stratified by age. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by age. \*P-values comparing age groups.



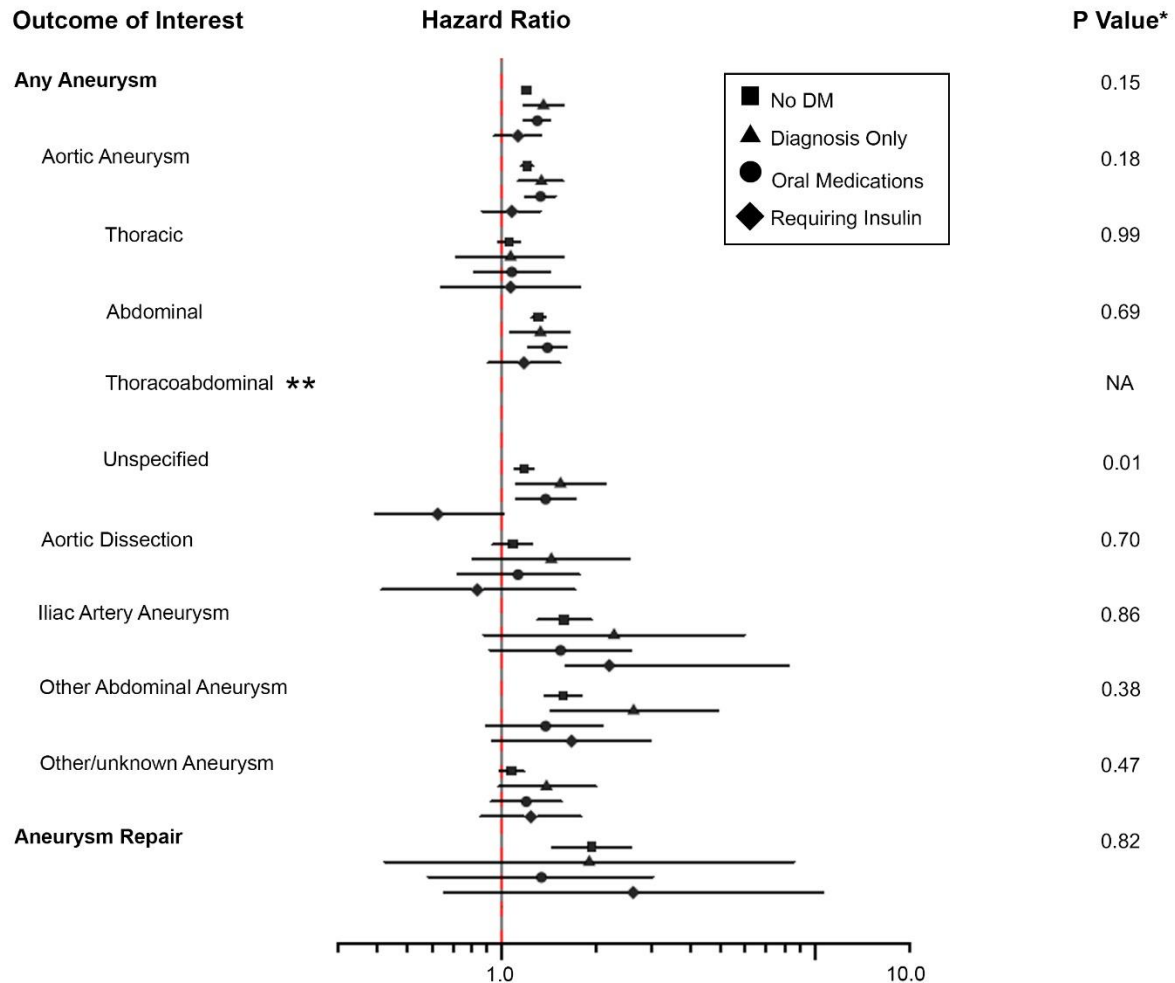
### eFigure 4. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Sex

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm stratified by sex. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by sex (i.e., is impact of FQ, compared to active comparator, different in females and males). \*P-value is comparing hazard ratios of males to females.



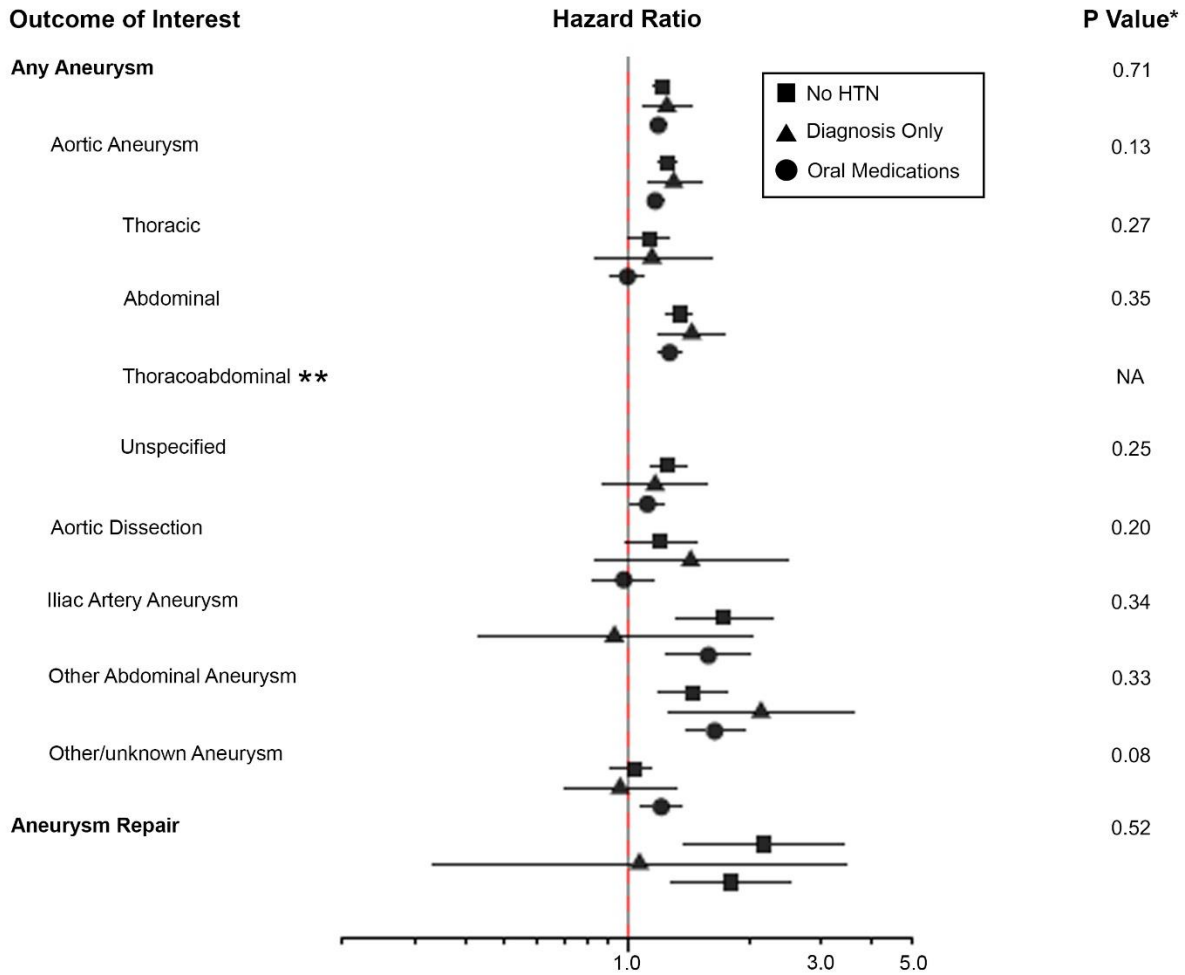
### eFigure 5. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Diabetes Status

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm stratified by diabetes status. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by diabetes status. \*P-value comparing at each sub-category level between disease severity. \*\*Thoracoabdominal Aortic Aneurysms were not able to be analyzed at this level due to low outcome incidence.



### Figure 6. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Hypertension Status

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm stratified by hypertension status. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by hypertension status. \*P-value comparing at each sub-category level between tiers of disease severity. \*\*Thoracoabdominal Aortic Aneurysms were not able to be analyzed at this level due to low cell counts across groups.





### eFigure 7. Association Between Fluoroquinolone Use and 90-Day Incidence of Aneurysm Formations Stratified by Hyperlipidemia Status

Effect of fluoroquinolone use, compared to active comparators, on 90-day incidence of aneurysm (including aortic dissection) stratified by hyperlipidemia status. Inverse-probability of treatment weights were used to account for potential confounding; weights and repeated observations were accounted for using robust sandwich estimators. Wald Chi-square test assessing potential effect measure modification by hyperlipidemia status. \*P-value comparing at each sub-category level between tiers of disease severity.

